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Lateralized auditory brain function in children with normal reading ability and in children with dyslexia

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ABSTRACT

We examined central auditory processing in typically- and atypically-developing readers. Concurrent EEG and MEG brain measurements were obtained from a group of 16 children with dyslexia aged 8–12 years, and a group of 16 age-matched children with normal reading ability. Auditory responses were elicited using 500 ms duration broadband noise. These responses were strongly lateralized in control children. Children with dyslexia showed significantly less lateralisation of auditory cortical functioning, and a different pattern of development of auditory lateralization with age. These results provide further evidence that the core neurophysiological deficit of dyslexia is a problem in the balance of auditory function between the two hemispheres.

1. Introduction

Developmental dyslexia is an unexplained difficulty in learning to read, despite adequate education and normal intelligence (Habib, 2000). It is thought to affect 5–10 per cent of school-aged children. The underlying causes remain unknown, but much current research focuses on explanations involving auditory processing problems, and/or abnormalities in hemispheric lateralisation of brain function.

Auditory processing explanations of dyslexia have been the subject of considerable interest and debate (e.g. Bishop, 2006; McArthur & Bishop, 2001; Ramus, 2006; Temple, 2002). In general, these explanations hold that reading problems stem from difficulties in processing and representing certain auditory features, which degrades the ability of the brain to accurately sample crucial elements in the speech stream (Goswami, 2011; Hari & Renvall, 2001; Tallal, 2004). These difficulties impair a child's ability to pair speech sounds with letters, which is a basic skill required for learning to read new words.

Theorists have long speculated that the biological basis of dyslexia is an imbalance of activity of the two hemispheres (Orton, 1925). Indeed this position has been supported by anatomical (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985), structural (Larsen, Hoien, Lundberg, & Odegaard, 1990; Leonard & Eckert, 2008), and functional neuroimaging (Illingworth & Bishop, 2009; Shaywitz et al., 1998) findings of atypical cerebral lateralization in dyslexic adults and children. Recent theoretical models of speech perception emphasise the importance of an asymmetric routing of different kinds of acoustic information to the two hemispheres (Poeppel, 2003; Zatorre, Evans, Meyer, & Gjedde, 1992) and current theories of dyslexia suggest that the maturation of phonological processing abilities is dependent on the appropriate development of information processing biases in the two hemispheres (Abrams, Nicol, Zecker, & Kraus, 2009; Goswami, 2011; Tallal, 2004). Others have suggested that altered patterns of auditory lateralization might be responsible for both pathological (e.g. dyslexia and schizophrenia) and supranormal (e.g. absolute pitch) cognitive function (Tervaniemi & Hugdahl, 2003).

Several recent magnetocencephalography (MEG) studies have reported reduced hemispheric asymmetry of auditory function in dyslexia using dipole source locations as a basis for an asymmetry index (Edgar et al., 2006; Heim, Eulitz, & Elbert, 2003; Paul, Bott, Heim, Eulitz, & Elbert, 2006). Heim et al. (2003) computed dipole source locations for the P100m response to a synthetic German syllable [ba:] and found a more symmetric source configuration in

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children with dyslexia compared to control children aged 8–15 years, while Edgar et al. (2006) reported a similar result for location of M100 sources of responses to non-linguistic stimuli in dyslexic and schizophrenic adults. Paul et al. (2006) attempted to replicate the results of Edgar et al. (2006) in a large sample of 64 dyslexic children aged 8–10 years. While these authors were unable to obtain reliable source locations for the P100m component, source locations for the later N260m component showed reduced asymmetry in the dyslexic children.

The reliability of dipole source locations is a significant problem for data from individual children, primarily because the accuracy of source modelling is critically dependent on the signal-to-noise ratio (SNR) of the event-related magnetic fields (ERFs) measured with MEG and event-related potentials (ERPs) measured with EEG. This SNR is typically much lower in children's ERFs and ERPs than in data obtained from adults (Luck, 2005; Pang, 2011). In practice this problem is more severe and intractable with MEG data: ERPs can be readily averaged across subjects to improve the SNR, while ERFs cannot. This is largely because EEG electrodes are placed in fixed anatomical positions on the head, while the MEG sensors are not.

In the present study we aimed to avoid this problem using an auditory lateralisation metric based on the amplitude of dipoles with fixed positions, in a paradigm that placed minimal demands on children's vigilance and attention to experimental stimuli. This lateralisation index provides a robust and reliable measure of functional brain asymmetry in typically developing children; and is a sensitive index of atypical auditory lateralisation in the brains of children with dyslexia.

2. Method

2.1. Subjects

Data were recorded from 16 children with dyslexia and 16 age-matched control children. Written consent was received from the parents of all children and all procedures were approved by the Macquarie University Human Participants Ethics Committee. Children were recruited from schools, clinics, and via newspaper advertisements. All children were aged from 7 to 12, had no history of neurological or sensory impairment as indicated on the background questionnaire (see test battery below) and spoke English as their first language at school and at home. The children with dyslexia scored at least 1 SD below the age-mean on the Castles and Coltheart 2 (CC2; Castles et al., 2009) non-word reading test or irregular word reading test (see test battery below). The control children scored within 1 SD of the age-mean on the CC2 non-word reading test and the irregular word reading test.

Children were assessed using a test battery designed to measure non-verbal IQ (NVIQ), reading proficiency, and phonological awareness. These tests included the Matrices Non-verbal subtest of the KBIT 2 (Kaufman & Kaufman, 2004), the Non-word repetition subtest of the NEPSY-II (Korkman, Kirk, & Kemp, 1998) and the Castles and Coltheart 2 (Castles et al., 2009). The Castles and Coltheart 2 has subtests that measure regular, irregular and non-word reading. Handedness was assessed with the Oldfield Handedness Questionnaire (Oldfield, 1971). Auditory thresholds were checked using an Otovation Amplitude T3 series audiometer (Otovation LLC, King of Prussia, PA). Subjects with pure-tone averages greater than 15 dB HL were excluded from the electrophysiological recordings.

Table 1 summarises the demographic and test results for the two groups. The two groups did not differ significantly in age, sex, or handedness. Nor did they differ on a non-word repetition task—a measure that is known to be particularly sensitive to spoken language impairment. As expected, the two groups did differ on measures of reading accuracy for non-words, irregular words, and regular words.

The two groups also differed on the measure of non-verbal IQ. The children with dyslexia, on average, performed close to the level expected for their age, while the controls, on average, performed above the average range. The participants also showed a wide range of scores on non-verbal IQ, with four dyslexic participants and two controls scoring more than 1 SD below their group means. On this issue we note that in recent years, there is growing evidence (and hence increasing acceptance) that intelligence is not a predictor of reading ability, and is not a predictor of response to reading intervention (see Gresham & Vellutino, 2010; Hulme & Snowling, 2009). Thus, IQ is rapidly being abandoned as a criterion for inclusion/exclusion into groups with dyslexia. Where relevant we have also partialled out the effect of IQ in statistical analyses to confirm that this variable did not play a role in our analyses.

2.2. Stimuli

Stimuli were 500 ms duration broadband noises of two kinds: *Noise only* stimuli, which result in a perception of a noise located in the centre of the head, and *Dichotic Pitch* (DP) stimuli, which were monaurally identical to the noise only stimuli but contained an interaural time shift for a narrow frequency band (Hautus & Johnson, 2005; Johnson, Hautus, & Clapp, 2003) resulting in the perception of a central noise and a lateralised pitch. The dichotic pitch stimuli were included to assess the possibility of binaural hearing deficits in the children with dyslexia (Dougherty, Cynader, Bjornson, Edgell, & Giaschi, 1998).

To produce the stimuli, we generated two independent broadband Gaussian noises of 500 ms duration at a sampling rate of 44,100 Hz. One noise was bandpass filtered (4th order Butterworth) with a centre frequency of 600 Hz and a half-power bandwidth of 50 Hz. The other noise was notch filtered using the same corner frequencies as the bandpass filter. The notch filter was designed so that the sum of the filter functions for the notch and bandpass filter was equal to one for all frequencies. Consequently, for these complementary filters, the sum of the two waveforms is a noise process with a flat spectrum (Dougherty et al., 1998). The bandpass filtered noise was duplicated and, to produce the DP stimuli, one copy was temporally delayed by 0.5 ms. For the noise only stimuli, no delay was introduced. The notch filtered noise was then added to each copy of the bandpass filtered noise, producing two spectrally identical noises. The bandwidth of the two spectrally-flat noises was determined by a bandpass 4th order Butterworth filter with corner frequencies 400 and 800 Hz. All stimuli were windowed with a Hanning ($\cos^2$) function with 10 ms rise and fall times. For the DP stimuli, the noise process with the temporally advanced narrow-band of frequencies was presented to the right ear of the listener and the other noise was presented to their left ear, leading to a perception of a right-lateralized pitch.

Stimuli were designed digitally using LabView software (Version 8.6, National Instruments, Austin, TX) and generated on two channels of a 16-bit D-A converter (Model NI USB 6251, National Instruments, Austin, TX). The level of the sounds was adjusted using programmable attenuators (Model PA4, Tucker Davis Technologies, Alachua, FL) to yield 70 dB SPL at the eardrum. Stimuli were delivered to listeners using insert earphones (Model ER-30, Etymotic Research Inc., Elk Grove Village, IL) with a random interstimulus interval (ISI) between 800 and 1200 ms, chosen because ISI's shorter than these are known to suppress some components of the auditory evoked response in younger children (Čeponienė, Cheour, & Näätänen, 1998; Gilley, Sharma, Dorman, & Martin, 2005; Sussman, 2008) due to developmental changes in refractoriness.

2.3. MEG and EEG acquisition

Prior to EEG and MEG measurements, EEG electrode caps and MEG marker coils were placed on the subject's head. Marker coil positions, electrode positions, and head shape were measured with a pen digitizer (Polhemus Fastrack, Colchester, VT). All measurements were carried out with the subject in a supine position in the MEG environment. MEG recordings were obtained in a magnetically shielded room (Fujihara Co. Ltd., Tokyo, Japan) using the KIT-Macquarie MEG160 (Model PQ1160R-N2, KIT, Kanazawa, Japan) consisting of 160 coaxial first-order gradiometers with a 50 mm baseline (Kado et al., 1999; Uehara et al., 2003). EEG was recorded using a 64-channel BrainAmp MR plus MEG-compatible EEG system (BrainProducts GmbH, Gilching, Germany). EEG electrodes were Ag/AgCl in a BrainCap MR electrode cap, consisting of 62 channels of EEG, 1 channel of EKG, and 1 channel of EOG, all referenced to Cz. Both MEG and EEG data were acquired using a sampling rate of 1000 Hz and a filter bandpass of 0.03–200 Hz.

2.4. Procedure

Hearing and cognitive tests were administered to participants prior to EEG/MEG setup. During the EEG/MEG recordings, children were permitted to ignore the experimental stimuli while viewing a movie of their choice, played with low-level video sound (McArthur, Bishop, & Proudfoot, 2003). The movie was projected via a data projector on to a screen located 120 cm above the participant's head. The projection subtended a visual angle of 12.3° (vertical) $\times$ 21.2° (horizontal), providing a comfortable viewing experience requiring few or no eye movements. Prior to the start of the experiment, participants were instructed to remain as still as possible during the recording session and to minimise eye movements and eyeblinks. Eye and head movements were continuously monitored via a closed circuit camera. When excessive movements were detected the experiment was paused and the movement instructions were re-issued to the participant. Four 10-min blocks of randomly interleaved noise only and DP stimuli were presented. Each block contained 216 stimuli, for a total of 432 of each of noise only and DP stimuli (864 trials in total). Stimulus blocks were presented consecutively with a short interval in between during which head position was measured. The head movement tolerance threshold was <5 mm for any marker coil from start to end of the recording session.

2.5. Pre-processing

Neurophysiological data were processed and analysed off-line using BESA Research version 5.3.1 (BESA GMbH, Grafelfing, Germany). EEG and MEG data were segmented and averaged into 600-ms epochs including a pre stimulus baseline of 100 ms. Averaged ERPs and ERFs were filtered with a bandpass of 0.16–40 Hz. EEG data were re-referenced to the average reference. EEG and MEG artefacts, including blinks and eye-movements, were rejected using the artefact scan tool in BESA 5.2.4, which rejects trials based on abnormally high amplitudes or abrupt rises or falls in amplitude (gradients). For each subject and condition, at least 90% of trials survived artefact rejection. This low rejection rate was achieved in part due to the instructions and monitoring procedures described above; and in part because the experimental environment was designed to be easy to tolerate, with a comfortable viewing position and an interesting video to watch.

2.6. Source modelling

For EEG data the head was modelled as a 4 shell ellipsoid with an outer radius of 71.4 mm and scalp/skull/csf thickness of 6.0, 7.0 and 1.0 mm respectively and brain, scalp, bone and csf conductivities 0.33, 0.33, 0.0042, and 1.0 S respectively. For MEG data the head model was a single shell sphere with an outer radius of 71.4 mm.

ERP/ERF sources for individual subjects were modelled using a model with fixed regional sources with locations derived from the grand average ERPs, and orientations derived from the individual's own data (Hine & Debener, 2007; Hoechstetter et al., 2000) for similar approaches to modelling ERF and ERP data respectively. ERP/ERF sources were modelled with two symmetric, bilateral regional sources. A master model was created by fitting sources to ERP waveforms grand averaged over all subjects, groups, and stimulus conditions. Sources were randomly seeded, and freely fitted (except for the symmetry constraint) to the grand average ERPs over a time window of 70–270 ms encompassing the main peaks of the ERP/ERFs.

The mean source locations from the ERP master model were used to calculate the EEG and MEG source activity waveforms of each individual subject in each group and stimulus condition. (We used the grand mean ERPs because they provided a more stable location estimate than could be calculated from any of the individual's EEG or MEG data. This is an unusual analysis strategy as MEG is generally considered to have superior spatial resolution to the EEG. However, as noted previously, children's ERPs and ERFs tend to be noisier and consequently less suitable for source localisation than adult's data. Had they been available, we could alternatively have used structural or functional MRI data for source locations.)

Regional sources have three orthogonal components: two tangential (parallel to the local head surface) and one radial (90° to the local head surface). The first tangential component generates the 'vertex potential' of the auditory ERP recorded on the scalp at fronto-central electrodes and an ERF distributed over temporal regions of the head. The orientation of the first tangential component was adjusted to the maximum amplitude within a window of 80–105 ms, the latency of the rising edge of the N100/N100m component for each subject. For ERPs the radial component corresponds to the auditory evoked 't-complex' recorded on the scalp at lateral temporal electrodes (Scherg, Vajsar, & Picton, 1989). The radial component was adjusted to explain the maximum activity perpendicular to the first tangential component at a latency of 120–140 ms. For ERFs there was no radial component as MEG is insensitive to purely radial sources. For both ERP and ERF data the second tangential component did not produce waveforms with any systematic activity and, therefore, this component was not further analysed. Source waveforms were generated for each subject and stimulus condition. For ERP data the source waveforms for the first tangential component and the radial component of regional sources in each hemisphere were used for statistical analyses.

Table 1
Demographic and cognitive characteristics of the dyslexia and control groups.

Measure	Dyslexia ($N=16$)		Controls ($N=16$)		Independent t-tests		
	M (*SD*)	*Min/Max*	*M* (*SD*)	*Min/Max*	*t*	*df*	*p*
Age (months)	9.55 (1.36)	7.1/12.0	9.44 (1.40)	7.1/12.0	0.22	30	0.83
Handedness (1=Right)	0.88 (0.34)	0/1	0.94 (0.25)	0/1	0.59	30	0.56
Non-verbal IQ (SS)	95.12 (18.20)	65/124	118.25 (15.01)	76/133	3.92	30	< 0.001
Non-word reading (*z*)	−1.28 (0.49)	−2.03/0.00	0.57 (0.83)	−0.67/2.13	7.67	30	< 0.001
Irregular-word reading (*z*)	−1.57 (0.74)	−2.51/−0.08	1.11 (0.97)	−0.20/2.77	8.80	30	< 0.001
Regular-word reading (*z*)	−1.46 (0.55)	−2.16/−0.39	1.11 (1.03)	−0.39/2.99	8.74	30	< 0.001
Repeating non-words (%)	40.88 (18.42)	9/75	54.16 (27.73)	16/99.6	1.60	30	0.12

Note: SS: standard score ($M=100$, $SD=15$); *z*: *z* score ($M=0$, $SD=1$); %: percentile.

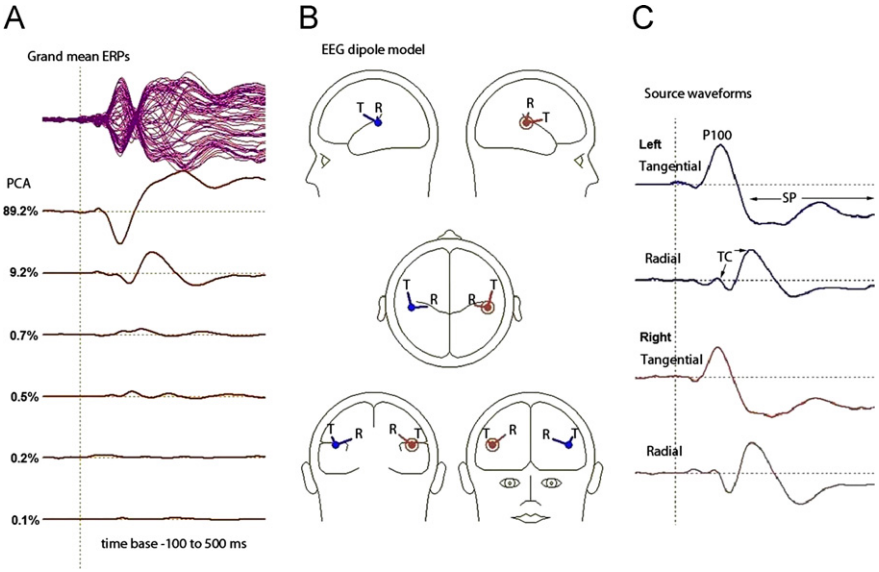

Fig. 1. EEG master source model based on grand mean ERPs: (A) butterfly plot at top shows all 62 grand mean ERP waveforms superimposed. PCA shows that the first two spatial components account for more than 98% of the ERP data. (B) Symmetric regional sources, consisting of 1 tangential (T) and 1 radial component (R), located in bilateral primary auditory cortices, accounted for approximately 96% of the data. (C) Source waveforms show excellent separation of P100/SP components from t-complex components. TC=T complex. SP=sustained potential.

As we had no strong hypotheses about the *timing* of differences between experimental conditions or between hemispheres, we employed a bootstrapping procedure to delineate the temporal profile of significant differences in the ERPs and ERFs. Time windows showing differences between conditions or hemispheres were determined using 95% confidence intervals for each difference source waveform based on 1000 bootstrap samples. A contrast was considered significant if the confidence interval of the difference source wave did not include zero. This bootstrapping procedure allowed us to locate the time windows of interest within the source waveforms without invoking a priori or arbitrary assumptions about the timing of experimental effects (Bledowski et al., 2004, 2006; Hine & Debener, 2007).

Using the time windows identified with the bootstrapping contrasts, concurrent main effects and interactions were analysed with ANOVA computed using the mean voltage over the time windows identified with the bootstrapping procedure. Epsilon values are given where it was necessary to mediate violations of the assumption of sphericity using the Greenhouse–Geisser correction.

3. Results

3.1. Event-related potentials and magnetic fields

Fig. 1 shows grand mean ERPs (averaged over all subjects, groups and stimuli) and the steps that were followed in constructing the master source model. Principal components analysis (PCA) decomposed the grand mean ERPs into 2 orthogonal spatial components which together accounted for 98.7% of the variance. A bilateral regional source model accounted for 98.1% of the variance in the grand mean ERPs. The two regional sources had Talairach coordinates of ± 47 mm, -24.4 mm, 14.9 mm (X, Y, Z), in Brodmann's area 41 corresponding to the transverse temporal gyri (primary auditory cortices).

The source waveforms in each hemisphere consisted of a tangential component and a radial component. The tangential component had a fronto-central scalp distribution and was characterised by the large P100 peak elicited by the sound onsets and a sustained potential (SP; (Picton, Woods, & Proulx, 1978)) which persisted for the duration of the sounds. The radial component consisted of the t-complex, a series of peaks with latencies of about 80, 105, 135 and 185 ms and with maximal amplitudes at lateral temporal electrodes T7 and T8.

The tangential component was also readily observable in the MEG data, consisting of a P100m peak and sustained field (SF; Hari, Aittoniemi, Jarvinen, Katila, & Varpula, 1980), and a surface distribution orthogonal to the EEG topography (Fig. 2). The radial component was not present in the MEG data, since MEG is largely insensitive to radially-oriented sources.

This master source model provides a simple account of the grand mean EEG data that confers two important features of our analysis strategy. First, it reduces the EEG data from 62 waveforms to 4 and reduces the MEG data from 160 waveforms to 2 (because the MEG is insensitive to purely radial sources). Second, it partitions the sources so that they are maximally sensitive to hemispheric differences: The grand averaged right and left hemisphere P100 source waveforms show a mean P100 latency difference of about 7 ms (right hemisphere 94 ms; left hemisphere 101 ms).

3.2. Binaural processing of dichotic pitch stimuli

Our analyses showed no significant group differences for processing of DP stimuli. To preserve the logical flow here we do not further describe the analysis of responses to binaural pitch in the present article, but see Section 4 for some further consideration of embedding of binaural and other sound features within broadband noises.

3.3. Age changes in latency of source waveforms

Previous work has demonstrated maturational changes in AEP (Bishop, 2007; Bishop, Anderson, Reid, & Fox, 2011; Cunningham, Nicol, Zecker, & Kraus, 2000; McArthur & Bishop, 2002; Sharma & Kraus, 1997) and AEF (Kotecha et al., 2009) peak latencies. We examined age changes using the P100/P100m source waveform peak latency as a landmark, as we found this to be the only AEP/AEF peak that could be unambiguously identified in both hemispheres and in all or nearly all individuals. For control subjects P100m latency showed a significant negative correlation ($r=-0.5$, $p<0.05$, 2-tailed) with age in the left hemisphere (Fig. 3). A linear fit to the data showed a latency decrease of 17 ms over the age range of our subjects. The right hemisphere P100m and the P100 in both hemispheres also all showed a negative correlation with age although these measures did not reach statistical significance. However, the data for dyslexic children showed no linear trends in any of the measures of peak latency.

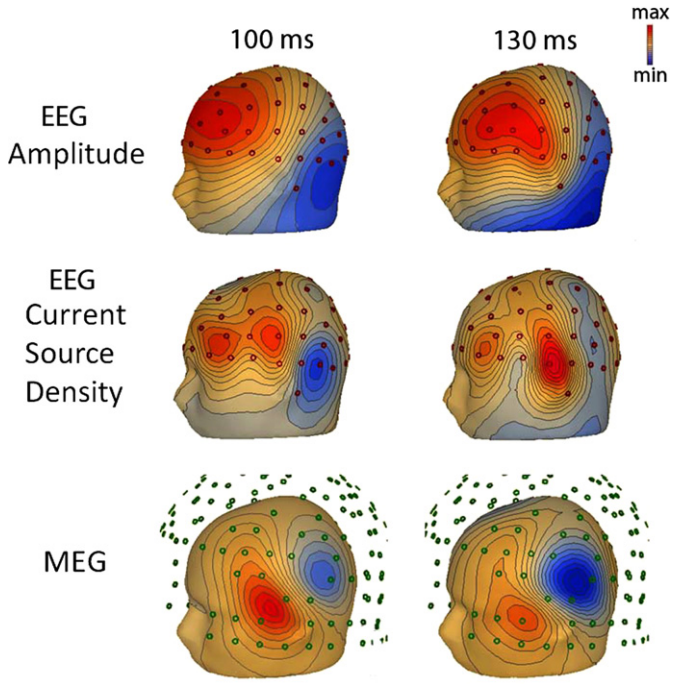

Fig. 2. Topographic contour maps for EEG grand mean ERPs and MEG grand mean ERFs, averaged over all subjects and conditions. EEG electrode positions and MEG sensor locations are indicated by circles.

3.4. Statistical analyses of source waveforms

For the EEG data, bootstrapping showed a significant difference in P100 peak latency between the two hemispheres: left hemisphere mean latency = 100.6 ms [95% CI = 93.7–106.9 ms], right hemisphere mean latency = 93.7 ms [95% CI = 89–100.6 ms]. The mean latency difference was 6.9 ms [95% CI = 1.7–11.1].

Bootstrapping comparisons of source waveform amplitudes for the two hemispheres showed non-overlapping CIs for the tangential component, during a time window of 110–150 ms (immediately following the P100 peak, Fig. 4). The overall ANOVA confirmed a significant main effect of hemisphere ($F(1,31)=5.1$, $p=0.03$) but no significant main effect of (or any interactions with) the group variable.

For the MEG, bootstrapping analysis showed significantly earlier P100m peaks latency in the right hemisphere compared to the left hemisphere (left hemisphere = 97.6 ms [95% CI = 91.4–104.3], right hemisphere = 90.7 ms [95% CI = 88.2–94.3 ms]).

Bootstrapping analysis of the MEG source waveforms showed significantly lower source amplitudes in the right hemisphere for the entire epoch after 60 ms latency (Fig. 4). ANOVA computed for the 60–500 ms window confirmed a highly significant main effect of

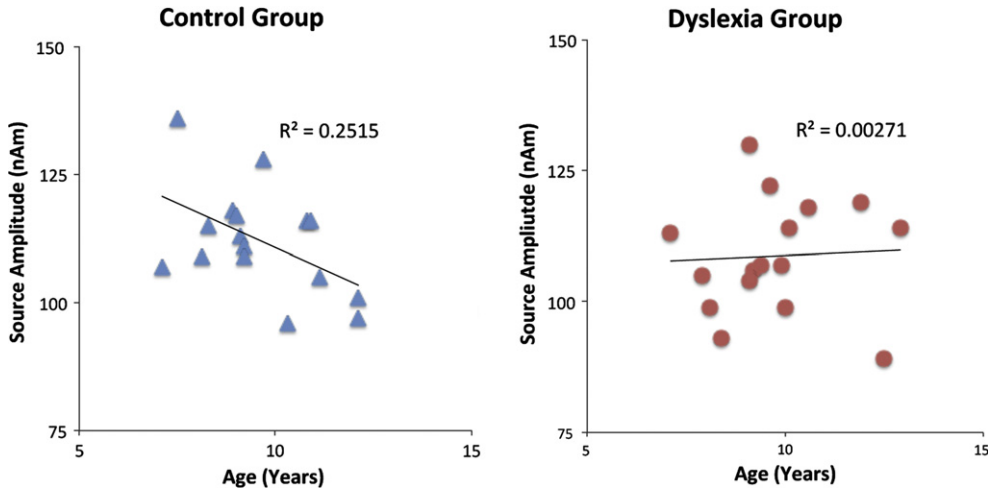

Fig. 3. Left hemisphere P100m latencies plotted against age for control and dyslexia groups.

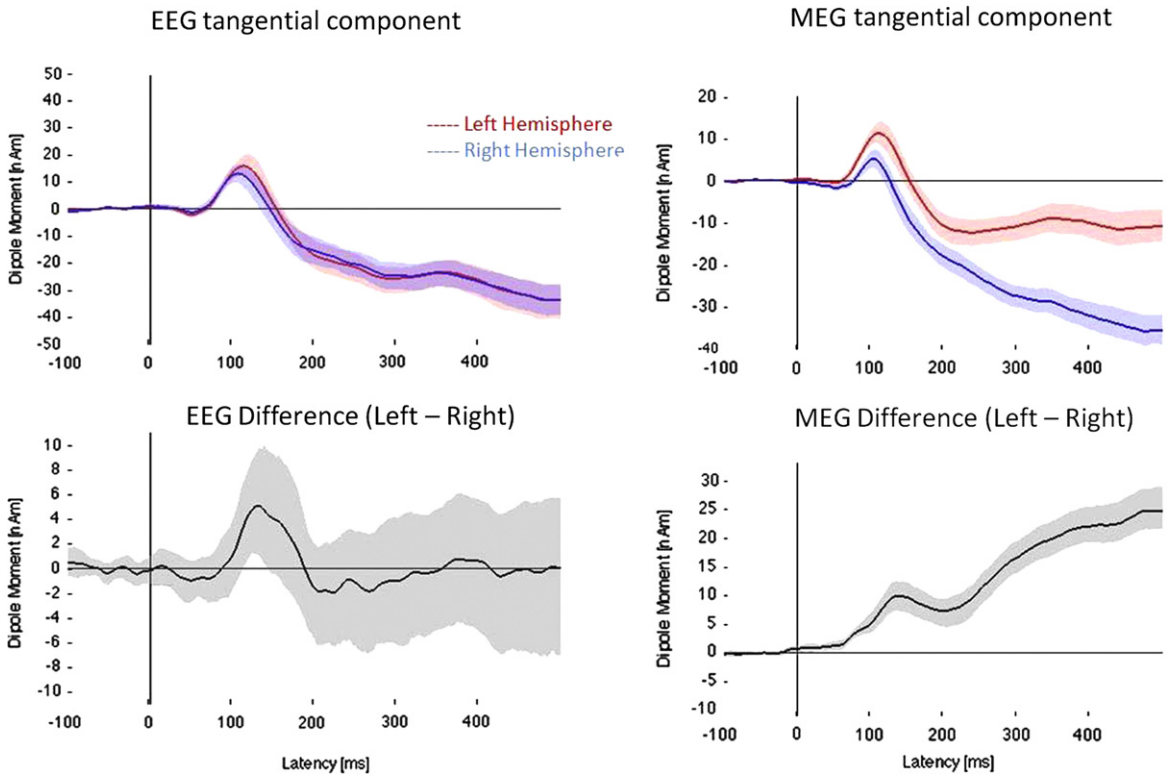

Fig. 4. Bootstrapping analysis of EEG and MEG source waveforms. Shaded regions represent 95% confidence intervals determined by bootstrapping. Latency regions of interest are where confidence intervals of difference waveforms (bottom) do not include zero.

hemisphere ($F(1,31)=179$, $p \ll 0.001$). ANOVA computed for the 60–500 ms window also showed a significant group × hemisphere interaction ($F(1,31)=6.7$, $p=0.02$). Fig. 5 shows that the interaction was such that the control group was relatively more negative on the right and more positive on the left than the dyslexic group. In other words, the controls showed relatively greater hemispheric asymmetry than the dyslexic children.

To further examine the group × hemisphere interaction revealed by the ANOVA of the MEG data, we calculated a laterality index (LI) as

LI = (LH − RH)/((LH + RH), where
LH = mean left hemisphere source amplitude (60–500 ms), and
RH = mean right hemisphere source amplitude (60–500 ms).

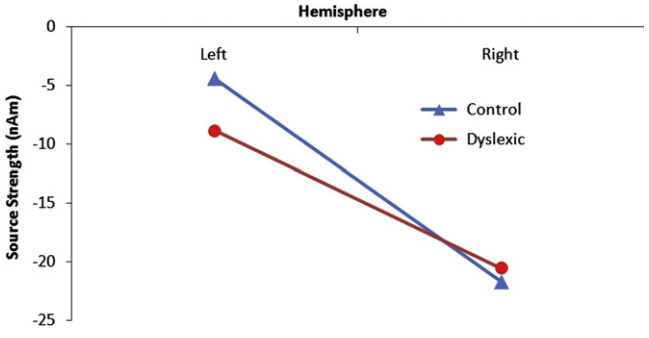

Fig. 5. Group × Hemisphere interaction for MEG data.

Negative values of the LI indicate left lateralization, while positive values indicate right lateralization. Because the computation of the LI requires that input values are positive, we subtracted the minimum value of each data vector (of mean amplitude for each subject) from each value in that vector prior to computing the LI. Since the ANOVA showed no significant main effects or interactions with stimulus type, we calculated a separate LI for each stimulus type in order to estimate the reliability of the indices (the overall correlation, or split-half reliability, between LIs for the noise only stimulus and the DP stimulus was .78 ($p < 0.01$)).

LIs calculated for the two stimulus types agreed closely and showed that considered as groups, controls were significantly more left lateralized than dyslexic children. For the noise only stimulus controls had a mean LI of −0.45 compared to an LI of −0.27 for dyslexics ($t(15)=0.01$, 1-tailed), while for the DP stimulus controls had a mean LI of −0.57 compared to a mean LI of −0.30 for dyslexics ($t(15)=0.004$). For the combined stimuli, controls had a mean LI of −0.50 while dyslexics had a mean of −0.28 ($t(15)=0.006$).

3.5. Age and laterality

When age was treated as a covariate of LI, the two groups showed strikingly different patterns. Control children showed no significant correlation between age and lateralization: noise only $r=-0.1$, DP $r=0.18$, both $r=0.04$ ($p > 0.05$ for all). In contrast, dyslexic children showed relatively strong correlations with age: noise only $r=-0.57$, DP $=-0.54$, both $r=-0.61$ ($p < 0.01$ for all). In other words, dyslexics but not controls became increasingly left lateralized within the age range. Fig. 6 shows that the divergence between the two groups is particularly evident at the younger end of the range, with a convergence of the linear trendlines at the older end of the range. In these groups, control children showed maximal lateralization at the lower bound and this was stable across the age range. In contrast, dyslexic children were much less lateralized at the lower age bound but approached control level of lateralization at the upper age bound.

4. Discussion

The present results demonstrate a robust pattern of auditory brain lateralisation in children aged 7–12; confirm previous reports of abnormal lateralisation of auditory function in dyslexia; and provide novel evidence for an abnormal developmental trajectory of auditory lateralisation in children with dyslexia. These findings bear on current theories of speech perception (Poeppel, 2003; Zatorre et al., 1992), and recent models of dyslexia that propose a crucial role for asymmetric auditory information processing for the maturation of phonological processing abilities (Abrams et al., 2009; Goswami, 2011; Tallal, 2004).

4.1. A neurophysiological index of asymmetric auditory processing

The adult auditory ERP measured by EEG is characterised by two main peaks: The P50, a positive peak with a latency of about 50 ms after stimulus onset, and the N100, a negative peak with a latency of about 100 ms. The corresponding responses measured by MEG are termed "P50m" and "N100m" respectively. Abrupt onsets of many kinds of acoustic stimuli, including the broadband noises used in the present experiment, are known to elicit asymmetric P50m and N100m responses in the two hemispheres (Chait, Simon, & Poeppel, 2004; Johnson & Hautus, 2010). In adults the N100m peak is about 10 ms earlier and larger in amplitude in the right hemisphere compared to the left hemisphere (Johnson & Hautus, 2010), while the earlier P50m response is significantly larger in the left hemisphere (Chait et al., 2004; Johnson & Hautus, 2010).

In children the most prominent auditory ERP is a circa 100 ms positivity termed the P100 (MEG: P100m) believed to be the precursor of the adult P50 response (Lippe, Martinez-Montes,

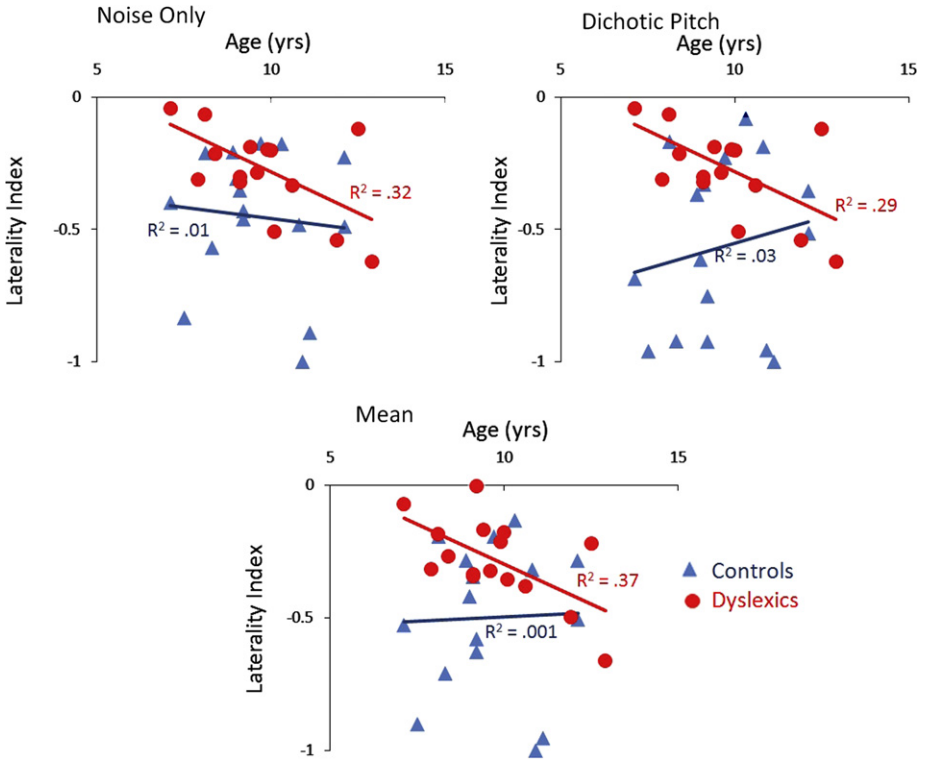

Fig. 6. Correlation between age and MEG laterality index.

Arcand, & Lassonde, 2009). The present data demonstrate that the P100m is strongly asymmetric in 7–12-year-old children with a peak that is about 7 ms earlier in the right hemisphere but significantly larger in the left hemisphere. These results confirm and extend previous findings from a study of 4-year-old children (Johnson, Crain, Thornton, Tesan, & Reid, 2010), which also showed significantly lower right hemisphere P100m amplitudes.

The hemispheric differences are not restricted to the P100m peak: our bootstrapping analyses showed that left hemisphere source amplitudes were significantly larger than right hemisphere source amplitudes from well before the P100m peak, until the end of the 500 ms analysis epoch, well past the P100m peak and encompassing the SF as well. Bootstrapping of the MEG difference waveforms (Fig. 4) indicates that hemispheric processing was not significantly different until about 60 ms, after which the processing activities of the two hemispheres increasingly diverge over time. Such a profile conforms well to the asymmetric sampling in time model (AST) of speech perception (Poeppel, 2003). In this model, the initial analysis of the speech signal is bilaterally symmetric; after this the neural representation is elaborated asymmetrically in time using different temporal analysis windows in the two hemispheres, in a manner analogous to two analogue to digital sampling devices with different internal timing clocks. The ERFs of Fig. 4 show such a profile of increasingly divergent activity in the two hemispheres over time.

However the hemispheric divergence over time is not a simple linear one, as would be expected if the two hemispheres simply run on different internal clocks: there are inflections at about 150 ms (a peak) and 220 ms (a trough). Such inflections suggests at least two significant departures from linear divergence, and these may mark the operation of processing stages involving lesser or greater degrees of interhemispheric transfers of information.

A reviewer of a previous version of this article has pointed that – since the children were attending to a movie with soundtrack during the experiment – another interpretation of these data is that they are the complex consequence of differential processing of the attended audio signal in the two hemispheres when randomly probed with nonspeech sounds. This is an intriguing (and perhaps no less interesting) possibility. However we think it is unlikely, due to the large number of trials (816), which would work against the survival over averaging of brain activity that is not strictly time-locked to the stimuli; and due to the fact that impulsive stimuli are known to elicit asymmetric brain responses (Chait et al., 2004; Johnson & Hautus, 2010).

A potential criticism of the LI metric used here is that it was (partly) based on auditory responses elicited by DP stimuli, which were perceptually lateralised to the right side. In fact our previous work in adults has shown that DP stimuli produce measureably contralateralised auditory responses (Johnson & Hautus, 2010; Johnson, Hautus, Duff, & Clapp, 2007). However, contralateralisation elicited by lateralised dichotic pitches is rather subtle in comparison to that elicited by monaural stimuli (see Johnson & Hautus, 2010 for review and discussion of this issue). In the present data from children, our analyses revealed no such contralateralisation of DP responses and the responses from DP and noise only stimuli were effectively the same. Further, our analyses showed no significant interactions between stimulus type and hemiphere. We conclude that any contralaterality in the DP responses in children must be below the noise floor of the data and should not significantly affect the LI index (see Fig. 6).

4.2. Atypical auditory lateralisation in dyslexia

The auditory lateralization index captures group differences that promise to be useful for studying atypical brain development. As a group, children with dyslexia showed significantly less hemispheric asymmetry than controls. Abnormal hemispheric asymmetry in dyslexia has been a theme in dyslexia research for many decades and is gaining new prominence with recent models that posit abnormalities of AST speech mechanisms to account for the perceptual and phonological difficulties experienced by individuals with dyslexia (Abrams et al., 2009; Goswami, 2011; Lehongre, Ramus, Villiermet, Schwartz, & Giraud, 2011).

Our cross-sectional data showed no association between age and laterality in control children, indicating that the left lateralization is complete by the time that children reach school age. Previous work by our group has shown that the P100m is also significantly left lateralized in four year olds (Johnson et al., 2010), suggesting that auditory asymmetry is present well before children begin to read. In striking contrast, the results showed a strong positive association between age and lateralization in the children with dyslexia. An interpretation of an abnormal trajectory of auditory development in dyslexia receives some further support from our finding that P100m latencies decreased with age in the control children but not in the children with dyslexia. These intriguing results indicate the need for follow up with longitudinal studies to more firmly establish the developmental trajectory of auditory lateralization in reading-delayed children.

Our cross-sectional data indicate that children with dyslexia show substantial lateralization differences from control children at the younger end of the range (8–9 yr) but approach or reach control group levels of lateralization by the end of the range (11–12 yr). If LI is really associated with reading disability, why does reading performance not normalise along with LI? One possibility is suggested by evidence from behavioural measures of the ability to hear tones in the presence of a masking noise. Wright and Zecker (2004) found that the thresholds of listeners with language-based learning problems (LP) were significantly higher than those of age matched controls, and that the pattern of impairment varied with age. Wright and Zecker (2004) accounted for these age-related variations in pattern of perceptual impairments by assuming that (1) LP children are about 2–4 years delayed in their performance on masking tasks, and (2) that the onset of puberty may crystallise some perceptual deficits so that they persist into adulthood. Our LI data agree well this account.

Two further issues merit consideration in interpreting atypical brain lateralisation in dyslexia. First, similar to data in many studies of dyslexia involving sensory processing, there is variability in laterality index of the dyslexic group. Fig. 5 shows that the LI difference is not present for all members of the group; at least 6 of the 16 fall within the range of the control group. This observation suggests that delayed or abnormal laterality is not a critical factor in the development of dyslexia (i.e., neither necessary nor sufficient). Nor are any of the other known risk factors for poor reading. This situation suggests that it is likely that there are a pool of many risk factors for dyslexia. Atypical laterality may be either one of a number of potential distal causes of dyslexia or one of a number of potential results of dyslexia.

A second issue that must be considered is that our data do not *directly* demonstrate a unique relationship between hemispheric laterality and reading or phonological skills. Our results, consistent with previous studies (Edgar et al., 2006; Heim et al., 2003; Paul et al., 2006), show that dyslexics *as a group* were significantly less lateralised than typically developing children. Within groups, however, brain lateralisation was not significantly correlated with any of the measures of reading ability. Since we selected our children for good or poor reading ability, the restricted ranges within each group likely work against such correlative analysis, and in the future it would be interesting to examine this possibility in larger samples with a greater range of reading abilities. On the other hand it is possible and perhaps likely, as discussed above, that the connection between brain laterality and reading ability is not a simple linear

relationship but rather a more complicated (and perhaps more interesting) story.

4.3. Binaural processing in dyslexia

While the focus of the present report is on neurophysiological responses to sound onsets, the continuous noise stimulus provides a convenient vehicle for embedding of additional sound features, including the binaural pitch used in the present experiment. Several psychophysical studies (Dougherty et al., 1998; Edwards et al., 2004) have previously reported an impaired ability to detect DP in children with dyslexia, but our neurophysiological results showed no group differences in processing of DP. Since our paradigm did not require children to perform any overt task, this indicates that group differences obtained with psychophysical studies may be at least partially due to differences in coping with task demands or attention or motivation, rather than differences in low-level (sensory) binaural processing abilities. To maintain the logical flow of the present article, we provide a more complete report of the binaural responses in a separate report. In addition to binaural pitch, we note that the broadband noises can readily be manipulated for studies including gap detection and sound lateralisation.

5. Conclusions

Developmental dyslexia has long been associated with problems in central auditory processing abilities and with atypical cerebral lateralization. Our data provide strong support for atypical lateralization of the auditory system in dyslexia, and show novel evidence for differences in the developmental trajectory of auditory function between children with dyslexia and children with normal reading abilities. These results are significant to the study of typical brain development, for several reasons. First, the LI as calculated here is fairly sensitive (nearly all children showed some degree of lateralization) and reliable (there was high agreement in the LIs calculated from the two types of sounds). Second, the MEG measurements are entirely noninvasive and do not require active attention to the stimuli, which are important considerations in conducting child studies.

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