

Sound envelope processing in the developing human brain: A MEG study



Huizhen Tang*, Jon Brock, Blake W. Johnson

ARC Centre of Excellence in Cognition and its Disorders, Macquarie University, Sydney, NSW 2109, Australia
Department of Cognitive Science, Macquarie University, Sydney, NSW 2109, Australia

See Editorial, pages 994–998

ARTICLE INFO

Article history:

Accepted 15 July 2015

Available online 11 September 2015

Keywords:

Auditory cortex

Auditory steady state response

Development

Envelope following response

Language acquisition

Temporal processing

HIGHLIGHTS

- The auditory cortical envelope following response was measured in preschool-aged children using a paediatric magnetoencephalography system.
- Results show that, relative to adults, children's auditory cortex has a limited capacity to encode temporal modulations at rates faster than about 25 Hz.
- These results suggest a protracted maturational time course in brain development for cortical processing of temporal modulations.

ABSTRACT

Objective: This study investigated auditory cortical processing of linguistically-relevant temporal modulations in the developing brains of young children.

Methods: Auditory envelope following responses to white noise amplitude modulated at rates of 1–80 Hz in healthy children (aged 3–5 years) and adults were recorded using a paediatric magnetoencephalography (MEG) system and a conventional MEG system, respectively.

Results: For children, there were envelope following responses to slow modulations but no significant responses to rates higher than about 25 Hz, whereas adults showed significant envelope following responses to almost the entire range of stimulus rates.

Conclusion: Our results show that the auditory cortex of preschool-aged children has a sharply limited capacity to process rapid amplitude modulations in sounds, as compared to the auditory cortex of adults.

Significance: These neurophysiological results are consistent with previous psychophysical evidence for a protracted maturational time course for auditory temporal processing. The findings are also in good agreement with current linguistic theories that posit a perceptual bias for low frequency temporal information in speech during language acquisition. These insights also have clinical relevance for our understanding of language disorders that are associated with difficulties in processing temporal information in speech.

© 2015 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Temporal modulations in the overall amplitude of sounds (“sound envelope”) contain critical information for the perception of speech (Drullman, 1995; Drullman et al., 1994; Rosen, 1992; Shannon et al., 1995). For example it is well known that the prosodic content

* Corresponding author at: Department of Cognitive Science, Macquarie University, Sydney, NSW 2109, Australia. Tel.: +61 298506789; fax: +61298506059.

E-mail address: joann.tang@mq.edu.au (H. Tang).

of a spoken sentence is conveyed within the slow temporal fluctuations of the sound envelope (Pelle and Davis, 2012; Rosen, 1992). Conversely, impaired temporal processing has long been associated with language problems including word deafness (Jorgens et al., 2008; Phillips and Farmer, 1990), deficits in speech discrimination (Ali and Jerger, 1992; Souza, 2000), and dyslexia (Ben-Yehudah et al., 2004; Boets et al., 2007; Lehongre et al., 2011; Menell et al., 1999; Putter-Katz et al., 2005; Walker et al., 2002).

Interest in the topic of auditory temporal processing has been stimulated by recent neurolinguistic models that propose an essential role in speech perception for neural mechanisms that

encode the speech envelope (Giraud and Poeppel, 2012; Goswami and Leong, 2013; Gross et al., 2013; Peelle and Davis, 2012). According to such models, intrinsic brain oscillations play a critical role in the analysis of speech, serving to partition the continuous speech signal down into manageable units and to align neural activity with the temporal rhythms of the speech stream (Giraud and Poeppel, 2012; Peelle and Davis, 2012). Speech is a dynamic signal that delivers units of critical information at quite different time scales (e.g. intonation/prosody at 500–1000 ms, syllables at 150–300 ms, and phonemic features at 20–80 ms). Therefore neural mechanisms are required for simultaneous sampling of these different speech units. The temporal sampling model proposed by Poeppel (2003) states that intrinsic auditory cortical oscillations in the theta range (3–7 Hz) and gamma range (30–50 Hz) are “tuned” to track and sample the temporal features of syllables and phonemes respectively. Logically, such models of speech perception must account for the maturation of temporal processing during the critical periods for language acquisition. However at the present time little is known about sound envelope processing in the developing brain.

Behavioural evidence from psychophysical studies suggests that temporal processing undergoes a protracted maturational time course. For example, performance in gap detection continues to improve with age from 3 to 6 years (Trehub et al., 1995; Wightman et al., 1989) and reaches adult levels of performance at about 8–10 years (Davis and McCroskey, 1980; Irwin et al., 1985). Likewise, detection of amplitude modulations (AM) does not reach mature levels until mid- to late-childhood (Hall and Grose, 1994; Moore et al., 2011). In general, children consistently demonstrate poorer auditory temporal resolution than adults (Banai et al., 2011; Fox et al., 2012; Hall and Grose, 1994; Hill et al., 2004; Moore et al., 2011; Trehub et al., 1995; Wightman et al., 1989). Nevertheless, the reported developmental profiles show considerable variability between studies. Some of this variability may result from children's failure to attend to repetitive stimuli and their failure to comply with experimental requirements. For these reasons, it is difficult to know how much of the difference in performance between children and adults is due to physiological differences in their auditory systems, and how much is due to attentional and motivational variables (Bishop et al., 2011). Consequently it is essential to obtain direct and objective neurophysiological data on temporal processing in the developing brain.

One direct and objective measure of temporal processing is the auditory steady-state response (ASSR), a brain response evoked by rapidly presented periodic stimuli and whose frequency components are stable in both amplitude and phase over a long temporal window (Regan, 1989). ASSRs recorded with electroencephalography (EEG) or magnetoencephalography (MEG) provide an objective and noninvasive metric of the extent to which a periodic stimulus “drives” a neurophysiological response, or conversely, the extent to which the brain response “follows” the temporal patterns of the physical stimulus (Picton et al., 2003). As an alternative to constant stimulation at individual modulation rates, one can characterise brain responses to stimuli that undergo rapid transition (e.g. sweeps) through a range of rates. Since the evoked brain responses to such sweeps are not “steady”, these evoked brain responses are referred to as envelope following responses (EFRs) (e.g. Lehongre et al., 2011; Miyazaki et al., 2013; Purcell et al., 2004).

Both ASSRs and EFRs can be characterised using their associated temporal modulation transfer functions (TMTFs). These transfer functions depict a system's sensitivity to amplitude modulations of an acoustic signal as a function of the modulation rate (Viemeister, 1979). TMTFs for the adult auditory cortex exhibit a low-pass filter profile characterised by a best modulation frequency (BMF) occurring at about 40 Hz and an upper cut-off point

at about 50–55 Hz, above which the strength of the response begins to decline steadily (Lehongre et al., 2011; Miyazaki et al., 2013; Picton et al., 2003; Poulsen et al., 2007, 2009; Purcell et al., 2004). This neurophysiological profile corresponds reasonably well to the psychophysical TMTF for the detection of the amplitude modulation of white noise (Viemeister, 1979).

While ASSRs/EFRs have been extensively characterised in the adult brain, the development of these responses during childhood is less well understood (Picton et al., 2003). Considering the abundant psychophysical evidence suggesting lower temporal resolution in children, it is somewhat paradoxical that EEG measurements of the ASSR/EFR in sleeping infants have identified the BMF to be at about 80 Hz, which is much higher than the BMF for adults (Picton et al., 2003; John et al., 2004; Nodarse et al., 2012). However, EEG responses to rates at about 40 Hz reside primarily in the auditory cortex, whereas responses in the 80–100 Hz range primarily involve subcortical (brainstem) responses (Purcell et al., 2004). This suggests that the difference between children's BMF at higher frequency, as compared to the lower BMF for adults, may simply reflect the earlier maturation of brainstem responses in children, as compared to their cortical response (Joris et al., 2004; Moore, 2002; Moore and Linthicum, 2007). The contribution of cortical responses in the infant studies may have been further reduced in previous studies because measurements were made when infants were either in sleep or sedated, both of which may have had suppressive effects on auditory processing in the cortex (Cohen et al., 1991; Goldstein et al., 1959; Lu et al., 2001). This suggestion is supported by a recent EEG study that examined the ASSR in children aged 6–9 years who were asked to maintain their attention to trains of tone-burst at a range of repetition rates during the recording (Tlumak et al., 2012). The data from this study showed that the children's ASSRs were adult-like at 80 Hz. In contrast, the ASSRs at 20 and 40 Hz in children were smaller than those of adults. Because the EEG ASSRs are dominated by brainstem responses at 80 Hz, but dominated by cortical response below about 50 Hz (Purcell et al., 2004), these findings can be taken as an indication of different developmental trajectories of temporal processing in the cortex and in peripheral regions (Moore, 2002). Interestingly, the magnitudes of responses at low repetition rates (i.e. 0.75 Hz, 1.25 Hz, 2.5 Hz, and 5 Hz) in school-aged children were larger than those obtained in adults (Tlumak et al., 2011, 2012).

To our knowledge there are no EEG/MEG data on the ASSR/EFR for children who are older than infants or younger than school age. Yet, the preschool years between 3 and 5 years represent a crucial period for the acquisition of language. Given the emerging importance of temporal processing in neurobiological models of language perception (Giraud and Poeppel, 2012; Goswami and Leong, 2013; Gross et al., 2013), it has become imperative to obtain objective neurophysiological data on cortical temporal processing capabilities in children during the years in which they are rapidly mastering the local language. To this end, the current study characterised the EFRs to a range of linguistically-relevant AM rates in a group of healthy, awake preschool-aged children and compared these responses to those of a reference group of healthy adults. In order to focus our measurements on the auditory cortex, EFRs were measured using MEG, which is relatively insensitive to subcortical signals, as compared to EEG (Baillet et al., 2001; Johnson et al., 2010; Nakasatp et al., 1994).

2. Method

2.1. Subjects

Twelve children (4 females) aged 3–5 years (mean = 49.3 months) participated in the study. All children were right-handed and

showed normal hearing based on their parents' reports. Twelve adult participants (7 female) were aged from 22 to 36 (mean = 28.8 years). All the adults were right-handed. Their hearing thresholds were measured using an Otovation Amplitude T3 series audiometer (Otovation LLC, King of Prussia, PA). All adults showed normal hearing thresholds (≤ 20 dB HL) for octave frequencies from 500 to 2000 Hz. All procedures were approved by the Human Subjects Ethics Committee at Macquarie University.

2.2. Acoustic stimulation

The acoustic stimulus was created in MATLAB (Mathworks: Natick, MA) and consisted of a 9-s AM sweep in the middle; and 0.3-s segments of unmodulated white noise both at the beginning and the end of the AM sweep. The unmodulated segments of white noise served to separate the envelope following response from the responses to sound onset and offset. The AM sweep was generated by modulating a 9-s white noise with an equal duration sweep changing exponentially from 1 Hz to 80 Hz. A noise carrier was used to eliminate any spectral cues from the stimulus, and the modulation rates encompassed the range of linguistically-relevant AM rates (Rosen, 1992). The modulation depth was 100%. The exponential function used to create the stimulus was:

$f(t) = f_0 \times \left(\frac{f_1}{f_0}\right)^{\frac{t}{t_1}}$, where $f(t)$ is the frequency changing by time, t , $f_0 = 1$ (Hz) is the starting frequency, $f_1 = 80$ (Hz) is the ending frequency, $t_1 = 9$ (s) is the sweep duration. The function therefore can be simplified as: $f(t) = 80^{t/9}$.

The temporal waveform of the complete stimulus and spectrogram of the sweep envelope are presented in Fig. 1. The sounds were delivered binaurally using insert earphones (Model ER-30, Etymotic Research Inc., Elk Grove Village, IL) at a level of 70–75 dB SPL.

2.3. Procedure

Participants listened to the stimuli passively while watching a muted movie. We adopted this passive listening strategy in order to make the experimental setup appealing enough for the child participants to remain in the MEG scanner for the duration of the experiment. Passive listening paradigms have been used in many previous EFR and ASSR studies (see Purcell et al., 2004; Picton et al., 2003).

Stimulus presentation was controlled using Experiment Builder 1.10.165 (SR Research: Mississauga, Ontario, Canada). The acoustic stimulus was presented with a mean inter-stimulus interval of 950 ms, randomly selected from a rectangular distribution between 900 ms and 1000 ms. 100 trials were presented in one block to children, while 200 trials were presented in two blocks to adults. For adult, there was a 5-min break between two blocks. In the present analyses, only the first 100 trials of adult data were included for comparison to the child data. The full set of adult data will be presented in a separate report. To effectively convey instructions to young children and minimise head movement artifacts during MEG recordings, a child-friendly data acquisition protocol was employed (Johnson et al., 2010). The whole experiment took about half an hour including the MEG set up for children; the more comprehensive recordings in adults required about 1 hour.

2.4. MEG recordings

Prior to data acquisition, the participants were fitted with five head position marker coils. The position of the five coils and the head shape of the subject were digitised using a Polhemus Fastrak digitiser (Colchester, VT). Head positions were recorded before and after each block to measure head movement. Brain activity was recorded using a whole-head 64-channel paediatric MEG system

(Model PQ1064R-N2m, KIT, Kanazawa, Japan) for children; and a whole-head 160-channel MEG system (Model PQ1160R-N2, KIT, Kanazawa, Japan) for adults. Both MEG systems consisted of first-order axial gradiometers with a 50 mm baseline and located in the same magnetically shielded room (Fujihara Co. Ltd., Tokyo, Japan). Sensor configurations for the two systems are described in detail in Johnson et al. (2010). All measurements were carried out with subjects in a supine position. MEG data were acquired continuously with a sampling rate of 1000 Hz and band-pass filtered between 0.03 Hz and 200 Hz using an analogue filter.

2.5. Analyses

MEG data were analysed using BESA Research Version 6.0 (BESA Research GmbH: Grafelfing, Germany). For both groups, the MEG data were coregistered to the template structural MRI implemented in BESA Research 6.0.

2.5.1. Dipole fitting

Data were analysed using a spatial filter consisting of bilateral dipoles fitted to auditory evoked fields (AEFs) elicited by the onsets of the acoustic stimuli (the P100m in children and the P50m in adults). AEFs were epoched from –100 to 400 ms with respect to the onset of each stimulus. The epoched data was averaged across trials and bandpass filtered between 2 and 20 Hz (Aiken and Picton, 2008). Symmetric dipoles were fitted within a latency window of 100–200 ms for each child subject and 50–100 ms for each adult subject. For both groups, mean dipole locations were in the superior temporal gyri in the vicinity of the primary auditory cortex in each hemisphere (Fig. 2 and Table 1).

Further analyses were conducted on the waveforms reconstructed from each dipole source. The dipole source analysis procedure takes into account the physical geometry of the measurement sensors with respect to individual head shapes (see Irimia et al., 2014 for a discussion of this issue), generating a stable and comparable source estimate from each data set and permitting comparison of brain responses recorded from the two different MEG systems (He et al., 2015).

2.5.2. Spontaneous cortical oscillations

To depict the ongoing brain activities in the absence of auditory stimulation, the power spectrograms of part of the inter-stimulus interval (–600–0 ms) were computed using the two bilateral source montage derived from the dipole fitting procedure.

2.5.3. Auditory evoked fields

Source waveforms were constructed from each dipole in each hemisphere for each subject.

2.5.4. Time–frequency analyses

Using the source montage of the bilateral auditory cortical sources derived from dipole fitting to the AEFs, spectral analyses were then carried out on the continuous source waveforms over a frequency range of 1–80 Hz within an epoch window from 600 ms pre-stimulus to 9600 ms post-stimulus. Time–frequency analyses were then conducted using the complex demodulation method implemented in BESA Research 6.0 (Hoechstetter et al., 2004), with a frequency step of 1 Hz and a time step of 50 ms.

Inter-trial phase coherence (ITPL), which quantifies phase consistency cross trials for each frequency and time point, was computed from the single trial time–frequency representation using the following formula.

$$\text{ITPL}(t, f) = \frac{1}{N} \sum_{k=1}^N e^{i\phi_k(t, f)}$$

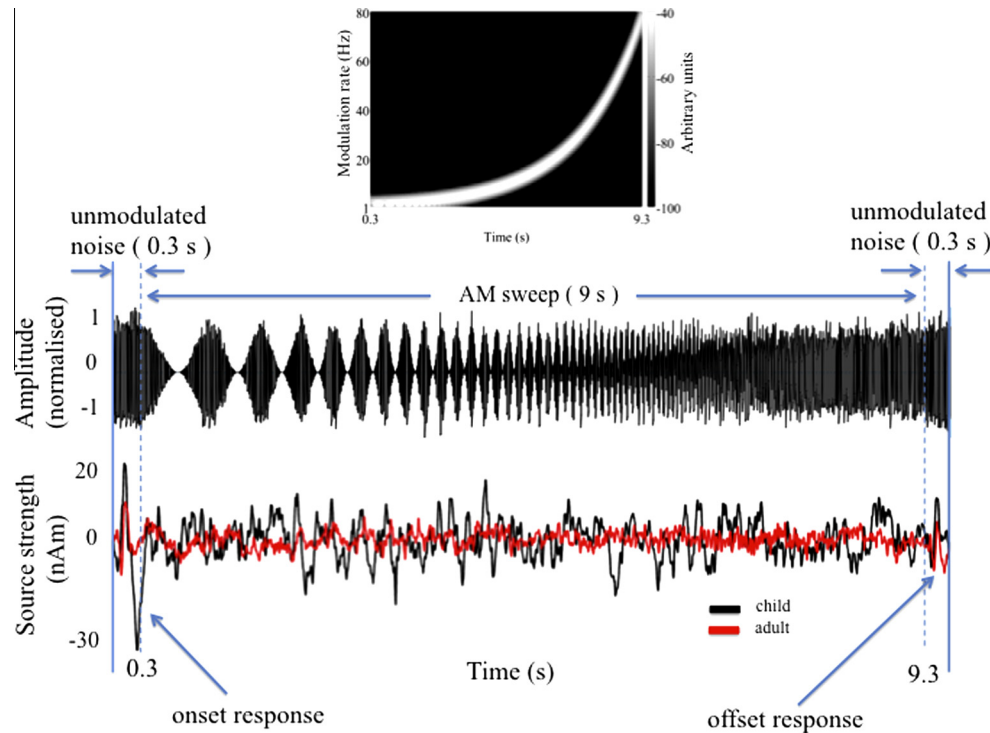


Fig. 1. Experimental paradigm. The acoustic stimulus (middle panel) had a total duration of 9.6 s, beginning and ending with 300 ms of unmodulated white noise. From 0.3 to 9.3 s the white noise carrier was amplitude modulated (100% modulated depth) with a logarithmic sweep over modulation rates from 1 to 80 Hz. The top panel shows the spectrogram of this logarithmic sweep. The bottom panel shows auditory cortex source waveforms (average of both hemispheres) for a representative child (black) and adult (red). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

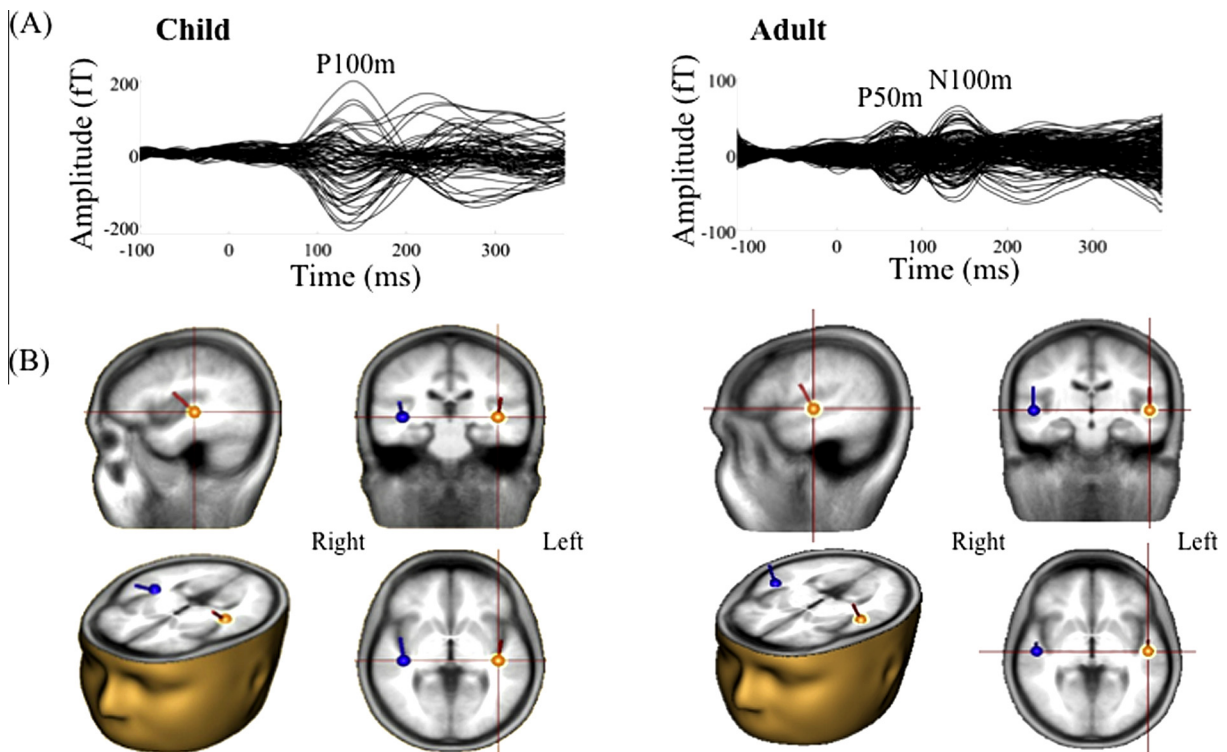


Fig. 2. (A) Overlaid sensor waveforms for a representative child and adult participant. (B) Grand mean dipole source locations for P100m (children) and P50m (adults).

where N = total number of trials; and $\varphi_k(f, t)$ = the phase in trial k .

The ITPL was used as an index of the EFR, because it offers a much more sensitive measure of stimulus-synchronised brain activity than response power (Ding and Simon, 2013).

Permutation tests (Maris and Oostenveld, 2007) were then carried out on the time–frequency data for each group using custom MATLAB scripts to determine the statistical significance of the envelope following pattern. The permutation tests were applied

Table 1

Talairach coordinates for grand mean dipole locations (mm).

		x (±)	y	z
Child	Mean	45.76	−14.53	9.13
	STD	4.79	10.93	12.93
Adult	Mean	51.12	−21.62	4.4
	STD	5.51	6.30	6.91

to the 0.3–9.3 s interval during which the temporal modulation rate of the stimulus swept from 1 Hz to 80 Hz. A primary threshold was used to identify the top 5% of values. This clustering algorithm used the sum of activities within a cluster. Only clusters surviving a permutation with 1000 iterations at the significance level of 0.05 were accepted.

To better visualise the relationship between stimulus modulation rate and brain response, a linearisation procedure was applied to convert the time axis to modulation rate m , based on the logarithmic function $m(t) = 80^{t/9}$ used to generate the AM. Model fitting was then performed in MatLab (MathWorks, Natick, MA) using the Curve Fitting Toolbox (version 3.4.1) to model the correlation between modulation rate and frequency of brain response. A linear model ($f = a * m + b$; here f is the frequency of brain response, m is the rate of modulation, a and b are two parameters set for free fitting) was used to fit the permuted data. This linear modeling was conducted separately for each group. Individual EFRs to AM at rate m were identified as the mean magnitude within the bin $[f - 1 \ f + 1]$. The vector strength of the defined EFR was then re-plotted against the frequency of the AM, in order to visualise the TMTF. Within each group, the same linear model generated from the permuted data was used to compute TMTF for each subject.

The ITPL values are proportional data (valued between 0 and 1). The distributions are not Gaussian and do not meet the distributional assumptions required for linear tests, such as ANOVA or t-tests. Therefore whenever linear tests were performed on ITPL values, the values were first converted to normalised values using the rationalized arcsine transform function (Studebaker, 1985).

3. Results

3.1. Spontaneous oscillations

Fig. 3 shows the average power of ongoing oscillations (combined hemispheres) as a function of its frequency in the absence of auditory stimulation. Both children and adults showed a prominent peak in the alpha band, with children showing a lower peak alpha frequency compared to adults (child: 8.67 ± 0.67 Hz, adult: 10.7 ± 1.27 Hz, $p < 0.001$), consistent with previous EEG measurements of peak alpha frequency in toddlers (Marshall et al., 2002; Saby and Marshall, 2012). Children showed significantly higher alpha amplitudes than adults (child: 28.77 ± 6.89 fT; adult: 16.82 ± 9.83 fT, $p < 0.001$). Fig. 3 shows that children's oscillations were larger in magnitude compared to adults throughout the low frequency range (< 10 Hz). While mean alpha amplitude was slightly larger in the right hemisphere in both groups (Fig. 3, inset), these differences were not statistically significant in either group.

3.2. AEFs

Fig. 4A shows grand averaged AEF source waveforms in the two groups. In children the most prominent auditory AEF is a circa 100 ms peak (mean latency, 117 ms) termed the P100m, believed to be the precursor of the adult P50m response (Johnson et al., 2010, 2013; Lippe et al., 2009). Surface topographic maps of the

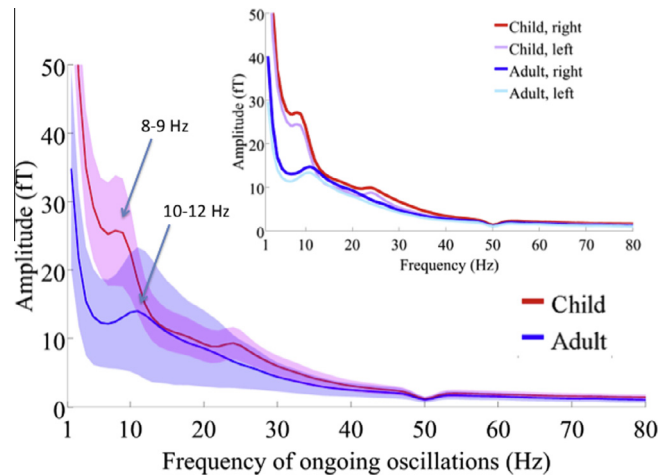


Fig. 3. Group mean profiles of spontaneous brain oscillations from auditory cortical sources measured in the absence of acoustic stimulation. Shading shows one standard deviation. Main figure shows average of two hemispheres, inset shows profiles for each hemisphere.

child P100m and adult P50m are shown in Fig. 4. Statistical analyses showed no significant hemispheric difference in amplitude or latency for any of the adult or child AEF peaks.

3.3. EFRs

Fig. 5 shows ITPL spectrograms and TMTFs for children and adults. From Fig. 5B and D, significant phase-locking was obtained for almost the full range of modulation rates with strongest phase-locking values in the range of 35–50 Hz (corresponding to the “auditory 40 Hz response”; see Galambos et al., 1981; Picton et al., 2003) in adults. In contrast, significant phase-locking was obtained in children only at modulation rates below ~25 Hz with maximal ITPL values at rates of 12–18 Hz (see Fig. 5A, C and E).

Fig. 5E presents the grand mean and standard error of TMTF in both participant groups. Greater ITPL values for adults are visible in two frequency ranges (7–11 Hz, and 15–80 Hz). T-tests (one-tailed) confirmed that these differences were statistically significant: 7–11 Hz: adults $\overline{\text{ITPL}}_{(7-11 \text{ Hz})} = 0.16$, $\text{SD}_{(7-11 \text{ Hz})} = 0.05$, children $\overline{\text{ITPL}}_{(7-11 \text{ Hz})} = 0.10$, $\text{SD}_{(7-11 \text{ Hz})} = 0.02$, $p = 0.006$; 15–80 Hz: adults $\overline{\text{ITPL}}_{(15-80 \text{ Hz})} = 0.19$, $\text{SD}_{(15-80 \text{ Hz})} = 0.10$, children $\overline{\text{ITPL}}_{(15-80 \text{ Hz})} = 0.10$, $\text{SD}_{(15-80 \text{ Hz})} = 0.01$, $p = 0.008$.

Fig. 6A and B shows ITPL spectrograms computed separately for right and left hemispheres in the two groups. Fig. 6C depicts the grand mean and standard error of hemispheric TMTFs in the two groups. Visual inspection of the children's plots indicates slightly greater ITPL values in the right hemisphere (Fig. 6A and C), at least within the 1–25 Hz range where EFRs were statistically significant in this group (Fig. 5C). T-test (two-tailed) confirmed that this difference is statistically significant: (mean left $\overline{\text{ITPL}}_{(1-25 \text{ Hz})} = 0.11$, $\text{SD}_{(1-25 \text{ Hz})} = 0.02$; mean right $\overline{\text{ITPL}}_{(1-25 \text{ Hz})} = 0.13$, $\text{SD}_{(1-25 \text{ Hz})} = 0.03$, $p = 0.004$).

Fig. 6D explicitly compares hemispheric lateralization in the two age groups. For this plot, a lateralization index (LI) was computed as $(\text{right ITPL} - \text{left ITPL}) / (\text{right ITPL} + \text{left ITPL})$, so that negative values indicate left lateralization and positive values indicate right lateralization. This plot indicates that children are more right lateralized than adults over a range of modulation rates between about 10–20 Hz. T-tests (two-tailed) were computed for the mean ITPL values over this range, and the results confirmed a significant difference in lateralization between the two groups (children $\overline{\text{LI}}_{(10-20 \text{ Hz})} = 0.03$, $\text{SD}_{(10-20 \text{ Hz})} = 0.03$; adults $\overline{\text{LI}}_{(10-20 \text{ Hz})} = 0.01$, $\text{SD}_{(10-20 \text{ Hz})} = 0.04$, $p = 0.005$).

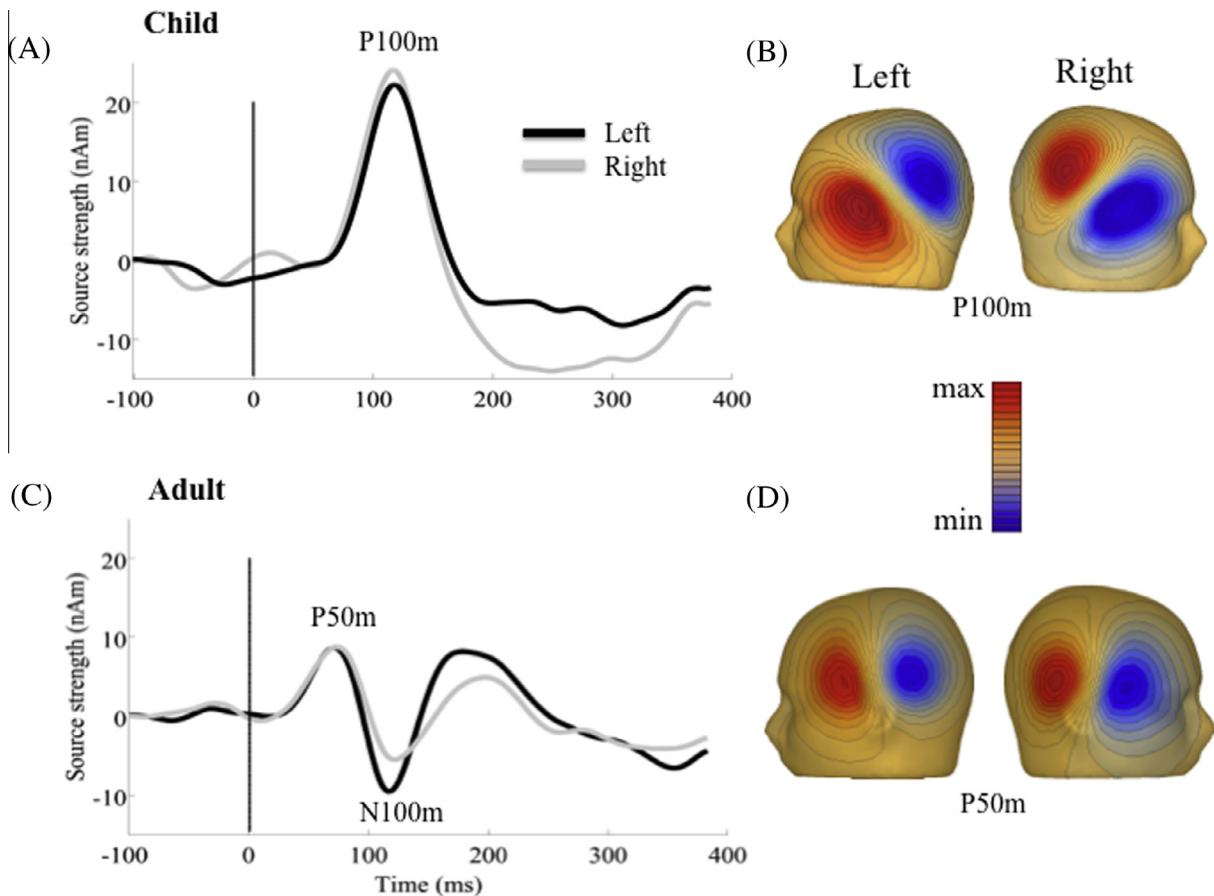


Fig. 4. Grand mean auditory event-related fields elicited by stimulus onsets and surface topographic distributions.

4. Discussion

The present results are the first comprehensive neurophysiological description of temporal envelope processing in the auditory cortex of preschool-aged children. The capacity to process temporal modulation is essential for speech perception and is presumably an important component of language acquisition. In agreement with psychophysical evidence for limited temporal processing capabilities in children, our data show that EFR phase-locking in children's auditory cortex drops off sharply at AM rates higher than about 15 Hz, with no detectable phase-locking at rates higher than about 25 Hz. The immature phase-locking profile of children stands in sharp contrast to the adult profile which shows robust phase-locking throughout the range of AM rates, with maximal ITPL values in the range of 30–50 Hz. Tying our results to the previous literature, we found that in the absence of acoustic stimulation, slow oscillatory activity of children's auditory cortex demonstrated higher power than adults, consistent with previous EEG work (Marshall et al., 2002; Saby and Marshall, 2012; Yordanova and Kolev, 2008). In addition, while EFRs were relatively weak, stimulus onsets elicited robust AEFs in the same children, arguing against the possibility that there were deficiencies in either the delivery of the acoustic stimuli or in the neuromagnetic measurements of the children.

4.1. Spontaneous brain rhythms

Our finding of a greater magnitude of MEG slow oscillations in children during the inter-stimulus intervals of the present experiment is in agreement with previous EEG studies describing

age-related changes of the brain oscillations in resting state (Gasser et al., 1988; Whitford et al., 2007; Yordanova and Kolev, 2008). Whitford et al. (2007) examined the EEG power in subjects aged from 10 to 30 years old. They found that slow wave (sub-alpha) EEG power declined as a function of age, with the most rapid decline during adolescence, and that this decline mirrored the age-related reduction in gray matter measured with structural MRI. The authors concluded that both the structural and neurophysiological changes were due to elimination of active cortical synapses during development.

Our finding of a lower alpha peak frequency in children is also entirely consistent with previous EEG findings (Marshall et al., 2002; Saby and Marshall, 2012; Srinivasan, 1999). For example, Srinivasan (1999) measured alpha EEG in a somewhat older cohort of children (aged 6–9 years) and reported differences in peak alpha frequency between children (mean 8.9 Hz) and adults (mean 10.1 Hz) that are very similar to those obtained in the present MEG study (8.7 Hz and 10.7 Hz respectively). In the EEG study, the measures of long-range alpha coherence also increased with age, indicating that the shift in peak alpha frequency is attributable to the establishment of long range cortico-cortical connections in the maturing neocortex. In general the maturation of the neocortex is characterised by a rearrangement of cortical networks and an increase in temporal precision and synchrony of network interactions, resulting in changes of peak oscillatory frequencies within the network and an increase in magnitude of ongoing high frequency oscillations (Uhlhaas et al., 2010). Reduced temporal precision and synchrony of the immature cortex is likely to be responsible for our finding of sharply reduced EFR capacity in auditory cortex of children, discussed below.

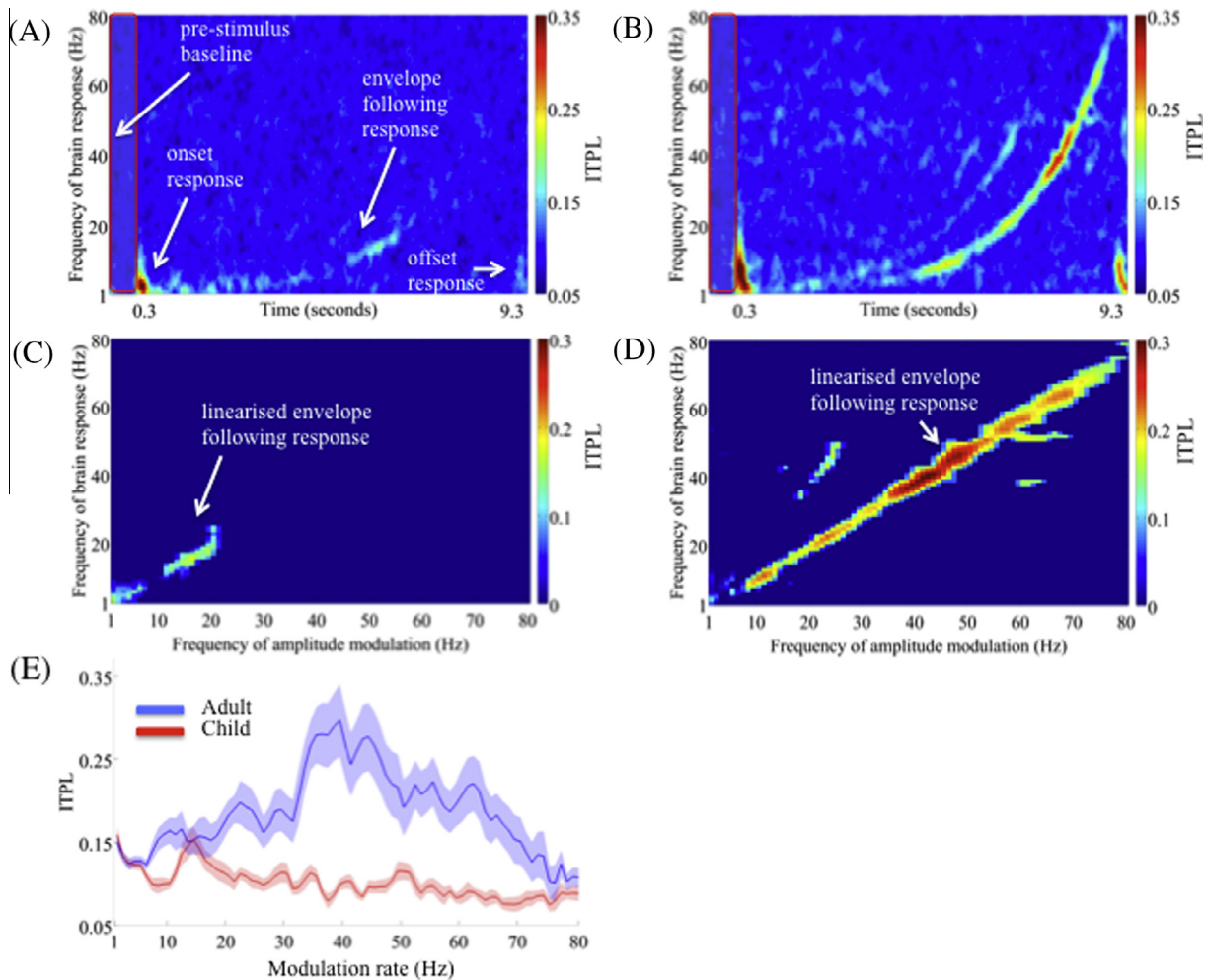


Fig. 5. Grand mean ITPL values measured from auditory cortical sources (average of two hemispheres) and indexed in (A) children and (B) adults. The pre-stimulus baseline is highlighted with a red rectangle. (C) ITPL values that survived permutation testing in children and (D) adults. Permutation tests were performed on data in A and B between 0.3 and 9.3 s (during the amplitude modulated portion of the stimulus). The exponential patterns in A and B are the envelope following responses plotted against time. Over the 0.3–9.3 s time epoch the stimulus was amplitude modulated over rates of 1–80 Hz in an exponential fashion. Consequently, the EFR follows the exponential pattern of modulation rates (Fig. 1, top). The linear patterns in C and D are the same data as A and B, thresholded with permutation testing and replotted by converting the time axis to amplitude modulation rate. This has the effect of linearizing the EFR pattern to directly show the relationship between AM rate and frequency of the following response. (E) Comparison of child and adult TMTFs. Shading indicates standard errors. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

It has been shown that the waking brain rhythms in the alpha range encompass at least three functionally and spatially different oscillations: the classic posterior alpha rhythm, the rolandic mu rhythm, and a lesser-known temporal rhythm (or possibly, set of rhythms) described by various investigators as “auditory alpha rhythm” (Weisz, 2011), “tau rhythm” (Lehtela et al., 1997), “third rhythm” (Niedermeyer, 1990) or “breach rhythm” (Niedermeyer, 1991). While the spatial filtering of the bilateral auditory cortical dipoles employed in this study suggests that our analyses should be biased to the auditory alpha rhythm, it is entirely possible that the alpha peaks in Fig. 3 represent some weighted combination of auditory alpha and the much larger amplitude posterior alpha and mu rhythms (Weisz, 2011). Therefore the present data cannot specify if the alpha peaks in Fig. 3 are modality specific (i.e. generated in auditory cortex) or not. This issue merits examination in future studies.

4.2. AEFs

AEFs elicited by sounds onsets in children’s auditory cortex showed a P100m peak with a mean latency of about 120 ms. The P100m, and its EEG equivalent, the P100, have been reported in

previous electrophysiological studies (Fujioka et al., 2006; Heim et al., 2003; Johnson et al., 2010; Paetau et al., 1995; Ponton et al., 2000; Sharma et al., 1997) and is considered to be an immature version of the P50m/P50 in the adult response. The latency and amplitude of this P100m/P100 component decrease with increasing age, achieving a peak latency of about 50 ms in the adult brain (Ponton et al., 2000; Sharma et al., 1997).

4.3. EFRs

Previous EEG studies of the ASSR/EFR in children have described a response that is at least partly and perhaps largely generated by subcortical sources (Purcell et al., 2004). MEG is considered to be relatively insensitive to subcortical sources, due to a much steeper dependence on distance from the measuring sensor compared to EEG (Baillet et al., 2001; Johnson et al., 2010; Nakasatp et al., 1994). While it is in principle possible to detect brainstem signals with MEG, it requires extraordinary efforts (e.g. thousands of trials) to achieve the signal-to-ratio required to extract subcortical responses such as wave V of the auditory brainstem response (ABR; Parkkonen et al., 2009). The present MEG results therefore represent responses that originate mainly or entirely from the

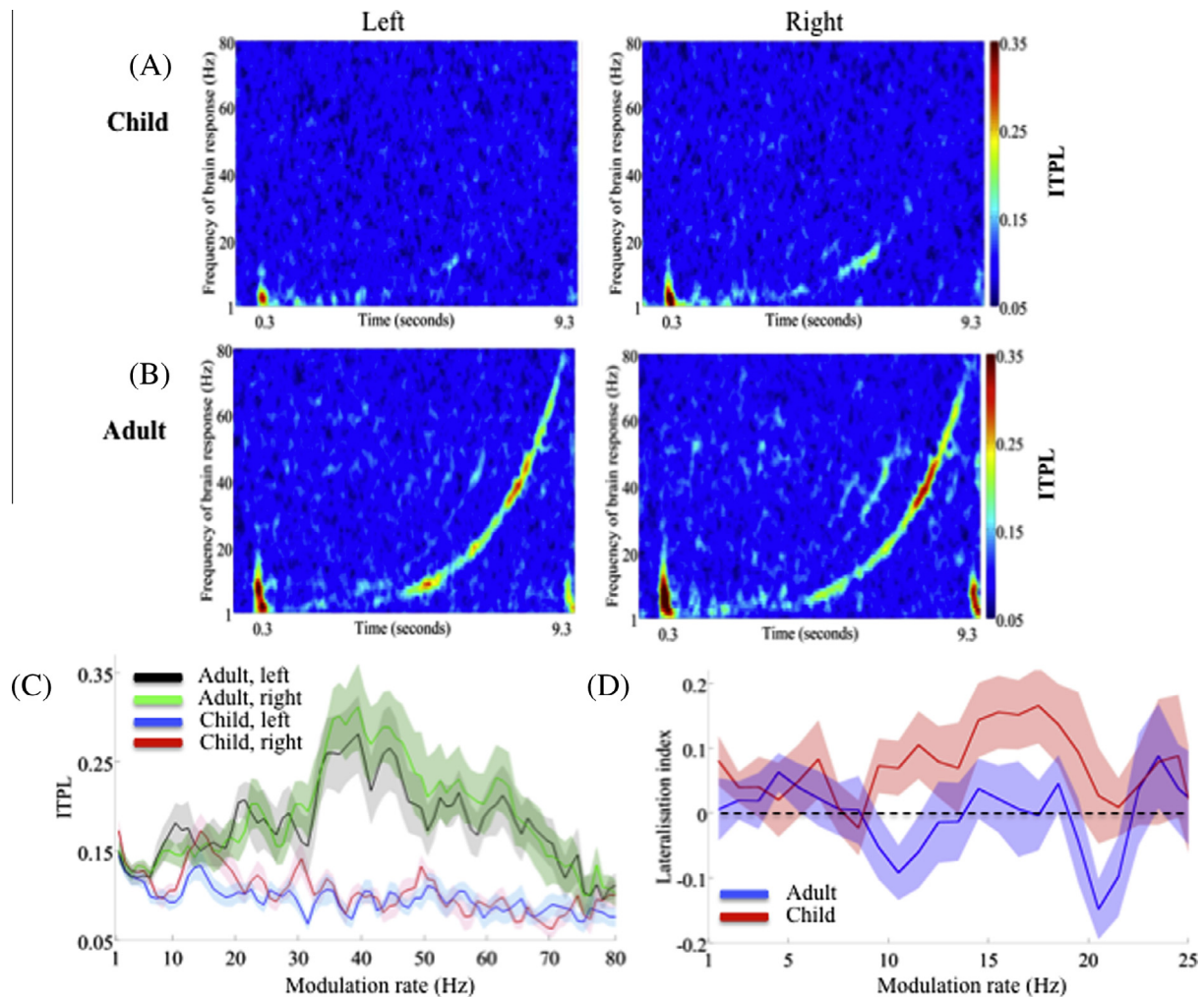


Fig. 6. Hemispheric comparison of EFRs for children and adults. (A) Grand mean spectrogram of ITPL in each hemisphere in children and (B) in adults. (C) Hemispheric comparison of ITPL values for both groups. (D) Between-group comparison of hemispheric lateralization index.

auditory cortex with little or no contribution from subcortical regions. The ability to focus our measurements specifically on cortical activity is important because the subcortical and cortical components of the auditory system have quite different temporal encoding capabilities in the mature brain. Single unit measurements show that the upper limit of synchronizing via phase-locking to the periodicity of a sound decreases progressively and markedly at higher levels of the auditory system, from about 4 kHz at the level of the auditory nerve to about 50 Hz at the level of primary auditory cortex (Joris et al., 2004). A further complication is that subcortical and cortical levels of the auditory system have quite different maturational trajectories (Moore, 2002; Moore and Linthicum, 2007).

Our results indicate that the immature auditory cortex has a limited capacity to encode and represent sound periodicities relative to the adult brain, with a sharp drop-off in phase-locking at rates higher than about 15 Hz and with no measurable following response to AMs faster than about 25 Hz. This indicates that sound envelope encoding, like other auditory cortical responses (Kraus et al., 1993; Moore, 2002; Moore and Linthicum, 2007; Ponton et al., 2000; Sharma et al., 1997; Sussman et al., 2008; Wunderlich and Cone-Wesson, 2006) has a prolonged maturational trajectory, with earlier development of responses to slow envelope periodicities and much later development of responding to high frequency modulations.

4.4. Further implications

The current study was designed to assess the temporal processing capabilities of auditory cortex in young children. While we used a non-speech (noise) stimulus in order to systematically characterise brain responses across a range of linguistically-significant temporal modulation rates, the results are relevant to theoretical frameworks that suggest an important role for temporal encoding mechanisms in speech perception and in language acquisition.

4.4.1. Implications for speech perception

Recent neurolinguistic models suggest that the neural mechanisms of encoding temporal modulation of speech envelope play an essential role in speech perception (Giraud and Poeppel, 2012; Peelle and Davis, 2012). Application of such models of speech perception to dyslexia draws on the logic that abnormal temporal sampling of speech will result in inaccurate representations of speech features and impaired speech processing. However it remains unclear what sampling rate is specifically affected and how this might impair phonological representations in dyslexia. A number of authors have suggested that the perceptual and phonological problems associated with dyslexia are specifically associated with impaired oscillatory processing in the slow theta range (Abrams et al., 2009; Giraud et al., 2005; Goswami, 2011). In the temporal sampling framework proposed by Goswami

(2011), impaired phase-locking of theta rhythms results in impaired syllable parsing and difficulties in perceiving the components of syllables. On the other hand, others have emphasised problems in temporal sampling at higher frequency gamma band rates, resulting in abnormal representations of phonemes (Lehongre et al., 2011).

Notably, the temporal sampling models described above are presently based entirely on neurophysiological data obtained from adults. The present study contributes to this issue with evidence that children show quite different cortical phase locking profiles than adults: The immature human auditory cortex emphasises low AM rates, and, in contrast to the adult reference group, show no measureable phase-locking at rates higher than about 25 Hz. These neurophysiological results are entirely consistent with behavioural evidence that children are strongly biased towards low frequency temporal information in the speech stream during language acquisition (Christophe and Dupoux, 1996; Christophe et al., 2003; Mehler and Christophe, 1995); with the fact that temporal modulations below about 20 Hz are most crucial for speech recognition/intelligibility (Drullman, 1995; Shannon et al., 1995; Smith et al., 2002); and with explanations of dyslexia that posit problems in sampling of low temporal rates in speech (Abrams et al., 2009; Giraud et al., 2005; Goswami, 2011). Temporal sampling models of language perception in general must accommodate the fact that children's temporal processing capabilities are sharply limited in comparison to adults.

4.4.2. Implications for language acquisition

Current views of language acquisition posit that the slow temporal rhythms associated with the prosodic content of speech are crucial for language acquisition (Peelle and Davis, 2012; Rosen, 1992). One proposal, known as the phonological bootstrapping hypothesis, contends that infants and young children depend on phrasal prosodic cues to initially segment continuous speech to form pre-lexical representations for early word learning (Christophe and Dupoux, 1996; Ramus et al., 1999). This provides a non-lexical method of finding word boundaries, which must exist for infants to acquire the words of a language (Christophe and Dupoux, 1996; Christophe et al., 2003; Ramus et al., 1999). On this view, prosodic cues are used by infants to segment the speech stream into prosodic units that are smaller than sentences but bigger than words. Lexical acquisition would then be performed on the basis of this prosody-segmented pre-lexical representation. Such a representation would be useful for the acquisition of phonology and syntax (Christophe and Dupoux, 1996; Ramus et al., 1999). In other words, prosody or rhythm plays an important role in speech processing and phonological bootstrapping is an essential ingredient of language acquisition (Christophe and Dupoux, 1996; Christophe et al., 2003; Mehler and Christophe, 1995). In this context our observed right hemispheric lateralization of EFRs in children is of interest because it has long been held that prosodic information is preferentially processed in the right hemisphere (Friederici and Alter, 2004; Gandour et al., 2004; Homae et al., 2006; Plante et al., 2006; Wartenburger et al., 2007).

4.5. Conclusions

These are the first MEG data on the auditory EFRs for healthy preschool-aged children, an age range that is under-represented in the neurophysiological and neuroimaging literatures. Our results show that the auditory cortex of preschool-aged children has a sharply limited capacity to process amplitude modulations in sound that are faster than about 25 Hz. These neurophysiological results are consistent with psychophysical evidence for a protracted maturational time course for auditory temporal processing and with current linguistic theories that posit a perceptual bias

for low temporal frequencies in speech during language acquisition. These insights also have clinical relevance for our understanding of language disorders associated with problems in processing temporal information in speech.

Acknowledgements

This work was supported by the HearingCRC and Australian Research Council Grants CE110001021 and DP1096160. We thank Stephen Crain for helpful discussions and comments about this manuscript.

Conflict of interest: None of the authors have potential conflicts of interest to be disclosed.

References

- Abrams DA, Nicol T, Zecker S, Kraus N. Abnormal cortical processing of the syllable rate of speech in poor readers. *J Neurosci* 2009;29:7686–93.
- Aiken SJ, Picton TW. Human cortical responses to the speech envelope. *Ear Hear* 2008;29(2):139–57.
- Ali AA, Jerger J. Phase coherence of the middle-latency response in the elderly. *Scand Audiol* 1992;21(3):187–94.
- Baillet S, Moshier JC, Leahy RM. Electromagnetic brain mapping. *IEEE Signal Process Mag* 2001;18(6):14–30.
- Banai K, Sabin AT, Wright BA. Separable developmental trajectories for the abilities to detect auditory amplitude and frequency modulation. *Hear Res* 2011;280(1–2):219–27.
- Ben-Yehudah G, Banai K, Ahissar M. Patterns of deficit in auditory temporal processing among dyslexic adults. *NeuroReport* 2004;15(4):627–31.
- Bishop DVM, Hardiman MJ, Barry JG. Is auditory discrimination mature by middle childhood? A study using time-frequency analysis of mismatch responses from 7 years to adulthood. *Dev Sci* 2011;14(2):402–16.
- Boets B, Wouters J, van Wieringen A, Ghesquiere P. Auditory processing, speech perception and phonological ability in pre-school children at high-risk for dyslexia: a longitudinal study of the auditory temporal processing theory. *Neuropsychologia* 2007;45(8):1608–20.
- Christophe A, Dupoux E. Bootstrapping lexical acquisition: the role of prosodic structure. *Linguist Rev* 1996;13(3–4):383–412.
- Christophe A, Nespor M, Guasti MT, Ooyen BV. Prosodic structure and syntactic acquisition: the case of the head-direction parameter. *Dev Sci* 2003;6(2):211–20.
- Cohen LT, Rickards FW, Clark GM. A comparison of steady-state evoked potentials to modulated tones in awake and sleeping humans. *J Acoust Soc Am* 1991;90(5):2467–79.
- Davis SM, McCroskey RL. Auditory fusion in children. *Child Dev* 1980;51(1):75–80.
- Ding N, Simon JZ. Power and phase properties of oscillatory neural responses in the presence of background activity. *J Comput Neurosci* 2013;34(2):337–43.
- Drullman R. Temporal envelope and fine structure cues for speech intelligibility. *J Acoust Soc Am* 1995;97(1):585–92.
- Drullman R, Festen JM, Plomp R. Effect of temporal envelope smearing on speech reception. *J Acoust Soc Am* 1994;95(2):1053–64.
- Fox AM, Reid CL, Anderson M, Richardson C, Bishop DV. Maturation of rapid auditory temporal processing and subsequent nonword repetition performance in children. *Dev Sci* 2012;15(2):204–11.
- Friederici AD, Alter K. Lateralization of auditory language functions: a dynamic dual pathway model. *Brain Lang* 2004;89(2):267–76.
- Fujioka T, Ross B, Kakigi R, Pantev C, Trainor LJ. One year of musical training affects development of auditory cortical-evoked fields in young children. *Brain* 2006;129:2593–608.
- Galambos R, Makeig S, Talmachoff PJ. A 40-Hz auditory potential recorded from the human scalp. *PNAS* 1981;78(4):2643–7.
- Gandour J, Tong Y, Wong D, Talavage T, Dziedzic M, Xu Y, et al. Hemispheric roles in the perception of speech prosody. *NeuroImage* 2004;23(1):344–57.
- Gasser T, Verleger R, Bacher P, Sroka L. Development of the EEG of school-age children and adolescents. I. Analysis of band power. *Electroencephalogr Clin Neurophysiol* 1988;69:91–9.
- Giraud K, Demonet JF, Habib M, Marquis P, Chauvel P, Liegeois-Chauvel C. Auditory evoked potential patterns to voiced and voiceless speech sounds in adult developmental dyslexics with persistent deficits. *Cereb Cortex* 2005;15:1524–34.
- Giraud AL, Poeppel D. Cortical oscillations and speech processing: emerging computational principles and operations. *Nat Neurosci* 2012;15(4):511–7.
- Goldstein MH, Kiang NYS, Brown RM. Responses of the auditory cortex to repetitive acoustic stimuli. *J Acoust Soc Am* 1959;31(3):356–64.
- Goswami U. A temporal sampling framework for developmental dyslexia. *Trends Cogn Sci* 2011;15(1):3–10.
- Goswami U, Leong V. Speech rhythm and temporal structure: converging perspectives? *Lab Phonol* 2013;4(1):67–92.
- Gross J, Hoogenboom N, Thut G, Schyns P, Panzeri S, Belin P, Garrod S. Speech rhythms and multiplexed oscillatory sensory coding in the human brain. *PLoS Biol* 2013;11(12):e1001752.

- Hall JW, Grose JH. Development of temporal resolution in children as measured by the temporal modulation transfer function. *J Acoust Soc Am* 1994;96(1):150–4.
- He W, Brock J, Johnson BW. Face processing in the brains of pre-school aged children measured with MEG. *NeuroImage* 2015;106:317–27.
- Heim S, Eulitz C, Elbert T. Altered hemispheric asymmetry of auditory P100m in dyslexia. *Eur J Neurosci* 2003;17(8):1715–22.
- Hill PR, Hartley DEH, Glasberg BR, Moore BCJ, Moore DR. Auditory processing efficiency and temporal resolution in children and adults. *J Speech Lang Hear Res* 2004;47(5):1022–9.
- Hoechstetter K, Bornfleth H, Weckesser D, Ille N, Berg P, Scherg M. BESA source coherence: a new method to study cortical oscillatory coupling. *Brain Topogr* 2004;16(4):233–8.
- Homae F, Watanabe H, Nakano T, Asakawa K, Taga G. The right hemisphere of sleeping infant perceives sentential prosody. *Neurosci Res* 2006;54(4):276–80.
- Irimia A, Erhart MJ, Brown TJ. Variability of magnetoencephalographic sensor sensitivity measures as a function of age, brain volume and cortical area. *Clin Neurophysiol* 2014;125(10):1973–84.
- Irwin RJ, Ball AKR, Kay N, Stillman JA, Rosser J. The development of auditory temporal acuity in children. *Child Dev* 1985;56(3):614–20.
- John MS, Brown DK, Muir PJ, Picton TW. Recording auditory steady-state responses in young infants. *Ear Hear* 2004;25(6):539–53.
- Johnson BW, Crain S, Thornton R, Tesan G, Reid M. Measurement of brain function in pre-school children using a custom sized whole-head MEG sensor array. *Clin Neurophysiol* 2010;121(3):340–9.
- Johnson BW, McArthur G, Hautus M, Reid M, Brock J, Castles A, Crain S. Lateralized auditory brain function in children with normal reading ability and in children with dyslexia. *Neuropsychologia* 2013;51(4):633–41.
- Jorgens S, Biermann-Ruben K, Kurz MW, Flugel C, Daehli Kurz K, Antke C, et al. Word deafness as a cortical auditory processing deficit: a case report with MEG. *Neurocase* 2008;14(4):307–16.
- Joris P, Schreiner C, Rees A. Neural processing of amplitude-modulated sounds. *Physiol Rev* 2004;84(2):541–77.
- Kraus N, McGee T, Carrell T, Sharma A, Micco A, Nicol T. Speech-evoked cortical potentials in children. *J Am Acad Audiol* 1993;4(4):238–48.
- Lehongre K, Ramus F, Villiermet N, Schwartz D, Giraud AL. Altered low-gamma sampling in auditory cortex accounts for the three main facets of dyslexia. *Neuron* 2011;72(6):1080–90.
- Lehtela L, Salmelin R, Hari R. Evidence for reactive magnetic 10-Hz rhythm in the human auditory cortex. *Neurosci Lett* 1997;222(2):111–4.
- Lippe S, Martinez-Montes E, Arcand C, Lassonde M. Electrophysiological study of auditory development. *Neuroscience* 2009;164(3):1108–18.
- Lu T, Liang L, Wang X. Temporal and rate representations of time-varying signals in the auditory cortex of awake primates. *Nat Neurosci* 2001;4(11):1131–8.
- Marshall PJ, Bar-Haim Y, Fox NA. Development of the EEG from 5 months to 4 years of age. *Clin Neurophysiol* 2002;113(8):1199–208.
- Maris E, Oostenveld R. Nonparametric statistical testing of EEG-and MEG-data. *J Neurosci Methods* 2007;164(1):177–90.
- Mehler J, Christophe A. Maturation and learning of language in the first year of life. In: *The cognitive neurosciences*. Cambridge, MA: The MIT Press; 1995. p. 943–54.
- Menell P, McAnally KI, Stein JF. Psychophysical sensitivity and physiological response to amplitude modulation in adult dyslexic listeners. *J Speech Lang Hear Res* 1999;42:797–803.
- Miyazaki T, Thompson J, Fujioka T, Ross B. Sound envelope encoding in the auditory cortex revealed by neuromagnetic responses in the theta to gamma frequency bands. *Brain Res* 2013;1506:64–75.
- Moore DR. Auditory development and the role of experience. *Br Med Bull* 2002;63:171–81.
- Moore DR, Cowan JA, Riley A, Edmondson-Jones AM, Ferguson MA. Development of auditory processing in 6 to 11 yr old children. *Ear Hear* 2011;32:269–85.
- Moore JK, Linthicum FH. The human auditory system: a timeline of development. *Int J Audiol* 2007;46(9):460–78.
- Nakasatp N, Levesque MF, Barth DS, Baumgartner C, Rogers RL, Sutherling WW. Comparisons of MEG, EEG, and ECoG source localization in neocortical partial epilepsy in humans. *Electroencephalogr Clin Neurophysiol* 1994;91(3):171–8.
- Nodaré EM, Abalo MCP, Fortuny AT, Hernández MV, Castellanos AL. Maturation changes in the human envelope-following responses. *Acta Otorrinolaringol Esp* 2012;63(4):258–64.
- Niedermeyer E. Alpha-like rhythmical activity of the temporal lobe. *Clin Electroencephalogr* 1990;21:210–24.
- Niedermeyer E. The “third rhythm”: further observations. *Clin Electroencephalogr* 1991;22:83–96.
- Paetau R, Ahonen A, Salonen O, Sams M. Auditory evoked magnetic fields to tones and pseudowords in healthy children and adults. *J Clin Neurophysiol* 1995;12(2):177–85.
- Parkkonen L, Fujiki N, Makela JP. Sources of auditory brainstem responses revisited: contribution by magnetoencephalography. *Hum Brain Mapp* 2009;30(6):1772–82.
- Peelle JE, Davis MH. Neural oscillations carry speech rhythm through to comprehension. *Front Psychol* 2012;3(320):1–17.
- Phillips DP, Farmer ME. Acquired word deafness, and the temporal grain of sound representation in the primary auditory cortex. *Behav Brain Res* 1990;40(2):85–94.
- Picton TW, John MS, Dimitrijevic A, Purcell D. Human auditory steady-state responses: respuestas auditivas de estado estable en humanos. *Int J Audiol* 2003;42(4):177–219.
- Plante E, Holland SK, Schmithorst VJ. Prosodic processing by children: an fMRI study. *Brain Lang* 2006;97(3):332–42.
- Poeppel D. The analysis of speech in different temporal integration windows: cerebral lateralization as ‘asymmetric sampling in time’. *Speech Commun* 2003;41(1):245–55.
- Ponton CW, Eggermont JJ, Kwong B, Don M. Maturation of human central auditory system activity: evidence from multi-channel evoked potentials. *Clin Neurophysiol* 2000;111(2):220–36.
- Poulsen C, Picton TW, Paus T. Age-related changes in transient and oscillatory brain responses to auditory stimulation in healthy adults 19–45 years old. *Cereb Cortex* 2007;17(6):1454–67.
- Poulsen C, Picton TW, Paus T. Age-related changes in transient and oscillatory brain responses to auditory stimulation during early adolescence. *Dev Sci* 2009;12(2):220–35.
- Purcell DW, John SM, Schneider BA, Picton TW. Human temporal auditory acuity as assessed by envelope following responses. *J Acoust Soc Am* 2004;116:3581–93.
- Putter-Katz H, Kishon-Rabin L, Sachartov E, Shabtai EL, Sadeh M, Weiz R, et al. Cortical activity of children with dyslexia during natural speech processing: evidence of auditory processing deficiency. *J Basic Clin Physiol Pharmacol* 2005;16(2–3):157–72.
- Ramus F, Nespor M, Mehler J. Correlates of linguistic rhythm in the speech signal. *Cognition* 1999;73:265–92.
- Regan D. Human brain electrophysiology: evoked potentials and evoked magnetic fields in science and medicine. Amsterdam: Elsevier; 1989.
- Rosen S. Temporal information in speech: acoustic, auditory and linguistic aspects. *Proc R Soc Lond A Math Phys Sci* 1992;336(1278):367–73.
- Saby JN, Marshall PJ. The utility of EEG band power analysis in the study of infancy and early childhood. *Dev Neuropsychol* 2012;37(3):253–73.
- Shannon RV, Zeng F-G, Kamath V, Wygonski J, Ekelid M. Speech recognition with primarily temporal cues. *Science* 1995;270(5234):303–4.
- Sharma A, Kraus N, McGee TJ, Nicol TG. Developmental changes in P1 and N1 central auditory responses elicited by consonant-vowel syllables. *Electroencephalogr Clin Neurophysiol* 1997;104(6):540–5.
- Souza PE. Older listeners’ use of temporal cues altered by compression amplification. *J Speech Lang Hear Res* 2000;43:661–74.
- Smith ZM, Delgutte B, Oxenham AJ. Chimaeric sounds reveal dichotomies in auditory perception. *Nature* 2002;416:87–90.
- Srinivasan R. Spatial structure of the human alpha rhythm: global correlation in adults and local correlation in children. *Clin Neurophysiol* 1999;110(8):1351–62.
- Studebaker GA. A rationalized arcsine transform. *J Speech Lang Hear Res* 1985;28(3):455–62.
- Sussman E, Steinschneider M, Gumenyuk V, Grushko J, Lawson K. The maturation of human evoked brain potentials to sounds presented at different stimulus rates. *Hear Res* 2008;236(1–2):61–79.
- Tlupak AI, Durrant JD, Delgado RE, Boston JR. Steady-state analysis of auditory evoked potentials over a wide range of stimulus repetition rates: profile in adults. *Int J Audiol* 2011;50(7):448–58.
- Tlupak AI, Durrant JD, Delgado RE, Boston JR. Steady-state analysis of auditory evoked potentials over a wide range of stimulus repetition rates: profile in children vs. adults. *Int J Audiol* 2012;51(6):480–90.
- Trehub SE, Schneider BA, Henderson JL. Gap detection in infants, children, and adults. *J Acoust Soc Am* 1995;98(5):2532–41.
- Uhlhaas PJ, Roux F, Rodriguez E, Rotarska-Jagiela A, Singer W. Neural synchrony and the development of cortical networks. *Trends Cogn Sci* 2010;14(2):72–80.
- Viemeister NF. Temporal modulation transfer functions based upon modulation thresholds. *J Acoust Soc Am* 1979;66(5):1364–80.
- Walker MM, Shinn JB, Cranford JL, Givens GD. Auditory temporal processing performance of young adults with reading disorders. *J Speech Lang Hear Res* 2002;45:598–605.
- Wartenburger I, Steinbrink J, Telkemeyer S, Friedrich M, Friederici AD, Obrig H. The processing of prosody: evidence of interhemispheric specialization at the age of four. *NeuroImage* 2007;34(1):416–25.
- Weisz N. Alpha rhythms in audition: cognitive and clinical perspectives. *Front Psychol* 2011;2:1–15.
- Wightman F, Allen P, Dolan T, Kistler D, Jamieson D. Temporal resolution in children. *Child Dev* 1989;60(3):611–24.
- Whitford TJ, Rennie CJ, Grieve SM, Clark CR, Gordon E, Williams LM. Brain maturation in adolescence: concurrent changes in neuroanatomy and neurophysiology. *Hum Brain Mapp* 2007;28(3):228–37.
- Wunderlich JL, Cone-Wesson BK. Maturation of CAEP in infants and children: a review. *Hear Res* 2006;212(1–2):212–23.
- Yordanova J, Kolev V. Event-related brain oscillations in normal development. In: Schmidt LA, Segalowitz SJ, editors. *Developmental psychophysiology: theory, systems and methods*. New York: Cambridge University Press; 2008. p. 15–68.