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4	Hemispheric Asymmetries in Rapid Temporal Processing at Age 7 Predict Subsequent Phonemic
5	Decoding 2 years later: a longitudinal event-related potential (ERP) study
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Abstract

2

The asymmetric sampling in time hypothesis (AST) suggests that the left and right secondary auditory 2 3 areas process auditory stimuli according to different sampling rates (Poeppel, 2003). We investigated 4 whether asymmetries consistent with the AST are observable in children at age 7 and whether they become more pronounced at age 9. Data were collected from 50 children who attended a 2-day research 5 program at age 7 (26 boys, 24 girls; M = 7.50 years, SD = 0.30) and were followed up 2 years later (M =6 7 9.47 years, SD = 0.30). At both time points, children were presented with tone-pairs, each composed of 8 two 50 ms, 1000 Hz, sinusoidal tones separated by inter-stimulus intervals (ISIs) of 25, 50, 100, or 200 9 ms. Stimuli were presented binaurally whilst the EEG was recorded. There was no significant effect of 10 age on Ta or Tb responses. Tb responses to the second tone of tone-pairs indicated a left-hemisphere preference for rapidly presented stimuli (50 ms ISI) and a right hemisphere preference for more slowly 11 12 presented stimuli (100 and 200 ms ISI). The results provide evidence that auditory areas of the left hemisphere preferentially respond to fast temporal rates, and those of the right hemisphere preferentially 13 respond to slow temporal rates in children at age 7 and 9. In 7-year-old children, leftward lateralization 14 of responses to rapidly presented tones predicted better phonemic decoding ability 2 years later, which 15 16 suggests that hemispheric specialization may be a precursor for subsequent phonemic decoding skills. Highlights: 17 18 1. We examined Ta and Tb responses to rapid and slow tone-pairs in children 19 2. Tb responses to rapid (50 ms) tone-pairs were enhanced over the left hemisphere 3. Tb responses to slow (100-200 ms) tone-pairs were enhanced over the right hemisphere 20

4. Lateralisation of Tb for rapid tones at age 7 predicts phonemic decoding at age 9.

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Keywords: Tb, asymmetric sampling in time, temporal integration, hemispheric asymmetry, event related potential, auditory processing, phonemic decoding, children

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1 1. Introduction

2 1.1. Multi-time resolution framework of speech processing

Speech is a rich composition of both temporal and spectral modulations. Temporal cues are 3 4 known to contribute significantly to the intelligibility of speech (Luo and Poeppel, 2007), even when the signal is spectrally degraded. We use temporal cues to identify auditory objects such as phonemes and 5 6 syllables, thus, sensitivity to temporal modulations in the phonemic and syllabic timescales is necessary for speech perception. Current research supports a multi-time resolution model of temporal processing 7 8 for speech perception called the Asymmetric Sampling in Time (AST) hypothesis (Poeppel, 2003). The 9 AST suggests that functional asymmetries of the left and right auditory areas facilitate the processing of the fast and slow modulations present in speech (phonemic/segmental and syllabic/suprasegmental). 10 Poeppel (2003) proposed that temporal integration windows of either a short (25-50 ms) or long (200-11 12 250 ms) duration provide an intrinsic framework by which we sample auditory information in chunks or phonological units. He further postulated that the privileged sampling rates associated with the temporal 13 integration windows are synonymous with the intrinsic oscillatory rates of neuronal ensembles in the left 14 and right auditory areas. According to the AST, neuronal ensembles in both the left and right primary 15 auditory areas are tuned to rapid temporal modulations 25-50 ms (20-40 Hz), which potentially 16 facilitates the higher-order decomposition of the signal into fast and slow modulations. In the secondary 17 auditory areas, the neuronal ensembles in the left and right hemispheres are differentially tuned to rapid 18 (25-50 ms = 20-40 Hz), and slow (200-250 ms = 4-5 Hz) modulations, respectively. The AST 19 hypothesis proposes a hierarchical, intrinsic neural framework, which is optimally suited to the 20 segmental and suprasegmental timescales of speech, and is necessary for the perception of phonemes 21 and syllables (Poeppel, 2003). 22

23 Numerous studies have investigated the predictions of the AST in adults using a range of neuroimaging techniques such as functional magnetic resonance imaging (fMRI; Boemio et al., 2005), 24 25 electroencephalography (EEG; Clunies-Ross et al., 2015), simultaneous fMRI and EEG (Giraud et al., 2007), and magnetoencephalography (MEG; Luo and Poeppel, 2007; 2012). In general, results have 26 supported the AST in that there is a leftward preference for the processing of rapid modulations and a 27 rightward preference for slow modulations. For example, Giraud and colleagues (2007) used 28 29 simultaneous EEG and fMRI to demonstrate that spontaneous fluctuations in EEG power in the gamma range (28-40 Hz) best correlated with endogenous neural activity in the left auditory cortex and 30

fluctuations in the theta (3-6 Hz) range best correlated with endogenous neural activity in the right auditory cortex. Despite substantial evidence for asymmetric temporal processing in adults, the developmental trajectory of temporal processing asymmetries is still unknown. Importantly, the role such asymmetries may play in the development of complex linguistic abilities is poorly understood (Vanvooren et al., 2014).

6 1.2. Auditory ERPs and temporal processing

In the current study, we used EEG to investigate hemispheric asymmetries in temporal 7 processing in children. As cortical processing of auditory signals occurs in the order of milliseconds, 8 techniques such as EEG or MEG provide high temporal resolution which is necessary for the detailed 9 analysis of such processes. However, previous research indicates that the activity of the auditory cortex 10 gives rise to both tangential (vertical) and radial (lateral) dipoles (Ponton et al., 2002). Whilst EEG is 11 sensitive to both tangential and radial dipoles, MEG is primarily sensitive to tangential dipoles (Irimia et 12 al., 2012). This difference is particularly important as the tangential dipole has been localised to the 13 superior surface of the temporal lobe (primary auditory cortex and belt areas of secondary auditory 14 cortex), and the radial dipole has been localised to the lateral surface of the temporal lobe (parabelt areas 15 of secondary auditory cortex) (Ponton et al., 2002; Ruhnau et al., 2011). The poor sensitivity of MEG to 16 radial dipoles means that the use of this technique in auditory processing research may mask critical 17 neural activity of secondary auditory areas. EEG is also a non-invasive, cost-effective neuroimaging 18 technique that is suitable for use in a wide range of age groups, from infants to the elderly. It is therefore 19 a valuable neuroimaging technique that can be used for a wide range of experimental paradigms and 20 populations. 21

The obligatory ERPs elicited by auditory stimuli are divided into fronto-central, and temporal components, generated by the tangential and radial dipoles, respectively (Albrecht et al., 2000; C Ponton et al., 2002). In previous years, it was suggested that the temporal components were simply an inversion of the components observed at fronto-central sites, however, differences in the maturation rates (Bishop et al 2011) and source dipoles strongly suggest that fronto-central and temporal ERPs are dissociable (Ponton et al 2002).

1 1.2.1. Fronto-central auditory ERPs

In adults, the fronto-central ERP waveform is the most often reported, and contains the P1 and N1. 2 The P1 is a positive deflection that peaks between 50-150 ms in adults, and 100-300 ms in children. It is 3 4 present from infancy and is thought to reflect early auditory processing in the cortex (Campbell et al., 2011; Shafer et al., 2015). The N1 is a negative deflection that peaks between 50-200 ms. It is the most 5 6 well-studied of the auditory ERPs due to its prominence in adults, however, the N1 is not clearly observed in children until approximately 10 years of age (Ruhnau et al., 2011). The P1-N1 components 7 8 are proposed to reflect acoustic feature processing (Wagner et al., 2013; Wagner et al., 2017) predominantly in the primary auditory cortex (Albrecht et al., 2000; Bishop et al., 2011; Ruhnau et al., 9 10 2011).

11 **1.2.2 Temporal auditory ERPs**

The temporal ERP waveform contains the Ta, and Tb components, commonly referred to as the 12 T-complex. It is the most prominent ERP component in children, and becomes less prominent 13 throughout adolescence and adulthood when the N1 becomes more prominent. The Ta is a positive 14 deflection that occurs between approximately 140-170 ms post-stimulus onset in childhood (Shafer et 15 al., 2015). Whilst the T-complex is proposed to reflect the activity of secondary auditory areas due to the 16 17 orientation of the dipole, some studies have localised the Ta to the primary auditory cortex (Bishop et al., 2011), and others report origins in secondary auditory areas (Ponton et al., 2002). The Tb is a 18 19 negative deflection that peaks between 140 and 200 ms in children, and has been localised to the secondary auditory cortex (Albrecht et al., 2000; Shafer et al., 2015; Tonnguist-Uhlen et al., 2003). 20

21 The T-complex has been implicated as a potential component for identifying individuals at risk of language difficulties (Shafer et al., 2011; Tonnquist-Uhlen et al., 2003). Like the P1-N1, the T-22 23 complex reflects acoustic feature processing, but is also shown to respond differentially depending on the phonological content (Wagner et al., 2013) and temporal rate of stimuli (Clunies-Ross et al., 2015). 24 The Ta appears less identifiable in individuals prior to the age of 7 years, and continues to increase in 25 amplitude before reaching peak amplitude at age 11 (Shafer et al., 2015; Tonnquist-Uhlen et al., 2003). 26 27 Some studies report that the Tb is identifiable from approximately 6 years of age (Tonnquist-Uhlen et al., 2003), whereas others report that it is more stable across individuals from age 7-8 years (Shafer et 28 29 al., 2015).

1 1.2.3 Functional utility of auditory ERPs

As fronto-central and temporal ERP components reflect areas of the primary and secondary 2 auditory areas, respectively, they can be used to differentiate between acoustic feature processing and 3 4 higher-level auditory processing. Clunies-Ross et al. (2015) examined asymmetries in N1, Ta and Tb responses elicited by tone-pairs with inter-stimulus intervals (ISIs) of 50 and 200 ms. No asymmetries 5 6 were observed for N1 and Ta responses to rapid and slow tone-pairs. The asymmetries in the Tb 7 component supported left hemisphere preference for the processing of rapidly presented stimuli (50 ms) 8 and a right hemisphere preference for slowly presented stimuli (200 ms). Their findings indicated that stimuli are processed in a hierarchical manner according to temporal features and also showed that the 9 10 Tb was particularly important when investigating functional asymmetries in temporal processing.

A previous study by Fox et al. (2012) examined the development of temporal processing in 11 children using the fronto-central components. The children were tested at 7- and 9 years, and 2 years 12 later, at 9 and 11 years. They used intra-class correlations (ICCs) to compare the fronto-central 13 waveforms elicited by single-tones and tone-pairs with varying ISIs. High ICCs indicated a low degree 14 of discrimination between tones, whilst low ICCs indicated a high degree of discrimination between 15 tones. They observed significant changes from time 1 to time 2 in ICCs for rapidly presented tone-pairs, 16 suggesting that the temporal discrimination of rapid tones improved between 7 and 9 years, and between 17 9 and 11 years. They also examined the relationship between rapid temporal processing and nonword 18 repetition. They found that ICCs for 50 ms ISI tone-pairs at the initial testing was a significant predictor 19 of nonword repetition two years later. They suggested that rapid temporal processing abilities contribute 20 to auditory decoding in subsequent years, consistent with the idea that early auditory temporal 21 processing likely facilitates the ability to discriminate phonological units (Poeppel, 2003). 22

23 1.3. Current study aims and hypotheses

The purpose of the current study was to extend the findings of Clunies-Ross et al. (2015) and Fox et al. (2012) in two ways. Our first objective was to look at the development of hemispheric asymmetries in temporal processing in children. Although Fox et al. (2012) examined the development of rapid temporal processing; they looked at fronto-central components only, and did not examine hemispheric asymmetries. Of the previous studies that have examined temporal processing asymmetries, most have focused on younger children (\leq 5 years of age), and have been relatively inconsistent.

Thompson et al. (2016) observed leftward lateralisation of high-frequency endogenous oscillations (20-1 2 50 Hz) in children aged 3 to 5 years-old, while Vanvooren and colleagues (2014) observed no lateralisation for processing of 20 Hz modulations in children of the same age. Rightward lateralisation 3 of temporal processing for slow modulations has been observed in infants (Telkemeyer et al., 2009) and 4 children aged 5 years-old (Vanvooren et al., 2014). However, Thompson et al. (2016) found no 5 lateralisation of low-frequency endogenous oscillations in children aged 3-5 years old. Thompson et al. 6 (2016) suggested that the bilateral representation of low-frequency oscillations (3-7 Hz) in 3-5-year-old 7 children might be due to the further maturation of the relevant neuronal populations in the right 8 hemisphere in mid-to-late childhood. 9

10 Given the mixed findings in younger children, the developmental trajectory remains unclear, and may be clarified with the investigation of temporal processing asymmetries in older children. As 11 12 Clunies-Ross et al. (2015) demonstrated the utility of temporal auditory ERPs for detecting functional asymmetries in temporal processing, we examined the Ta and Tb responses to tone-pairs with short (25, 13 50 ms) and long (100, 200 ms) ISIs in children at age 7, and again 2 years later at age 9. Previous studies 14 have observed marked development of T-complex components (Bishop et al., 2011; Tonnquist-Uhlen et 15 16 al., 2003) and associated complex linguistic skills between 7 and 9 years of age (Vandewalle et al., 17 2012). Therefore, hemispheric asymmetries in this age band could provide further clarification regarding the emergence of functional asymmetries and may also inform the relevance of these asymmetries for 18 19 higher-order linguistic processes.

20 Our second objective was to investigate whether the lateralisation of rapid temporal processing to the left secondary auditory areas (as indexed by the Tb) is associated with the subsequent development 21 of phonological representations necessary for decoding letter strings. Poeppel (2003) suggested that the 22 23 hierarchical decomposition of auditory signals facilitates the isolation and identification of 24 distinguishable units within the speech signal. The ability to isolate segmental and suprasegmental units 25 of speech is essential for the development of phonological skills, such as phonemic decoding (Goswami, 2011; Vanvooren et al., 2014). Like the nonword repetition task used by Fox et al. (2012), phonemic 26 27 decoding also requires the use of phonological output lexicon and oromotor skills, but does not require auditory discrimination of sounds. Furthermore, phonemic decoding requires the mapping of graphemes 28 29 to phonological representations, and taps the integrity of phonological representations as it requires the 30 ordering and combining of these representations according to phonological rules (Wolf et al., 1998). In

light of the relationship between the ERP index of rapid auditory processing and subsequent nonword
 repetition observed by Fox et al. (2012), we hypothesised that the leftward lateralisation of rapid
 temporal processing (indexed by the Tb) at age 7 would be associated with subsequent phonemic
 decoding at age 9.

5 **2. Methods**

6 2.1. Participants

7 The current study examined the archival auditory ERP data of children reported in Fox et al. (2012) and Bishop et al. (2011). The children attended Project K.I.D.S., a 2-day research program aimed 8 at investigating the cognitive, social and emotional development of children. Children were initially 9 10 tested at age 7 years in July of 2007 or 2008, and were retested 2 years later in July of 2009 or 2010. Parents provided informed written consent for their children to take part in the study. Data were 11 12 excluded from individuals with a history of neurological disorders, and from whom reliable auditory evoked responses were not elicited by the single tone at sites of interest (Fox et al., 2010). The final 13 sample consisted of 50 children (26 boys, 24 girls; M = 7.50 years, SD = 0.30, range 7 years 0 months to 14 8 years 4 months; M = 9.47 years, SD = 0.30, 9 years 0 months to 10 years 4 months). 15

16 **2.2. Auditory stimuli**

The auditory stimuli were composed of standard 50 ms, 1000 Hz sinusoidal tones with 2 ms 17 ramped onset and offset. Sound intensity was calibrated using a 1-second continuous 1000 Hz sinusoidal 18 80 dB SPL tone measured by a Bruel and Kiaer sound level meter. There were six stimulus types: a 19 20 single tone stimulus, and five tone-pair stimuli. The tone-pairs were each composed of two tones that were separated by varying interstimulus intervals (ISIs; 25, 50, 100, 200, and 600 ms). Each trial was set 21 to 1500 ms in duration, and the stimulus onset times were randomly jittered between 0-200 ms from the 22 start of each trial (Woldorff, 1993). In addition, the 600 ms ISI tone-pairs were presented to determine 23 whether a reliable auditory ERP was elicited (Fox et al., 2010; Fox et al., 2012). The maturation of 24 auditory ERPs elicited by single tones has been reported previously by Bishop et al. (2011), and auditory 25 26 ERPs elicited by tone-pairs (Fz only) have been reported previously by Fox et al. (2012).

1 2.3. Measurement of phonological processing

The Sight Word Efficiency and Phonemic Decoding Efficiency subtests of the Test of Word Reading Efficiency (TOWRE) measure sight word reading fluency and phonological decoding (Torgeson et al., 1999). The Sight Word Efficiency subtest is composed of four columns of real words (104 words in total) and the Phonemic Decoding Efficiency subtest is composed of three columns of nonwords (63 nonwords in total). For each subtest the participant must read aloud as many items as they can in 45 seconds. For each subtest, the raw score is the number of items pronounced correctly in 45 seconds.

9 The TOWRE has high internal consistency between 0.86 and 0.98 (Torgeson et al., 1999) and high test-retest reliability between 0.82 and 0.97(Tanna, 2009). The Sight Word Efficiency and 10 Phonemic Decoding Efficiency subtests also have high inter-rater reliability (r > 0.99 and 0.98, 11 respectively; Marinus et al., 2013). The TOWRE has adequate construct validity, correlating highly with 12 other measures of reading ability such as the Woodcock Reading Mastery Tests-Revised (Sight Word 13 Efficiency r = 0.89 to 0.91; Phonemic Decoding Efficiency r = 0.89 to 0.91; Tanna, 2009). The 14 descriptive statistics for Sight Word Efficiency and Phonemic Decoding Efficiency scores are presented 15 in Table 1. 16

17 Table 1.

Descriptive Statistics of Raw Score Performance on the Sight Word Efficiency and Phonemic Decoding
Efficiency Subtests at Age 7 and Age 9.

	Subtest of	of the TOWRE
	Sight Word Efficiency	Phonemic Decoding Efficiency
	M(SD)	M(SD)
Age 7	53.86 (13.19)	25.62 (9.71)
Age 9	70.80 (6.82)	39.90 (8.43)

20 N = 50

In the present study, performance on the Sight Word Efficiency and Phonemic Decoding Efficiency subtests improved significantly from 7 to 9 years of age t(49) = 11.37, p < .001, d = 1.61, and

23 t(49) = 14.51, p <.001, d = 2.05, respectively.

1 **2.3. Procedure**

Participants were fitted with an EasyCap[™] at the beginning of each testing session. Auditory 2 stimuli were presented to participants binaurally via a set of Sennheiser HD 265 adjustable headphones 3 4 placed over the ears in a quiet room. A passive task was used to reduce the influence of attention to stimuli on ERP amplitudes (Lang et al., 1995; McArthur et al., 2003; Naatanen, 1995). Participants were 5 6 instructed to ignore the tones and were provided with reading materials (picture books with minimal text) and hand-held electronic games (audio switched off) to aid their distraction. If at any time the 7 8 participant's chosen activity was interfering with the EEG recording (e.g. excessive eye movements), they were instructed to change activities. Stimuli were presented binaurally to avoid asymmetric 9 10 activation of the left and right auditory cortices caused by monaural presentation (Mahajan and McArthur, 2013). Participants completed the TOWRE Sight Word Efficiency test first, followed by the 11 12 Phonemic Decoding Efficiency subtest as in the standardized administration instructions.

13 **2.4. EEG data acquisition**

Data were acquired using SCANTM 4. Electrophysiological activity was continuously recorded 14 via electrodes located at 33 scalp locations (Fp1, Fp2, F3, F4, F7, F8, Fz, FC1, FC2, FC5, FC6, FCz, 15 FT9, FT10, C3, C4, Cz, T7, T8, CP1, CP2, CP5, CP6, P3, P4, P7, P8, Pz, PO9, PO10, O1, O2, Iz). 16 17 Channel impedances were limited to below 10 k Ω prior to recording. The EEG was amplified using a NuAmps 40-channel amplifier, digitised at a sampling rate of 250 Hz, and filtered online using a 0.01-18 30 Hz band-pass filter. AFz was set as the ground and the electrode located at the right mastoid was set 19 as the reference. Data were processed offline using SCANTM 4. A common-averaged reference was 20 21 calculated offline, and data were re-referenced to the common-averaged reference. Vertical ocular artifacts were removed via a regression algorithm (Semlitsch et al., 1986) using the recordings from two 22 23 ocular leads placed 2 cm above and below the left eye. The EEG was digitally filtered offline using a 1-30 Hz zero phase-shift band-pass filter (12 dB roll-off) (Bishop et al., 2011). Epochs were segmented 24 25 from 100 ms pre-stimulus onset to 1000 ms post-stimulus onset. Averaged waveforms were baselinecorrected around the 100 ms pre-stimulus interval. Epochs that contained artifacts exceeding \pm 150 μ V 26 27 were rejected. The mean numbers of epochs included per participant after epoch rejection are included in Table 2. 28

1 Table 2.

			Stimulus	5		
-	Single	25 ms	50 ms	100 ms	200 ms	600 ms
Age 7	158.98	158.64	158.56	158.60	159.58	158.54
	(19.58)	(20.10)	(19.99)	(19.51)	(20.09)	(19.93)
Age 9	163.82	163.22	163.34	163.68	164.52	163.80
	(18.50)	(18.03)	(18.69)	(18.45)	(18.60)	(18.27)

2 Mean Number of Epochs Per Participant at Age 7 and Age 9 for the Single Tone and Tone-pairs.

N = 50

4 **2.6.** Correction for response overlap

As we were interested in the electrophysiological response to the second tone of each tone-pair, 5 6 we corrected for the overlap between the ERPs elicited by the first and second tone of each tone-pair stimulus. We subtracted individual-averaged single tone waveforms from each individual-averaged tone-7 8 pair waveform for each participant. The subtraction allowed us to isolate the response elicited by the 9 second tone of each tone-pair (Clunies-Ross et al., 2015; Fox et al., 2010; Sable et al., 2004). In order to 10 compare Ta and Tb responses across ISIs, the waveforms were then stimulus-locked such that the onset of the second tone was set to time zero, and were baseline-corrected using the 100 ms pre-stimulus 11 interval of the corrected waveform. The waveform corrected for response overlap shall be hereafter 12 referred to as the corrected waveform. 13

14 2.7. Topographic distribution of ERPs

The topographic distribution of the Ta and Tb of the single tone waveforms, and the corrected waveforms indicated that the Ta and Tb were largest at temporal (T7 and T8) sites. The Ta and Tb were, therefore, extracted at these sites. The grand-averaged waveforms synchronised to the onset of the first tone are presented in Figure. 1 and the grand-averaged corrected waveforms synchronised to the onset of the second tone are presented in Figure. 2. In the following sections, references to and discussions of data refer to the Ta and Tb elicited by the second tone of the tone-pairs.

21

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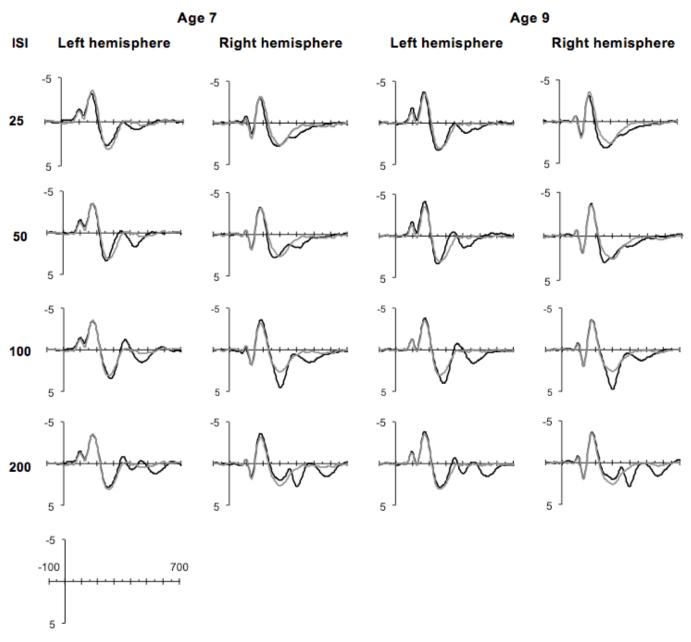


Figure 1. Grand-averaged ERP waveforms synchronised to the onset of tone 1 of tone-pairs with ISIs of
25, 50, 100 and 200 ms (black), with the single tone waveforms superimposed (grey). The amplitudes of
the waveforms recorded at T7 and T8, are presented in microvolts (μV) on the y-axis, and time is
presented in milliseconds (ms) on the x-axis.

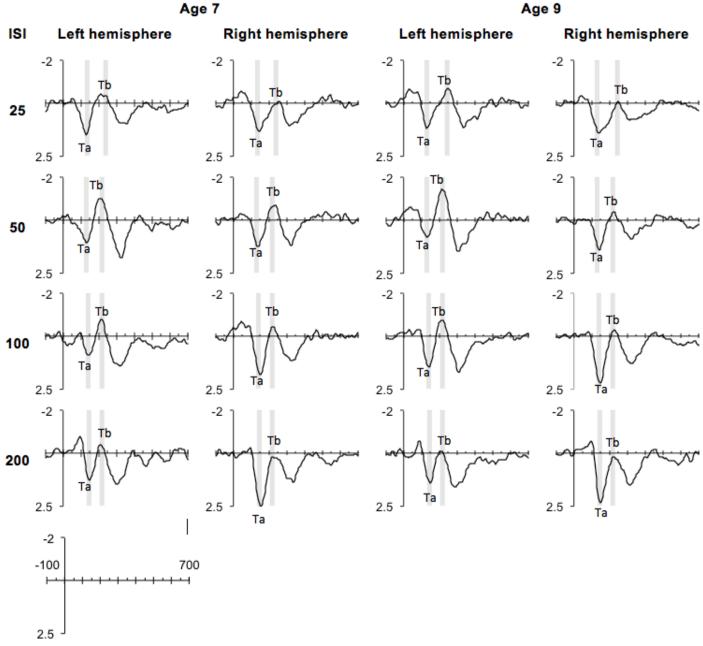


Figure 2. Grand-averaged ERP waveforms corrected for response overlap, and synchronised to the onset
of the second tone of tone-pairs. Waveforms were recorded at T7 (left hemisphere) and T8 (right
hemisphere), at age 7 (left) and 9 (right). The amplitudes of the waveforms are presented in microvolts
(µV) on the y-axis, and time is presented in milliseconds (ms) on the x-axis. Grey vertical bars illustrate
the latency intervals used to calculate the mean amplitude for Ta and Tb.

6 **2.8. Extraction of mean amplitudes**

7

Latency windows were established for each ISI at age 7 and 9 to take into account differences in

the latency of the relevant peaks. Peak latencies were identified from the grand-averaged waveforms at T7 and T8, and the mean amplitudes were calculated based on a 20 ms window, centred on the peak latency (Clunies-Ross et al., 2015; Hakvoort et al., 2014). In Figure 2, grey vertical bars illustrate the latency intervals over which the mean amplitudes were calculated. Mean amplitudes for the Tb were measured relative to the mean amplitude of the previous positivity (Ta).

6 2.9. Laterality index of rapid temporal processing

One of our primary objectives was to examine the relationship between the lateralisation of rapid 7 8 temporal processing and phonological awareness. To do so, we calculated a laterality index (LI) using 9 Tb responses to the second tone of the 50 ms ISI tone-pairs. The Tb response was selected for analysis 10 as it has been found to reflect asymmetries in temporal processing (Clunies-Ross et al., 2015). The LI was calculated as the difference between the Tb responses of the left and right hemisphere to 50 ms ISI 11 tone-pairs (LI = Left – Right). A negative LI indicated leftward lateralisation of the Tb response and a 12 positive LI indicated a rightward lateralisation of the Tb response. LIs were calculated for both ages. 13 (Age 7: M = -0.09, SD = 2.92, range = -7.94 to 7.46, Age 9: M = -0.57, SD = 2.62, range: -8.16 to 5.45). 14

15 **2.10. Data analysis**

All data were subject to preliminary screening measures prior to statistical analyses to ensure that 16 all the assumptions of ANOVA and regression were met. Data were winsorised to reduce the effect of 17 spurious outliers as outlined by Wilcox (2001). No more than four values were winsorised per variable. 18 Skew and kurtosis coefficients were used to assess the normality of the data. The skew and kurtosis 19 coefficients of all variables fell within the acceptable range (± 2 ; George and Mallery, 2010). 20 21 Multivariate outliers were screened by calculating Mahalanobis distance for each case, per analysis. No multivariate outliers were detected (p > .001). Two repeated-measures ANOVAs were conducted. Ta and 22 Tb mean amplitudes were subject to separate 2x2x4 repeated-measures ANOVAs, with age (7, 9) 23 hemisphere (left, right) and ISI (25 ms, 50 ms, 100 ms, 200 ms) treated as the within-subject variables. 24 We accounted for violations of the assumption of sphericity using the Greenhouse-Geisser correction. 25 Significance values based on the Greenhouse-Geisser correction are reported with the uncorrected 26 27 degrees of freedom. Regression analyses were conducted where the laterality indices (LI) (calculated for the Tb response to the 50 ms ISI tone-pair at age 7 and 9) were treated as the predictors and performance 28

1 on the Sight Word Efficiency and Phonemic Decoding Efficiency subtests measured at age 7 and 9 were

- 2 treated as dependent variables.
- 3 **3. Results**
- 4 Table 3.
- 5 Descriptive Statistics of the Mean Amplitudes (μV) for the Ta and Tb peaks at Age 7 and Age 9, for each
- 6 ISI and Hemisphere.

	LH	DU		
		RH	LH	RH
ISI	M (SD)	M (SD)	M (SD)	M(SD)
25 ms	1.30 (1.38)	1.22 (1.72)	1.12 (1.31)	1.30 (1.52)
50 ms	0.97 (1.61)	1.18 (1.41)	0.77 (1.51)	1.22 (1.32)
100 ms	0.85 (1.60)	1.75 (1.50)	1.40 (1.62)	2.13 (1.58)
200 ms	1.27 (1.84)	2.36 (1.41)	1.34 (1.62)	2.21 (1.63)
25 ms	-1.60 (2.01)	-1.25 (2.22)	-1.78 (1.75)	-1.38 (2.18)
50 ms	-1.90 (2.18)	-1.81 (1.99)	-2.15 (1.90)	-1.60 (1.79)
100 ms	-1.54 (2.27)	-2.16 (2.24)	-2.09 (1.96)	-2.40 (1.75)
200 ms	-1.65 (1.95)	-2.18 (2.02)	-1.35 (1.84)	-1.94 (1.88)
	25 ms 50 ms 100 ms 200 ms 25 ms 50 ms 100 ms	25 ms 1.30 (1.38) 50 ms 0.97 (1.61) 100 ms 0.85 (1.60) 200 ms 1.27 (1.84) 25 ms -1.60 (2.01) 50 ms -1.90 (2.18) 100 ms -1.54 (2.27)	25 ms 1.30 (1.38) 1.22 (1.72) 50 ms 0.97 (1.61) 1.18 (1.41) 100 ms 0.85 (1.60) 1.75 (1.50) 200 ms 1.27 (1.84) 2.36 (1.41) 25 ms -1.60 (2.01) -1.25 (2.22) 50 ms -1.90 (2.18) -1.81 (1.99) 100 ms -1.54 (2.27) -2.16 (2.24)	25 ms 1.30 (1.38) 1.22 (1.72) 1.12 (1.31) 50 ms 0.97 (1.61) 1.18 (1.41) 0.77 (1.51) 100 ms 0.85 (1.60) 1.75 (1.50) 1.40 (1.62) 200 ms 1.27 (1.84) 2.36 (1.41) 1.34 (1.62) 25 ms -1.60 (2.01) -1.25 (2.22) -1.78 (1.75) 50 ms -1.90 (2.18) -1.81 (1.99) -2.15 (1.90) 100 ms -1.54 (2.27) -2.16 (2.24) -2.09 (1.96)

7 Note. N = 50; LH = Left hemisphere (T7), RH = Right hemisphere (T8)

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15 **3.1.** Analysis of Variance of the Ta mean amplitudes

1 Table 4.

Variable	df	F	Е	р	n_p^2
age	1, 49	0.40	-	.532	.008
hemisphere	1, 49	13.31	-	.001	.214
ISI	3,147	9.93	.745	.001	.168
age x hemisphere	1, 49	0.01	-	.921	.000
age x ISI	3, 147	2.08	.846	.117	.041
hemisphere x ISI	3, 147	5.28	.689	.006	.097
age x hemisphere x ISI	3, 147	0.60	.904	.603	.012

2 Analysis of Variance of Ta Mean Amplitudes with Age, Hemisphere and ISI as Within-Subject Variables.

3 *Note.* N = 50

The interaction between hemisphere and ISI was broken down by conducting two repeatedmeasures ANOVAs (one for each hemisphere) with ISI as the within-subjects variable. The Ta mean amplitudes averaged across ages are presented in Figure 3. There was a significant main effect of ISI on Ta mean amplitudes measured over the right hemisphere such that Ta amplitudes increased with increasing ISI, illustrated in panel A of Figure 3. ($F(3, 147) = 16.03, p < .001, \varepsilon = .750, n_p^2 = .247$). Ta amplitudes measured over the left hemisphere did not vary significantly as a function of ISI (F(3, 147) = $1.54, p = .219, \varepsilon = .674, n_p^2 = .030$).

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16 **3.2** Analysis of Variance of the Tb mean amplitudes

1 Table 5.

Variable	df	F	Е	р	n_p^2
age	1, 49	0.26	-	.612	.005
hemisphere	1, 49	0.17	-	.682	.003
ISI	3, 147	2.99	.785	.046	.057
age x hemisphere	1, 49	.478	-	.493	.010
age x ISI	3, 147	1.40	.836	.251	.028
hemisphere x ISI	3, 147	3.76	.810	.019	.071
age x hemisphere x ISI	3, 147	.260	.871	.828	.005

2 Analysis of Variance of Tb Mean Amplitudes with Age, Hemisphere and ISI as Within-Subject Variables.

3 Note. N = 50

The interaction between hemisphere and ISI was broken down by conducting two repeated-measures ANOVAs (one for each hemisphere), with ISI as the within-subjects variable. The mean Tb responses averaged across ages are presented in Figure 3. Tb responses measured over the left hemisphere were enhanced to 50 ms ISI tone-pairs (quadratic trend, F(1, 49) = 4.06, p < .05, $n_p^2 = .077$). Tb responses measured over the right hemisphere were enhanced to 100 and 200 ms ISI tone-pairs (linear trend, F(1, 49) = 9.48, p < .01, $n_p^2 = .162$).

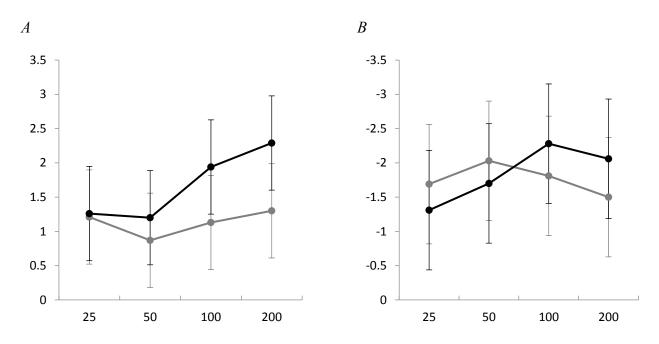


Figure 3. Ta (panel A) and Tb (panel B) mean amplitudes collapsed across time-points, measured over
the left (grey) and right hemispheres (black) are plotted for each ISI. Amplitudes are displayed on the yaxis and are measured in microvolts (µV). The error bars reflect 95% confidence intervals for the
interaction between hemisphere and ISI, for the respective component.

3.3. Lateralisation of rapid temporal processing and performance on the Sight Word Efficiency
and Phonemic Decoding Efficiency subtests at age 9.

- 7 *Table 6.*
- 8 Predictors of Sight Word Efficiency and Phonemic Decoding Efficiency at Age 9

Outcome	Predictors	R^2	В	SE B	β	t	р
Sight Word Efficiency	LI 50 ms ISI - 7	.007	- 0.20	0.34	009	- 0.60	.550
Sight Word Efficiency	LI 50 ms ISI - 9	.008	0.23	0.38	0.09	0.624	.536
Phonomia Docading	LI 50 ms ISI - 7	.114	- 0.98	0.39	-0.34	-2.49	.016
Phonemic Decoding	LI 50 ms ISI - 9	.002	0.16	0.47	0.05	0.34	.738

9 Note. N = 50

10 The LI measured at age 7 was a significant predictor of performance on the Phonemic Decoding 11 Efficiency subtest of the TOWRE at age 9, such that the greater the lateralisation of the Tb at age 7, the 12 better they performed on the Phonemic Decoding Efficiency subtest 2 years later. The LI at age 9 was not predictive of performance on the Phonemic Decoding Efficiency at age 9, nor were the LIs at age 7
and 9 predictive of performance on the Sight Word Efficiency subtest at age 9.

3 4. Discussion

4 The AST hypothesis states that acoustic information is processed hierarchically within the left and right auditory areas of the brain, and this has been well supported by research on adult samples. 5 6 Current findings support the theory that neuronal ensembles in the primary auditory areas are tuned to rapid temporal modulations 25-50 ms (20-40 Hz). Neuronal ensembles in the left and right secondary 7 8 auditory areas are differentially tuned to rapid (25-50 ms = 20-40 Hz), and slow (200-250 ms = 4-5 Hz) 9 modulations, respectively. Although the AST proposes that hemispheric asymmetries are intrinsic and 10 likely to emerge prior to adulthood, investigations in children have been sparse and inconsistent. It is still unclear when these functional asymmetries appear to develop and behave in an adult-like way 11 (Telkemeyer et al., 2009). Therefore, we sought to characterise hemispheric asymmetries in rapid and 12 slow temporal processing in children at age 7 and 2 years later at age 9. Our results show that 13 hemispheric asymmetries in children at 7 - 9 years resemble that seen in young adults, suggesting that 14 hemispheric specialisation for fast and slow modulations is present at this age. We also provide evidence 15 for the relationship with hemispheric specialisation of rapid auditory processing and subsequent 16 phonemic decoding ability. 17

18 4.1. Hemispheric asymmetries in Ta response

We observed hemispheric asymmetries in patterns of Ta responses to rapid and slow tone-pairs. 19 There was no significant difference between Ta responses across all ISIs over the left hemisphere, 20 suggesting that the associated auditory areas in the left hemisphere may function according to a short 21 temporal integration window, and that the generator of the Ta in the left hemisphere may be mature at 22 age 7. Over the right hemisphere, Ta responses to the 25 and 50 ms ISI tone-pairs were attenuated 23 relative to Ta responses to the 100 and 200 ms ISI tone-pairs, suggesting that the generators of the Ta in 24 the right hemisphere are functioning according to a longer integration window of approximately 100 ms. 25 The longer integration window could reflect the later development of the Ta generators in the right 26 27 hemisphere, which is consistent with previous reports by Mahajan and McArthur (2013) who found that the Ta peak over the right hemisphere continued to develop throughout adolescence, suggesting that the 28 29 functional development of the left and right hemispheres differs. As the reported neural generators of the Ta are inconsistent, the functional implications of hemispheric asymmetries in the development of the
 Ta require further investigation.

3 4.2. Hemispheric asymmetries in the Tb response

4 Previous findings in adults support a left hemisphere specialisation for rapid temporal modulations and a right hemispheric specialisation for slow temporal modulations (Boemio et al., 2005; 5 6 Clunies-Ross et al., 2015; Jamison et al., 2006; Luo, and Poeppel, 2007; 2012). At present, our understanding of when this develops during childhood is not clear (Vanvooren et al., 2014). By 7 8 examining the Tb responses to auditory stimuli presented with varying ISIs, we investigated whether the 9 left and right secondary auditory areas exhibit preferential processing of rapid and slow temporal 10 modulations. Based on the AST, we predicted that the left hemisphere would preferentially respond to rapidly presented tones with ISIs of ~ 50 ms, whereas the right hemisphere would preferentially respond 11 to slower temporal modulations ~ 200 ms (Poeppel, 2003). Consistent with the AST, we observed the 12 preferential processing of both rapid and slow auditory stimuli over the left and right hemispheres, 13 respectively. 14

As can be seen in panel B of Figure. 3, Tb responses were largest over the left hemisphere when 15 tones were separated by 50 ms, suggesting a left hemisphere preference for rapidly presented stimuli. 16 17 This is consistent with the conjecture that a large proportion of neuronal populations in the left secondary auditory areas are tuned to rapid temporal rates and, therefore, preferentially respond to 18 19 rapidly presented stimuli (Poeppel, 2003). The presence of a distinct Tb response to the 25 ms ISI tonepairs, in particular, suggests that there are neuronal ensembles in the left hemisphere capable of 20 21 responding to stimuli presented as quickly as 25 ms. These results provide evidence of left hemisphere specialisation for rapid temporal processing in children aged 7 and 9 years, and are consistent with 22 23 previous findings of Thompson et al. (2016) who observed leftward lateralisation of high-frequency (20-50Hz) endogenous cortical oscillations at the younger ages of 3-5 years. 24

Over the right hemisphere, Tb responses were largest for the 100 and 200 ms ISI tone-pairs, indicating a preference for slower presentation rates. In Figure 1. it can be seen that over the right hemisphere, at both ages 7 and 9, the Tb response to the second tone of tone pairs is not present at ISIs of 25 and 50 ms, but emerges at the longer ISIs of 100 and 200 ms. The preferential processing of the 100 and 200 ms ISI tone-pairs in the right hemisphere is consistent with previous findings of right hemisphere preference for the processing of slowly unfolding auditory stimuli (Abrams et al., 2008;
Clunies-Ross et al., 2015; Luo and Poeppel, 2007; 2012). Interestingly, the Tb response to the 100 ms
ISI tone-pairs over the right hemisphere was as large as that of the 200 ms ISI tone-pairs, despite
representing a much faster modulation rate than the frequently discussed 200-250 ms. This finding
suggests that finer tuning of neuronal ensembles in the right secondary auditory areas may occur beyond
the age of 9.

7 The same pattern of hemispheric asymmetries was observed at age 7 as at age 9, suggesting that 8 neuronal tuning to specific modulations did not change significantly over this time. This was particularly unexpected given that studies have demonstrated marked development in the Ta and Tb over this 9 10 developmental period (Bishop et al., 2011; Tonnquist-Uhlen et al., 2003). However, this may suggest that there are differences between the maturation rates of Ta and Tb neural generators, and the 11 12 maturation of their functional properties. Nevertheless, our results clearly demonstrate that hemispheric preferences for fast and slow modulations are present in children at age 7 and 9. In the context of 13 previous findings by Thompson et al (2016) and Vanvooren et al (2014), our results suggest that 14 temporal processing asymmetries may become more consistent from at least 7 years. Earlier 15 16 inconsistencies across studies of younger children may reflect reduced prominence of functional 17 asymmetries, and therefore, difficulty identifying such asymmetries consistently.

Similar to the current study, Clunies-Ross et al. (2015) conducted an experiment with young 18 adults, which examined Tb responses to tone-pairs separated by ISIs of 50 and 200 ms. They found that 19 Tb responses to the second tone of the 50 ms ISI tone-pairs were enhanced over the left hemisphere 20 relative to the right hemisphere (d = 0.45), providing evidence for a left hemisphere advantage for 21 rapidly presented tones. In the present study, the left hemisphere advantage for rapidly presented tones 22 23 was not found to be as prominent in children (d = 0.16) as was found in young adults, suggesting that 24 although the hemispheric asymmetries are present at age 7 and remain stable until age 9, further tuning 25 of the neuronal populations in the right hemisphere may occur between childhood and young adulthood.

26 4.3 Rapid temporal processing: left-hemisphere vs. bilateral

Together, functional asymmetries in the processing of tone-pairs with short and long ISIs provide evidence for a left hemisphere preference for the processing of rapidly presented stimuli and a right hemisphere preference for slowly presented stimuli. Previous research investigating asymmetries in

temporal processing have drawn inconsistent conclusions as to whether neuronal ensembles functioning 1 according to a short temporal integration window are distributed bilaterally or primarily in the left 2 hemisphere. Some researchers have observed bilateral rapid temporal processing (Boemio et al., 2005; 3 Luo and Poeppel, 2012), whilst others have demonstrated a left hemisphere advantage (Okamoto et al., 4 2009; Zaehle et al., 2004). Vanvooren et al. (2014) proposed that the inconsistency in reports of 5 asymmetries in rapid temporal processing might be due to the differences in methodology and the type 6 of neuroimaging techniques used. Our current findings and the findings of previous research (Clunies-7 Ross et al., 2015) demonstrate how the Ta and Tb can be used to differentiate between auditory areas in 8 9 which rapid temporal processing occurs bilaterally and those in which it occurs primarily in the lefthemisphere. The present data do not provide evidence for bilateral rapid auditory processing in primary 10 11 auditory areas as proposed by Poeppel (2003) in the AST, potentially due to the slower development of 12 right hemisphere neural generators (Mahajan and McArthur, 2013). However, our results support a left hemisphere preference for the processing of rapidly presented stimuli, and, consistent with the AST, the 13 observed asymmetry was reflected by the Tb of the T-complex, which is proposed to originate from the 14 secondary auditory areas (Tonnquist-Uhlen et al., 2003). 15

4.4. Hemispheric asymmetries in rapid temporal processing at age 7 predict phonemic decoding at age 9.

Our results suggest that children who showed greater leftward lateralisation of rapid temporal 18 processing at age 7 performed better on the Phonemic Decoding Efficiency subtest 2 years later. The LI 19 at age 7 accounted for 11.4 % of variance in Phonemic Decoding Efficiency performance at age 9, 20 demonstrating that greater leftward hemispheric specialisation for rapid temporal processing may 21 contribute to subsequent phonemic decoding ability (Fox et al., 2012; Tallal, 2004; Tallal et al., 1993; 22 23 Tallal and Gaab, 2006). This suggests that perhaps one must be able to differentiate phonological sounds before being able to form mental representations of the sounds (Tallal, 1980; Tallal et al., 1993), map 24 25 them onto letters, and be able to use their knowledge of grapheme to phoneme associations to decode and accurately read aloud written words. Further evidence in support of this idea comes from the lack of 26 27 association between the LI at age 9 and Phonemic Decoding Efficiency at age 9. In sum, lateralisation of rapid temporal processing at age 7, as indexed by the Tb, appears to be a moderate predictor of future 28 29 phonemic decoding ability, rather than current phonemic decoding ability. As expected, LIs measured at age 7 and 9 did not predict sight word reading ability at age 9. Our findings are consistent with the 30

notion that sight word reading ability is more dependent on familiarity with real words, than
 phonological ability (Espy et al., 2004). This adds further support for the contribution of rapid temporal
 processing to performance on tasks that accessing phonological representations.

4 One of the key ideas in the literature pertaining to hemispheric specialisation is that greater 5 lateralisation or specialisation of a particular function or process allows for better efficiency, and in turn, 6 better performance. Our findings suggest that left hemisphere specialisation of rapid temporal processing 7 is associated with better outcomes on tests of phonemic decoding ability, and further suggest that this 8 lateralisation may be a precursor for the future development of more complex linguistic skills. It builds on previous research by Fox et al. (2012), by demonstrating the relationship between the leftward 9 10 lateralisation of rapid temporal processing and subsequent phonemic decoding of written language, in addition to repeating nonwords. 11

12 **4.5.** Conclusion

In the present study, we provide evidence of functional asymmetries in temporal processing in 13 children at age 7 and 9. Tb responses to the second tone of a tone-pair stimulus were largest when 14 separated by 50 ms in the left hemisphere, and 100-200 ms in the right hemisphere. Our findings suggest 15 that neuronal populations in the left secondary auditory cortex preferentially respond to rapidly 16 17 presented stimuli and neuronal populations in the right secondary auditory cortex preferentially respond to slowly presented stimuli, consistent with the predictions of the AST hypothesis (Poeppel, 2003). 18 19 Although the pattern of asymmetry did not change over the 2 year period investigated in the present study, we suggest that asymmetries may further mature after the age of 9, as left-hemisphere advantage 20 21 for rapid temporal processing was not as prominent as has been seen in adults (Clunies-Ross et al., 2015) and right hemisphere advantage did not appear as finely tuned to ~200 ms stimuli as observed in adults. 22

Our results demonstrate auditory stimuli presented as quickly as 25 ms are discriminable in the auditory ERP of children as young as 7. The lateralisation of an individual's Tb response to the 50 ms ISI tone-pair at age 7 was a significant predictor of phonemic decoding ability two years later, suggesting that hemispheric specialisation of rapid temporal processing may be a precursor to subsequent phonemic decoding ability. Finally, our findings provide support for previous suggestions that the Tb may be an important ERP for the investigation of the relationship between auditory processing and complex language abilities.

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