




## Children with amblyaudia show less flexibility in auditory cortical entrainment to periodic non-speech sounds

Sara Momtaz, Deborah Moncrieff, Meredith A. Ray & Gavin M. Bidelman


**To cite this article:** Sara Momtaz, Deborah Moncrieff, Meredith A. Ray & Gavin M. Bidelman (2023) Children with amblyaudia show less flexibility in auditory cortical entrainment to periodic non-speech sounds, *International Journal of Audiology*, 62:10, 920-926, DOI: [10.1080/14992027.2022.2094289](https://doi.org/10.1080/14992027.2022.2094289)

**To link to this article:** <https://doi.org/10.1080/14992027.2022.2094289>

 [View supplementary material](#) 

 [Published online: 13 Jul 2022.](#)

 [Submit your article to this journal](#) 

 [Article views: 136](#)

 [View related articles](#) 

 [View Crossmark data](#) 

# Children with amblyaudia show less flexibility in auditory cortical entrainment to periodic non-speech sounds

Sara Momtaz<sup>a</sup> , Deborah Moncrieff<sup>a</sup>, Meredith A. Ray<sup>b</sup>  and Gavin M. Bidelman<sup>a,c,d</sup> 

<sup>a</sup>School of Communication Sciences and Disorders, University of Memphis, Memphis, TN, USA; <sup>b</sup>Division of Epidemiology, Biostatistics, and Environmental Health, School of Public Health, University of Memphis, Memphis, TN, USA; <sup>c</sup>Institute for Intelligent Systems, University of Memphis, Memphis, TN, USA; <sup>d</sup>Department of Speech, Language and Hearing Sciences, Indiana University, Bloomington, IN, USA

## ABSTRACT

**Objective:** We investigated auditory temporal processing in children with amblyaudia (AMB), a subtype of auditory processing disorder (APD), *via* cortical neural entrainment.

**Design and study samples:** Evoked responses were recorded to click-trains at slow vs. fast (8.5 vs. 14.9/s) rates in  $n = 14$  children with AMB and  $n = 11$  age-matched controls. Source and time–frequency analyses (TFA) decomposed EEGs into oscillations (reflecting neural entrainment) stemming from bilateral auditory cortex.

**Results:** Phase-locking strength in AMB depended critically on the speed of auditory stimuli. In contrast to age-matched peers, AMB responses were largely insensitive to rate manipulations. This rate resistance occurred regardless of the ear of presentation and in both cortical hemispheres.

**Conclusions:** Children with AMB show less rate-related changes in auditory cortical entrainment. In addition to reduced capacity to integrate information between the ears, we identify more rigid tagging of external auditory stimuli. Our neurophysiological findings may account for domain-general temporal processing deficits commonly observed in AMB and related APDs behaviourally. More broadly, our findings may inform communication strategies and future rehabilitation programmes; increasing the rate of stimuli above a normal (slow) speech rate is likely to make stimulus processing more challenging for individuals with AMB/APD.

## ARTICLE HISTORY

Received 19 August 2021

Revised 16 June 2022

Accepted 21 June 2022

## KEYWORDS

Auditory processing disorders (APD); event-related brain potentials (ERPs); gamma/beta band response; hemispheric asymmetries; phase-locking; time–frequency analysis

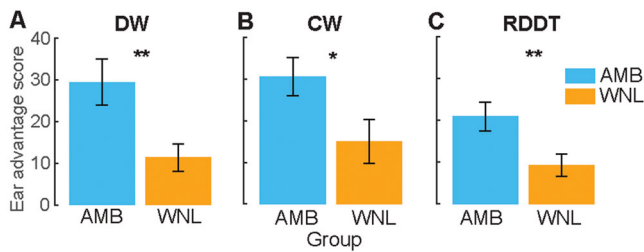
## Introduction

Auditory temporal processing refers to the detection, identification, integration, and segregation of sound events over time (Picton 2013). Temporal processing impairments are observed in a variety of patient populations, such as schizophrenia (Luthra 2021), Parkinson’s disease (Grondin 2010), attention-deficit/hyperactivity disorder (ADHD) (Toplak, Dockstader, and Tannock 2006), and dyslexia (Tallal 1980). Some have suggested that difficulties “hearing in time” might present in individuals with auditory processing disorder (APD), where temporal processing deficits could manifest as poorer auditory perceptual abilities (Tallal 1980; Picton 2013; Kopp-Scheinflug and Tempel 2015). However, while there is growing evidence (Chowsilpa, Bamiou, and Koochi 2021), temporal processing is an often suggested but still unproven hypothesis of APDs and remains controversial (Merzenich et al. 1996; Zhang and Tomblin 1998; Dawes et al. 2009; Billiet and Bellis 2011).

APD itself is characterized by symptoms of hearing difficulty without deficits in pure tone peripheral sensitivity, *per se*. It likely comprises at least 5% of clinical hearing referrals (Moore 2006). While not observed in all cases nor a sole deficit (Dawes et al. 2009), several reports have documented temporal processing issues in APD populations (Tallal, Sainburg, and Jernigan 1991; Kopp-Scheinflug and Tempel 2015). Indeed, most clinical APD batteries explicitly test a broad spectrum of temporal

processing skills suggesting these faculties might be important in describing at least some forms of APDs. Presumably, temporal processing deficits during childhood could negatively affect speech-language acquisition, which relies heavily on the accurate encoding of fine timing information in sound (Picton 2013). This has led to the use of rhythm and time synchronization paradigms in rehabilitative and therapeutic approaches (Grondin 2010) to improve both basic auditory and more general cognitive abilities such as attention and memory (Tallal 1980; Picton 2013). Nevertheless, due to the heterogeneity of APD, there might be a range of different temporal difficulties which span both speech and non-speech domains and might manifest differently for more/less challenging stimuli (slow vs. faster rate sounds).

AMB is identified by abnormally asymmetric results from dichotic listening (DL) tests that may stem from genetic factors (Morell et al. 2007) or from periods of auditory deprivation during early critical periods of brain development (Whitton and Polley 2011). Asymmetric DL has been attributed to poor inter-hemispheric connectivity (Musiek and Weising 2011; Momtaz, Moncrieff, and Bidelman 2021) or to weaknesses in directing attention to complex auditory stimuli (Tallus et al. 2015). While there is an undisputed role of attention in DL results (Hiscock, Inch, and Kinsbourne 1999; Alho et al. 2012), an abnormal asymmetry may also reflect an excitatory–inhibitory imbalance within early-stage sensory filters as proposed by Broadbent



**Figure 1.** Group comparison of behavioral ear advantage scores in dichotic listening tests. (A) Dichotic words (DW) test. (B) Competing words (CW) test. (C) Random Dichotic Digits Test (RDDT). AMBs show stronger ear advantage scores (i.e. larger asymmetry) for all three tasks. Solid lines denote normal curve fits. AMB: amblyaudia; WNL: within normal limit. Error bars =  $\pm 1$  s.e.m. \* $p < 0.05$ , \*\* $p < 0.01$ .

(1958). An imbalance in brainstem neural processes may also generate hypoactivity of the non-dominant ear and/or hyperactivity of the dominant ear. Regardless of underlying mechanism (e.g. imbalance of ear-specific inputs, attentional allocation, etc.), asymmetric patterns in DL can be identified in nearly 50% of children suspected of APD (Moncrieff et al. 2016). While more global issues in cognition, language, and attention might also impact APDs (McFarland and Cacace 2009; Moore et al. 2010), another possible factor of perceptual deficits in AMB children might involve aberrant auditory temporal processing.

In previous work, we explored this possibility by comparing children with/without AMB by evaluating time–frequency responses (i.e. neural oscillations) from multichannel EEG (Momtaz, Moncrieff, and Bidelman 2021). We showed that children with AMB had unusually large  $\beta/\gamma$  brain rhythms in response to relatively slow, click-train stimuli, suggesting a hyper-synchronization in their “neural entrainment” to complex, non-speech sounds. Entrainment is defined as the brain’s inherent ability to temporally synchronize its activity with exogenous rhythmic stimuli (Obleser and Kayser 2019). AMB’s larger responses were accompanied by an imbalance in functional connectivity between hemispheres characterized by poor neural transmission from right to left hemisphere despite this group’s abnormally large right ear advantage (REA) behaviourally. Our previous findings led us to infer that behavioral asymmetries in children with AMB might be due to a lack of appropriate sensory processing *via* reduced inhibition, poorer cross-talk between auditory cortices and especially poorer neural entrainment during even passive listening (Momtaz, Moncrieff, and Bidelman 2021). We further speculated that the inability of AMB listeners to properly entrain might result in less flexibility in how the brain adapts to changes in the sound environment, thereby rendering difficulties in extracting (or suppressing) important acoustic features needed for perception. Still, our stimulus design was limited to only a single, relatively slow click-train stimulus. Here, by explicitly manipulating the rate of stimulus presentation, we formally test our previously asserted hypothesis that AMB is associated with less flexible neural entrainment to rapid auditory stimuli, analogous to deficient pace-maker.

To this end, we recorded multichannel EEGs in children diagnosed with AMB and their age-matched peers in response to rapid non-speech stimuli. We measured neural oscillatory activity extracted from the left and right auditory cortex to assess auditory entrainment and spectrotemporal details of the EEG. Varying the rate of stimulus presentation (slow vs. fast) allowed us to directly compare the flexibility in temporal processing (i.e. adaptability to fast vs. slow stimulus rates) in AMB vs. within normal limit (WNL) children. One rate was comparable to that

found in normal speech [i.e. published data from Momtaz, Moncrieff, and Bidelman (2021)], while the other exceeded what might be expected of typical production (Assaneo and Poeppel 2018). However, our use of non-speech stimuli allowed us to characterize whether AMBs showed differences in domain-general auditory temporal processing devoid of lexical-semantic confounds carried in the speech stimuli used in most DL tasks (Alho et al. 2012; Moore et al. 2020). Our findings show that while WNL children easily entrain to rapid auditory stimuli, children with AMB are largely insensitive to changes in rate. Our data reveal a new AMB deficit in general auditory-sensory processing (i.e. neural tagging of sounds) independent of attention and linguistic processing.

## Materials and methods

### Participants

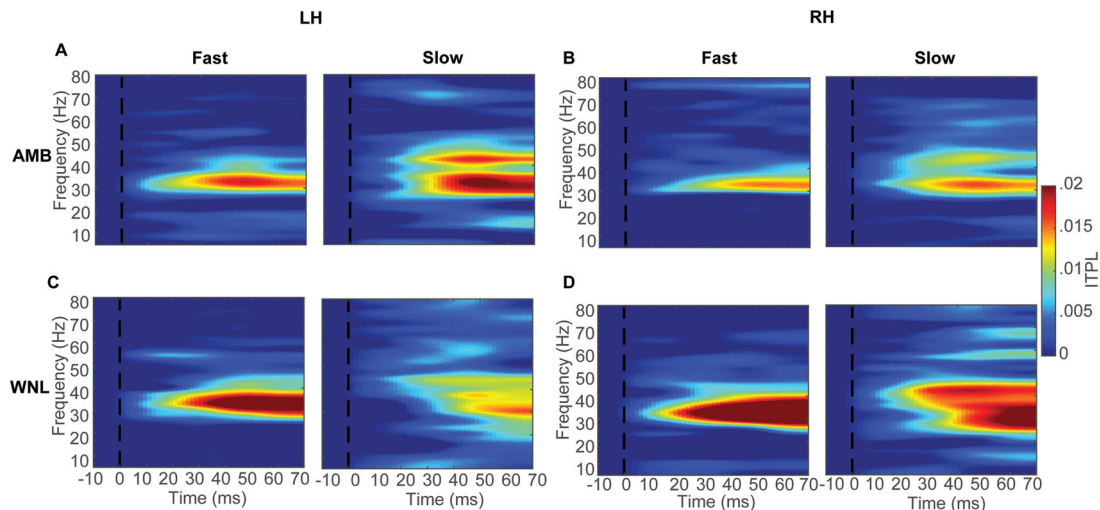
The sample included  $n = 25$  native English-speaking children (9–12 years) who were classified into two groups (WNL;  $n = 11$ , amblyaudia [AMB;  $n = 14$ ]) based on their behavioral scores on DL tests. Groups were similar in age (AMB:  $10.1 \pm 1.7$  years, WNL:  $10.8 \pm 1.1$  years,  $t_{23} = -1.48$ ,  $p = 0.15$ ) and gender (AMB: 10/4 male/female; WNL 7/4 male/female; Fisher exact test,  $p = 1$ ). None had a history of neurological impairment, head injury, chronic disease, or hearing loss ( $\leq 25$  dB HL screened from 500 to 4000 Hz; octave frequencies). They were recruited from APD evaluation clinic referrals and flyers distributed throughout the community. Participants’ parents gave written informed consent in compliance with a protocol approved by the Institutional Review Board at the University of Pittsburgh.

### Behavioural evaluation

Children who produced abnormal scores ( $< 10$ th percentile from normative data) consistent with AMB (low non-dominant ear and large asymmetry) on at least two of three dichotic tests (Randomised Dichotic Digits Test [RDDT]; Strouse and Wilson 1999; Moncrieff and Wilson 2009; Dichotic Words Test; Moncrieff 2015; competing words subtest from the SCAN-C; Keith 1986; presented through earphones at 50 dB HL in a sound-treated room) were placed into the AMB group. Details of the behavioral evaluation are reported in Momtaz, Moncrieff, and Bidelman (2021) and supplemental. Children with normal scores on at least two of the dichotic tests were placed into the WNL group. Scores from a parent checklist of listening difficulties were significantly poorer among the AMB children for listening related to integration [ $F_{(1,26)} = 5.09$ ,  $p = 0.033$ ] and prosody [ $F_{(1,26)} = 13.74$ ,  $p < 0.001$ ]. One child in the AMB group had a diagnosis of mixed language disorder and second demonstrated reading difficulties but had not been diagnosed with a reading disorder. None in the WNL group had been diagnosed with any disorder.

For each test, right and left ear scores were converted to dominant and non-dominant so that the difference in performance between ears (reflecting interaural asymmetry) remained positive. AMB is distinguished by an abnormally large interaural asymmetry and is diagnosed when at least two DL tests indicate greater than average interaural asymmetry.

Groups well separated in terms of their DL performance (Figure 1). Most listeners showed a REA as measured by their ear advantage scores (i.e. difference in behavioral performance between non-dominant and dominant ears). However, children



**Figure 2.** ITPL spectrograms for (A, C) left hemisphere and (B, D) right hemisphere per group and stimulus rate. Strong neural synchrony of ITPL maps is demonstrated between 30 and 40 Hz. AMB: amblyaudia; WNL: within normal limits; LH/RH: left/right hemisphere; ITPL: inter-trial phase-locking.

with AMB showed larger ear advantages compared to WNL listeners in all three dichotic tests including DW [ $t_{24} = 2.67$ ,  $p = 0.013$ ], CW [ $t_{22} = 2.14$ ,  $p = 0.044$ ], and RDDT [ $t_{24} = 2.55$ ,  $p = 0.017$ ]. These findings confirm a large interaural asymmetry in AMB compared to the WNL group (Moncrieff et al. 2016).

### EEG recording procedure

#### Stimuli

Neural responses were elicited by click trains presented at two different rates. Individual clicks were 385  $\mu$ s biphasic pulses. Stimuli were presented monaurally (passive listening) at 70 dB nHL via ER-3A insert earphones. Two different presentation rates (i.e. interstimulus intervals) were used: slow (8.5/s) and fast (14.9/s). A total of 1000 sweeps were collected per condition.

#### EEG recording

Data recording and analysis were identical to our previous study on AMB and neural oscillations (Momtaz, Moncrieff, and Bidelman 2021). Briefly, EEGs were recorded from 64 electrodes at 10–20 scalp locations (Oostenveld and Praamstra 2001). Electrode impedances were  $<5$  k $\Omega$ . EEGs were digitized using Neuroscan Synamp<sup>2</sup> amplifiers at 10 Hz. Data were re-referenced to the common average offline for analysis. Continuous EEGs were processed in BESA Research 7.0 (BESA, GmbH, Gräfelting, Germany). Recordings were epoched [−10–56 ms] into single trials, bandpass filtered (10–2000 Hz), and baseline corrected to the pre-stimulus interval per trial. Prior to TFA, we rejected artifactual trials exceeding  $\pm 500$   $\mu$ V and those with a  $>75$   $\mu$ V amplitude gradient between consecutive samples. This resulted in 877–1000 artifact-free trials. Critically, trial counts did not differ between groups for either left ( $t_{48} = -0.32$ ,  $p = 0.74$ ) or right ( $t_{34} = 0.74$ ,  $p = 0.46$ ) ear recordings, nor for fast ( $t_{47} = 1.11$ ,  $p = 0.26$ ) vs. slow ( $t_{47} = -0.83$ ,  $p = 0.40$ ) stimulus rates indicating similar overall signal-to-noise ratio.

#### EEG source and time–frequency analysis

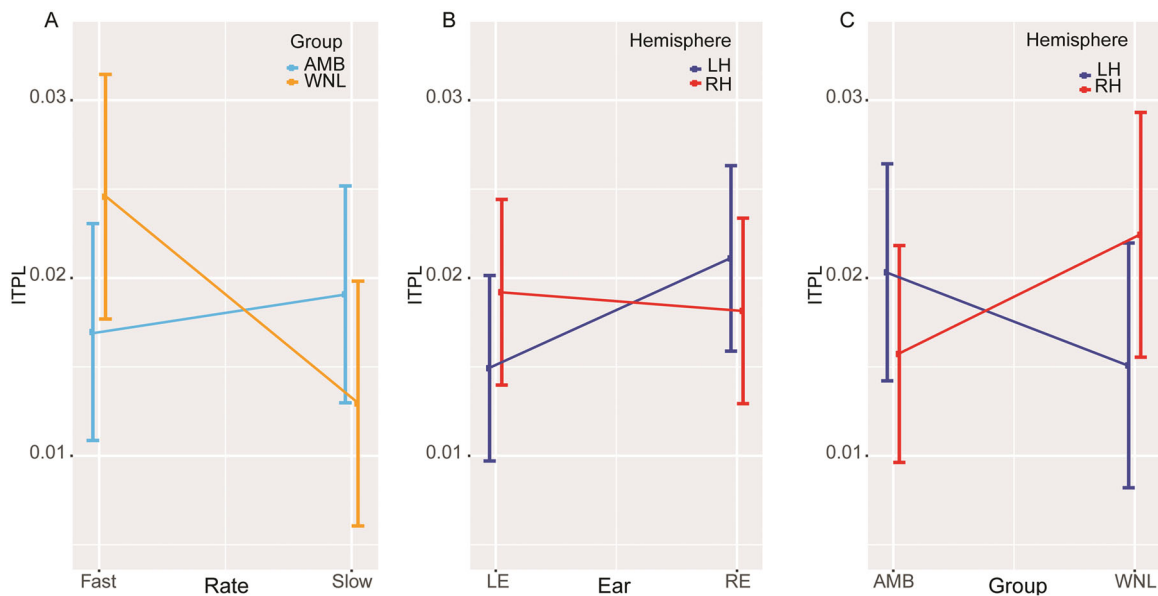
Single-trial scalp potentials were transformed into source space using BESA's Auditory Evoked Potential (AEP) source montage (Bidelman and Momtaz 2021). This dipole model contains regional sources in bilateral AC [Talairach coordinates ( $x, y, z$ ; in

mm): *left* = (−37, −18, 17) and *right* = (37, −18, 17)]. We extracted and averaged the time courses from the radial and tangential dipoles as these orientations capture the majority of variance describing the auditory cortical ERPs (Picton et al. 1999). This approach reduced the 64-channel data to two source dipole channels localizing current activity in left and right AC (Momtaz, Moncrieff, and Bidelman 2021). Single-trial source activity was then submitted to TFA.

The TFA transformation was computed using a sliding window analysis on each epoch (complex demodulation; Papp and Ktonas 1977) in 20 ms/2.5 Hz resolution step sizes (10–80 Hz bandwidth). We then computed inter-trial phase-locking (ITPL) (Lachaux et al. 1999) at each time–frequency point across single trials (Momtaz, Moncrieff, and Bidelman 2021). ITPL maps reflect the change in neural synchronization (0 = random noise; 1 = perfect phase-locking) relative to baseline (−10 to 0 ms) (Bidelman 2015). Note that ITPL is invariant to amplitude (it depends only on trial phase consistency) rendering it impervious to amplitude scaling inaccuracies that might emerge from our use of adult head templates for source analysis (Momtaz, Moncrieff, and Bidelman 2021). Oscillation responses are most prominent to click train stimuli near the  $\sim 33$  Hz band of the EEG (Momtaz, Moncrieff, and Bidelman 2021). Hence, we extracted the time course of the high- $\beta$ /low- $\gamma$  frequency band (33 Hz) from each ITPL spectrogram (Supplemental Figure S1). We then measured the peak ITPL strength and latency from each band time course to quantify group effects per hemispheric source, ear, and rate of presentation.

#### Statistical analysis

We used  $2 \times 2 \times 2 \times 2$  random effects rank-based (robust) ANOVAs (R<sup>®</sup> version 4.0.3; R Foundation for Statistical Computing; Vienna, Austria) and the *lme4* (Bates et al. 2015) and *robustlmm* (Koller 2016) R packages (R Core Team 2020) to assess latency and ITPL strength differences in  $\beta$ -band responses. Note this package reports omnibus ANOVA results as *t*- (rather than *F*-) values. Fixed factors included group (2 levels: WNL, AMB ear (2 levels: LE and RE), hemispheres (2 levels: LH and RH), and rate of presentation (2 levels: fast and slow); subjects served as a random effect. The dependent variables were minimally truncated and skewed so we elected to use a robust approach to account for the distribution of these variables. However, we



**Figure 3.** Neural oscillation strength differentially varies between groups according to stimulus rate, hemisphere, and ear. (A) rate\*group interaction. WNLs showed decreased ITPL strength at a slow vs. fast rate. In stark contrast, no rate effects were observed in AMBs. (B) ear\*hemisphere interaction. LH ITPL was stronger for RE vs. LE presentation for both groups. No ear differences were observed for RH responses. (C) group\*hemisphere interaction. This interaction is stratified by ear and rate. Overall, AMB showed increased ITPL in the LH whereas WNL showed increased ITPL in the RH. Note values are plotted on the untransformed scale whereas the statistical analyses were conducted using non-parametric (ranked-based) ANOVAs. Error bars = 95% CI.

note that standard parametric, mixed-model ANOVAs (*lme4* package, R) yielded identical results (data not shown). Backward model selection was used to arrive at the most parsimonious model. For example, if the highest order interaction term was significant, all lower-ordered interaction terms and main effects were retained in the model. If the highest-order interaction term was insignificant, it was removed, and the next highest-ordered interaction term(s) were then considered. To examine significant interactions, we stratified by the different covariates within the interaction term. The significance level was set at  $\alpha = 0.05$ .

We used correlations (Spearman's *rho*) to evaluate relationships between neural oscillations (i.e. slow vs. fast entrainment) and behavior (i.e. DL scores). For these analyses, a laterality index for the neural measures was computed as the difference in peak ITPL between ears (i.e. laterality =  $ITPL_{RE} - ITPL_{LE}$ ) (Jerger and Martin 2004; Momtaz, Moncrieff, and Bidelman 2021). LH and RH responses were averaged given the lack of hemisphere effect in the omnibus ANOVAs. Neural laterality was then regressed against listeners' three different ear advantage scores (per RDDT, DWT, and CW test), computed as the difference in behavioral performance between their dominant and non-dominant ears.

## Results

A detailed analysis of the behavioral data is reported in Momtaz, Moncrieff, and Bidelman (2021). Here, we focus on new rate effects in neural entrainment in children with AMB.

### EEG time-frequency data

Figure 2 shows ITPL spectral maps across ear, rate, group, and hemispheres. In our backward model selection, neither the main nor interaction effects occurred for latency measures. However, ITPL in the  $\beta$  frequency band was strongly modulated by stimulus rate, ear of presentation, hemisphere, and group, but within several two-way interactions. Our final model using ranked-based (robust)

ANOVA on ITPL was:  $ITPL_{amp} \sim rate + group + ear + hemi + rate*group + ear*hemi + group*hemi + (1|subject)$ . This model revealed significant two-way interactions on neural oscillation strength including rate  $\times$  group [ $t_{169} = -3.76, p = 0.0002$ ], ear  $\times$  hemisphere [ $t_{169} = -1.99, p = 0.04$ ], and group  $\times$  hemisphere [ $t_{169} = 3.27, p = 0.001$ ] (Figure 3). No other higher-order interaction terms were significant. To understand the components of these interactions, we examined post-hoc tests for each factor in each two-way term, collapsing across the other remaining factors that were not significant in the respective bivariate interaction.

Focusing first on the rate  $\times$  group interaction (averaging over levels of ear, hemisphere; Figure 3(A)), we found stronger ITPL strength in the fast compared to the slow rate for the WNL group ( $p < 0.0001$ ) but not for the AMB group ( $p = 0.3819$ ). This suggests that regardless of ear and hemisphere, AMBs showed less flexibility in neural entrainment to changes in stimulus rate.

Focusing next on the ear  $\times$  hemisphere interaction (averaging over levels of rate and group; Figure 3(B)), we found stronger ITPL strength for RE compared to LE presentation in LH responses ( $p = 0.0159$ ). No ear effect was observed in RH ( $p = 0.6821$ ). These findings suggest neural responses in LH were overall stronger for right vs. left ear presentation regardless of stimulus rate and group.

We next focussed on the group  $\times$  hemisphere interaction (averaging over levels of rate and ear; Figure 3(C)). The WNL group showed stronger ITPL responses in the RH compared to LH ( $p = 0.0071$ ). In contrast, this hemispheric effect was not significant in the AMB group ( $p = 0.058$ ). These findings suggest a differential pattern of neural entrainment in AMBs vs. WNL listeners with regard to hemisphere.

### Brain-behaviour correlations

The correspondence between neural ear laterality (at slow and fast rates) and all three behavioral ear advantage scores was evaluated using correlational analysis. We previously found that the degree of ear asymmetry in neural oscillation strength to slow

(8.5/s) rate auditory stimuli were associated with behavioral performance on the DW test (Momtaz, Moncrieff, and Bidelman 2021). However, for the fast rate (14.9/s) stimuli in this study, we did not find a relationship between the degree of ear asymmetry in neural oscillation strength and any of the three DL tests (all  $ps > 0.199$ ).

## Discussion

Extending our prior work on the brain basis of DL deficits, we show differences in phase-locked neural oscillations among AMB children that depend critically on the speed of auditory stimuli. In contrast to WNL children whose neural entrainment was sensitive to rate, AMB children showed responses that were largely insensitive to rate manipulations. This resistance to rate was observed regardless of the ear of presentation and in both cortical hemispheres. Our data imply that in addition to any deficits in cognition, language, or more global issues (McFarland and Cacace 2009; Moore et al. 2010), AMB is characterized by a varying capacity in how the brain temporally tags rapid auditory stimuli. Thus, in addition to a reduced capacity to integrate information between the ears (Momtaz, Moncrieff, and Bidelman 2021), AMB appears characterized by functional deficits in temporal processing in the form of less flexibility (more rigidity) in how the auditory system passively entrains to external sounds.

### Neural entrainment differs based on the ear of presentation and hemispheres regardless of rate and group

We should note that ITPL values reported herein are notably smaller (roughly order of magnitude) in this compared to other auditory EEG studies. At least three reasons might account for lower values in our data. First, prior work assessing phase-locked neural oscillations *via* EEG overwhelmingly used scalp (electrode-level) signals rather than dipole source current waveforms as used here. While ITPL is robust to subtle fluctuations in amplitude (Cohen 2014; p. 251), source signals are considerably smaller, resulting in ITPL values that are roughly  $\times 10$  lower than what is observed for scalp data (Bidelman 2018; Hämäläinen, Ortiz-Mantilla, and Benasich 2019). Second, our source responses reflect phase-locked activity localized to left/right auditory cortex, and do not measure phase-locked activity that could entrain to our periodic stimuli in other brain areas (e.g. brainstem and non-auditory regions) (Herdman et al. 2002; Bidelman 2018; Lerousseau et al. 2021). Lastly, ITPL magnitudes depend strongly on trial counts (Cohen 2014; p. 346), with values decreasing 10-fold over the course of the first  $\sim 500$  stimulus presentations. Typical ERP studies employ  $<100$ – $200$  trials resulting in what are large (likely overinflated) estimates of ITPL. In contrast, very high (1000+) trial counts produce ITPLs in the range of 0–0.1 (Cohen 2014; p. 346), comparable to what we observe in our data.

Our results show that right ear stimulus presentation produced stronger neural entrainment in the LH regardless of group, whereas no ear-effect was observed in RH responses. Clicks are fast onset stimuli which might evoke stronger LH recruitment comparable to rapid features of speech (e.g. consonants). This pattern is also expected given the crossed nature of the auditory neuroanatomy which leads to the typical REA and dominance in the contralateral pathway from RE to LH. Larger neural responses for the dominant contralateral auditory pathway (Jerger and Martin 2004) regardless of stimulus properties confirm the advantage of the contralateral over the ipsilateral

pathway as posited by the structural model of auditory processing (Kimura 1967). The REA results in an interaural asymmetry of the contralateral auditory pathway that is biased to the right ear in 75–80% of right-handed and 60% of left-handed individuals, respectively (Kimura 1967). Indeed, the majority ( $\sim 80\%$ ) of our AMB listeners were RE dominant when assessed by DL tests composed of *linguistic* materials. The fact that we find a similar REA for click entrainment suggests the REA may occur irrespective of stimulus nature (i.e. for both linguistic and non-linguistic stimuli). This finding gives credence to a “low-level deficit” account of AMB (Momtaz, Moncrieff, and Bidelman 2021) that is sensory in nature. By extension, such auditory-sensory deficits are unlikely to be acquired late (e.g. during speech development) and could originate or at least be exacerbated by early insults to hearing during infancy (e.g. chronic conductive hearing loss) (Wilmington, Gray, and Jahrsdoerfer 1994; Whitton and Polley 2011). Here, we assume that the LH is more sensitive to the inputs of the dominant right ear and hence produces a larger response when the stimuli are presented to the RE as opposed to the LE. Whereas the RH mainly receives the input from the nondominant ear and hence would not be as flexible to the inputs of different ears.

### Neural entrainment in AMB is rate insensitive

Extending our prior study (Momtaz, Moncrieff, and Bidelman 2021), we found that changing the speed of auditory stimulation reveals a fundamentally different pattern in neural phase-locking between AMB and WNL children that is rate-dependent. Whereas control children showed stronger ITPL strength at fast vs. slow click rates, ITPL strength was surprisingly invariant in children with AMB. Though our data reveal a rate (in)sensitivity in AMB, future studies could explore this further by evaluating more extreme rates (slower and faster) than those used here to map a rate sensitivity profile (i.e. input/output function).

Differences in the resonant frequency of rhythmic entrainment (Baltus and Herrmann 2016) could explain these group differences in the ability to entrain to rapid sounds. The precise interplay of neural excitation/inhibition can generate oscillations at a  $\gamma$ -band frequency that is dependent on stimulus parameters such as rate (Baltus and Herrmann 2016). Therefore, higher stimulation rates may drive activation and boost  $\gamma$  oscillations, which could explain the increment in  $\gamma$  responses for fast vs. slow rates we find in WNLs. On the other hand, the lower ITPL strength in AMBs at faster rates could be a neural correlate of the temporal processing deficits observed in some APDs and dyslexia (ASHA. 1996; Bellis 2011; Granados Barbero et al. 2021; Momtaz, Moncrieff, and Bidelman 2021). Alternatively, weaker  $\gamma$  responses might also be attributed to poorer perceptual-cognitive processes for rapid stimuli (Başar-Eroglu et al. 1996), which is also consistent with the dichotic and other listening difficulties observed in AMB (Momtaz, Moncrieff, and Bidelman 2021). Less robust entrainment in AMBs at faster rates also implies poorer temporal resolution in auditory processing. Interestingly, optimizing stimulus presentation rates shows promise in improving aspects of auditory processing (Baltus and Herrmann 2016). Therefore, tuning external stimulus delivery to the preferred (characteristic) internal entrainment clock (which seems less flexible in AMB) might help increase the coupling between acoustic features and brain activity, ultimately leading to better and perhaps less burdensome auditory processing (e.g. Merzenich et al. 1996).

Across languages, the speed of conversational speech (i.e. syllable rate) unfolds at a near-universal rate between 2 and 8 Hz (Poeppl and Assaneo 2020). Auditory cortical activity (Giraud et al. 2000), psychophysical performance (Viemeister 1979), and speech comprehension (Versfeld and Dreschler 2002) decline rapidly for modulations outside this range. Thus, both speech acoustics and auditory perception are bound by a common, fundamental upper limit of ~8–10 Hz. Non-speech aside, our fast (14.9/s), and slow (8.5/s) rate stimuli might therefore be described as straddling this critical acoustic-perceptual boundary that constrains auditory temporal processing. In this regard, it is tempting to suggest that the AMB group's stronger responses at slower rates (Figure 3(A) here; Momtaz, Moncrieff, and Bidelman 2021) might reflect the fact these stimuli are paced at the normal speech-like rate listeners are exposed to in their everyday environment. In contrast, they show inflexibility to entrain to higher (non-speech) rates where their normally developing peers show robust phase-locking. These findings parallel other electrophysiological studies showing listeners with more adept hearing skills (cf. WNL in this study) better track not only acoustic periodicities that are among their regular experiences but also do so for more complex signals that extend beyond those found in their everyday language experience (Krishnan et al. 2010; Bidelman, Gandour, and Krishnan 2011). Conceivably, the relative breakdown of neural entrainment in the AMB group at higher rates might reflect the fact those sounds are faster than what is observed in everyday speech rhythms (Poeppl and Assaneo 2020). Future studies could test this hypothesis by parametrically varying, for example, time-compressed speech.

Our stimuli were also limited to periodic signals. It is conceivable that individuals with AMB might also have difficulties nimbly switching between periodic and aperiodic acoustic events, as is characteristic of speech. Nevertheless, it should be emphasized these limits were observed using passively evoked, non-speech, repetitive click stimuli. Consequently, our data expose an AMB deficit in general auditory-sensory processing (i.e. neural tagging of sounds) that appears independent of attention and linguistic processing, *per se*. Still, future studies comparing non-speech vs. speech stimulus presentation are needed to test these possibilities and verify whether deficits in AMB's "internal entrainment clocking mechanism" is also observed for speech/linguistic materials and tasks which tap attentional processing.

## Acknowledgments

We thank Drs. Karen Bell and Caitlin Price for comments on earlier versions of this manuscript. Requests for data and materials should be directed to G.M.B. [gbidel@indiana.edu].

## Author contributions

D.W.M. designed the experiment and collected the data; S.M. and M.A.R. analysed the data; all authors wrote the article.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

## Funding

This work was supported by the National Institute on Deafness and Other Communication Disorders of the NIH under award number R01DC016267 (G.M.B.), the U.S. Department of Education under

award number H325K100325 (D.M.), and the Lions Hearing Research Foundation (D.M.).

## ORCID

Sara Momtaz  <http://orcid.org/0000-0001-6585-3141>  
Meredith A. Ray  <http://orcid.org/0000-0001-5312-3774>  
Gavin M. Bidelman  <http://orcid.org/0000-0002-1821-3261>

## References

- Alho, K., J. Salonen, T. Rinne, S. V. Medvedev, K. Hugdahl, and H. Hämäläinen. 2012. "Attention-Related Modulation of Auditory-cortex Responses to Speech Sounds during Dichotic Listening." *Brain Research* 1442: 47–54. doi:10.1016/j.brainres.2012.01.007.
- ASHA. 1996. "Central Auditory Processing: Current Status of Research and Implications for Clinical Practice." *American Journal of Audiology* 5: 41–52. doi:10.1044/1059-0889.0502.41.
- Assaneo, M. F., and D. Poeppl. 2018. "The Coupling between Auditory and Motor Cortices is Rate-restricted: Evidence for an Intrinsic Speech-motor rhythm." *Science Advances* 4 (2): eaao3842. doi:10.1126/sciadv.aao3842.
- Baltus, A., and C. S. Herrmann. 2016. "The Importance of Individual Frequencies of Endogenous Brain Oscillations for Auditory Cognition – A Short Review." *Brain Research* 1640: 243–250. doi:10.1016/j.brainres.2015.09.030.
- Başar-Eroglu, C., D. Strüber, M. Schürmann, M. Stadler, and E. Başar. 1996. "Gamma-band Responses in the Brain: A Short Review of Psychophysiological Correlates and Functional Significance." *International Journal of Psychophysiology* 24 (1–2): 101–112. doi:10.1016/S0167-8760(96)00051-7.
- Bates, D., M. Maechler, B. Bolker, and S. Walker. 2015. "Fitting Linear Mixed-Effects Models Using lme4." *Journal of Statistical Software* 1–48. doi: 10.48550/arXiv.1406.5823.
- Bellis, T. J. 2011. *Assessment and Management of Central Auditory Processing Disorders in the Educational Setting: From Science to Practice*. San Diego, CA: Plural Publishing.
- Bidelman, G. M. 2015. "Induced neural Beta Oscillations Predict Categorical Speech Perception Abilities." *Brain and Language* 141: 62–69. doi:10.1016/j.bandl.2014.11.00.
- Bidelman, G. M. 2018. "Subcortical Sources Dominate the Neuroelectric Auditory Frequency-Following Response to Speech." *NeuroImage* 175: 56–69. doi:10.1016/j.neuroimage.2018.03.060.
- Bidelman, G. M., J. T. Gandour, and A. Krishnan. 2011. "Cross-domain Effects of Music and Language Experience on the Representation of Pitch in the Human Auditory Brainstem." *Journal of Cognitive Neuroscience* 23 (2): 425–434. doi:10.1162/jocn.2009.21362.
- Bidelman, G. M., and S. Momtaz. 2021. "Subcortical Rather than Cortical Sources of the Frequency-Following Response (FFR) relate to Speech-in-noise Perception in Normal-hearing Listeners." *Neuroscience Letters* 746: 135664. doi:10.1016/j.neulet.2021.135664.
- Billiet, C. R., and T. J. Bellis. 2011. "The Relationship between Brainstem Temporal Processing and Performance on Tests of Central Auditory Function in Children with Reading Disorders." *Journal of Speech, Language, and Hearing Research* 54: 228–242. doi:10.1044/1092-4388(2010/09-0239).
- Broadbent, D. E. 1958. "Effect of Noise on an "Intellectual" Task." *The Journal of the Acoustical Society of America* 30 (9): 824–827. doi:10.1121/1.1909779.
- Chowsilpa, S., D.-E. Bamiou, and N. Koohi. 2021. "Effectiveness of the Auditory Temporal Ordering and Resolution Tests to Detect Central Auditory Processing Disorder in Adults With Evidence of Brain Pathology: A Systematic Review and Meta-Analysis." *Frontiers in Neurology* 12: 656117. doi:10.3389/fneur.2021.656117.
- Cohen, M. X. 2014. *Analyzing Neural Time Series Data: Theory and Practice*. Cambridge, MA: MIT Press.
- Dawes, P., T. Sirimanna, M. Burton, I. Vanniasagaram, F. Tweedy, and D. V. M. Bishop. 2009. "Temporal Auditory and Visual Motion Processing of Children Diagnosed with Auditory Processing Disorder and Dyslexia." *Ear & Hearing* 30 (6): 675–686. doi:10.1097/AUD.0b013e3181b34cc5.
- Giraud, A. L., C. Lorenzi, J. Ashburner, J. Wable, I. Johnsrude, R. Frackowiak, and A. Kleinschmidt. 2000. "Representation of the Temporal Envelope of Sounds in the Human Brain." *Journal of Neurophysiology* 84 (3): 1588–1598. doi:10.1152/jn.2000.84.3.1588.

- Granados Barbero, R., A. Vos, P. Ghesquière, and J. Wouters. 2021. "Atypical Processing in Neural Source Analysis of Speech Envelope Modulations in Adolescents with Dyslexia." *European Journal of Neuroscience* 54 (11): 7839–7859. doi:10.1111/ejn.15515.
- Gronlund, S. 2010. "Timing and Time Perception: A Review of Recent Behavioral and Neuroscience Findings and Theoretical Directions." *Attention, Perception, & Psychophysics* 72 (3): 561–582. doi:10.3758/APP.72.3.561.
- Hämäläinen, J. A., S. Ortiz-Mantilla, and A. Benasich. 2019. "Change Detection to Tone Pairs during the First Year of Life – Predictive Longitudinal Relationships for EEG-based Source and Time-frequency Measures." *NeuroImage* 198: 83–92. doi:10.1016/j.neuroimage.2019.05.034.
- Herdman, A. T., O. Lins, P. Van Roon, D. R. Stapells, M. Scherg, and T. W. Picton. 2002. "Intracerebral Sources of Human Auditory Steady-state Responses." *Brain Topography* 15 (2): 69–86. doi:10.1023/a:1021470822922.
- Hiscock, M., R. Inch, and M. Kinsbourne. 1999. "Allocation of Attention in Dichotic Listening: Differential Effects on the Detection and Localization of Signals." *Neuropsychology* 13 (3): 404–414. doi:10.1037/0894-4105.13.3.404.
- Jerger, J., and J. Martin. 2004. "Hemispheric Asymmetry of the Right Ear Advantage in Dichotic Listening." *Hearing Research* 198 (1–2): 125–136. doi:10.1016/j.heares.2004.07.019.
- Keith, R. W. 1986. *Scan: A Screening Test Auditory Processing Disorders*. San Diego, CA: Psychological Corporation Harcourt Brace Jovanovich, Incorporated.
- Kimura, D. 1967. "Functional Asymmetry of the Brain in Dichotic Listening." *Cortex* 3 (2): 163–178. doi:10.1016/S0010-9452(67)80010-8.
- Koller, M. 2016. "Robustlmm: an R Package for Robust Estimation of Linear Mixed-effects Models." *Journal of Statistical Software* 75 (6): 1–24. doi:10.18637/jss.v075.i06.
- Kopp-Scheinplugg, C., and B. L. Tempel. 2015. "Decreased Temporal Precision of Neuronal Signaling as a Candidate Mechanism of Auditory Processing Disorder." *Hearing Research* 330 (Pt B): 213–220. doi:10.1016/j.heares.2015.06.014.
- Krishnan, A., J. T. Gandour, C. J. Smalt, and G. M. Bidelman. 2010. "Language-dependent Pitch Encoding Advantage in the Brainstem is Not Limited to Acceleration Rates that Occur in Natural Speech." *Brain and Language* 114 (3): 193–198. doi:10.1016/j.bandl.2010.05.004.
- Lachaux, J. P., E. Rodriguez, J. Martinerie, and F. J. Varela. 1999. "Measuring Phase Synchrony in Brain Signals." *Human Brain Mapping* 8 (4): 194–208. doi:10.1002/(SICI)1097-0193(1999)8:4<194::AID-HBM4>3.0.CO;2-C.
- Lerousseau, J. P., A. Trébuchon, B. Morillon, and D. Schön. 2021. "Frequency Selectivity of Persistent Cortical Oscillatory Responses to Auditory Rhythmic Stimulation." *The Journal of Neuroscience* 41 (38): 7991–8006. doi:10.1523/JNEUROSCI.0213-21.2021.
- Luthra, S. 2021. "The Role of the Right Hemisphere in Processing Phonetic Variability Between Talkers." *Neurobiology of Language* 2 (1): 138–151. doi:10.1162/nol\_a\_00028.
- McFarland, D. J., and A. T. Cacace. 2009. "Modality Specificity and Auditory Processing Disorders." In: Cacace AT, McFarland DJ, eds. *Controversies in Central Auditory Processing Disorder*. San Diego: Plural, 199–216.
- Merzenich, M. M., W. M. Jenkins, P. Johnston, C. Schreiner, S. L. Miller, and P. Tallal. 1996. "Temporal processing Deficits of Language-learning Impaired Children Ameliorated by Training." *Science* 271 (5245): 77–81. doi:10.1126/science.271.5245.77.
- Momtaaz, S., D. Moncrieff, and G. M. Bidelman. 2021. "Dichotic Listening Deficits in Amblyaudia are Characterized by Aberrant Neural Oscillations in Auditory Cortex." *Clinical Neurophysiology* 132 (9): 2152–2162. doi:10.1016/j.clinph.2021.04.022.
- Moncrieff, D. 2015. "Age- and Gender-Specific Normative Information from Children Assessed with a Dichotic Words Test." *Journal of the American Academy of Audiology* 26 (7): 632–644.
- Moncrieff, D., W. Keith, M. Abramson, and A. Swann. 2016. "Diagnosis of Amblyaudia in Children Referred for Auditory Processing Assessment." *International Journal of Audiology* 55 (6): 333–345. doi:10.3109/14992027.2015.1128003.
- Moncrieff, D., and R. H. Wilson. 2009. "Recognition of randomly presented one-, two-, and three-pair dichotic digits by children and young adults." *Journal of the American Academy of Audiology* 20: 58–70. doi: 10.3766/jaaa.20.1.6.
- Moore, D. R. 2006. "Auditory Processing Disorder (APD): Definition, Diagnosis, Neural Basis, and Intervention." *Audiological Medicine* 4 (1): 4–11. doi:10.1080/16513860600568573.
- Moore, D. R., M. A. Ferguson, A. M. Edmondson-Jones, S. Ratib, and A. Riley. 2010. "Nature of Auditory Processing Disorder in Children." *Pediatrics* 126 (2): e382–390–e390. doi:10.1542/peds.2009-2826.
- Moore, D. R., K. Hugdahl, H. J. Stewart, J. Vannest, A. J. Perdew, N. T. Sloat, E. K. Cash, and L. L. Hunter. 2020. "Listening Difficulties in Children: Behavior and Brain Activation Produced by Dichotic Listening of CV Syllables." *Frontiers in Psychology* 11: 675. doi:10.3389/fpsyg.2020.00675.
- Morell, R. J., C. C. Brewer, D. Ge, H. Snieder, C. K. Zalewski, K. A. King, D. Drayna, and T. B. Friedman. 2007. "A Twin Study of Auditory Processing Indicates that Dichotic Listening Ability is a Strongly Heritable Trait." *Human Genetics* 122 (1): 103–111. doi:10.1007/s00439-007-0384-5.
- Musiek, F. E., and J. Weihing. 2011. "Perspectives on Dichotic Listening and the Corpus Callosum." *Brain and Cognition* 76 (2):225–232. doi:10.1016/j.bandc.2011.03.011.
- Obleser, J., and C. Kayser. 2019. "Neural Entrainment and Attentional Selection in the Listening Brain." *Trends in Cognitive Sciences* 23 (11): 913–926. doi:10.1016/j.tics.2019.08.004.
- Oostenveld, R., and P. Praamstra. 2001. "The Five Percent Electrode System for High-resolution EEG and ERP Measurements." *Clinical Neurophysiology* 112 (4): 713–719. doi:10.1016/s1388-2457(00)00527-7.
- Papp, N., and P. Ktonas. 1977. "Critical Evaluation of Complex Demodulation Techniques for the Quantification of Bioelectrical Activity." *Biomedical Sciences Instrumentation* 13: 135–145.
- Picton, T. 2013. "Hearing in Time: Evoked Potential Studies of Temporal Processing." *Ear and Hearing* 34 (4): 385–401. doi:10.1097/AUD.0b013e31827ada02.
- Picton, T. W., C. Alain, D. L. Woods, M. S. John, M. Scherg, P. Valdes-Sosa, J. Bosch-Bayard, and N. J. Trujillo. 1999. "Intracerebral Sources of Human Auditory-Evoked Potentials." *Audiology & Neuro-Otology* 4 (2): 64–79. doi:10.1159/000013823.
- Poeppl, D., and M. F. Assaneo. 2020. "Speech Rhythms and Their Neural Foundations." *Nature Reviews Neuroscience* 21 (6): 322–334. doi:10.1038/s41583-020-0304-4.
- R Core Team. 2020. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing.
- Strouse, A., and R. H. Wilson. 1999. "Stimulus Length Uncertainty with Dichotic Digit Recognition." *Journal of the American Academy of Audiology* 10 (4): 219–229. doi: 10.1055/s-0042-1748483.
- Tallal, P. 1980. "Auditory Temporal Perception, Phonics, and Reading Disabilities in Children." *Brain and Language* 9 (2): 182–198. doi:10.1016/0093-934x(80)90139-x.
- Tallal, P., R. L. Sainburg, and T. Jernigan. 1991. "The Neuropathology of Developmental Dysphasia: Behavioral, Morphological, and Physiological Evidence for a Pervasive Temporal Processing Disorder." *Reading and Writing* 3 (3–4): 363–377. doi:10.1007/BF00354968.
- Tallus, J., A. Soveri, H. Hämäläinen, J. Tuomainen, and M. Laine. 2015. "Effects of Auditory Attention Training with the Dichotic Listening Task: Behavioural and Neurophysiological Evidence." *PLOS One* 10 (10): e0139318. doi:10.1371/journal.pone.0139318.
- Toplak, M. E., C. Dockstader, and R. Tannock. 2006. "Temporal Information Processing in ADHD: Findings to Date and New Methods." *Journal of Neuroscience Methods* 151 (1): 15–29. doi:10.1016/j.jneumeth.2005.09.018.
- Versfeld, N. J., and W. A. Dreschler. 2002. "The Relationship between the Intelligibility of Time-compressed Speech and Speech in Noise in Young and Elderly Listeners." *Journal of the Acoustical Society of America* 111 (1): 401–408. doi:10.1121/1.1426376.
- Viemeister, N. F. 1979. "Temporal Modulation Transfer Functions Based Upon Modulation Thresholds." *The Journal of the Acoustical Society of America* 66 (5): 1364–1380. doi:10.1121/1.383531.
- Whitton, J. P., and D. B. Polley. 2011. "Evaluating the Perceptual and Pathophysiological Consequences of Auditory Deprivation in Early Postnatal Life: A Comparison of Basic and Clinical Studies." *Journal of the Association for Research in Otolaryngology* 12 (5): 535–547. doi:10.1007/s10162-011-0271-6.
- Wilmington, D., L. Gray, and R. Jahrsdoerfer. 1994. "Binaural Processing After Corrected Congenital Unilateral Conductive Hearing Loss." *Hearing Research* 74 (1–2): 99–114. doi:10.1016/0378-5955(94)90179-1.
- Zhang, X., and J. B. Tomblin. 1998. "Can Children with Language Impairment be Accurately Identified Using Temporal Processing Measures? A Simulation Study." *Brain and Language* 65 (3): 395–403. doi: 10.1006/brln.1998.1999.