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ORIGINAL ARTICLE

The frequency-following response as an assessment of spatial processing

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ABSTRACT

Objective: It is important to detect children with difficulties distinguishing speech-in-noise early. Prompt identification may be assisted by an evoked potential. The aims of the present study were: 1) to evaluate the frequency-following response (FFR) as a measure of binaural processing and spatial listening and, 2) to investigate the relationship between the FFR and a behavioural measure of binaural processing and spatial listening.

Design: A single group, repeated measures design. The FFR was recorded in two different spatial conditions and amplitudes compared to spatial listening ability.

Study Sample: Thirty-two children (aged 6.0 to 13.1 years) with a range of spatial processing abilities as measured behaviourally using the Listening in Spatialised Noise Sentences test (LiSN-S).

Results: FFR waveforms were elicited using speech-like stimuli in co-located and separated conditions. A significant ($p \leq 0.005$) spatial advantage effect was observed with larger amplitudes in the separated condition. No correlations were observed between FFR amplitude and LiSN-S results.

Conclusions: The FFR shows promise as a measure of binaural processing and spatial listening, but could be measuring different processes to those measured by the LiSN-S.

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Paediatric; anatomy & physiology; behavioural measures; conditions/pathology/disorders

Introduction

The ability to understand speech in noise is reliant on the separation and streaming of acoustic signals arriving at the two ears. Signals are separated based on interaural timing and intensity differences (ITDs and IIDs) as well as spectral cues. Phase, level and spectral differences between the ears occur because of varying distances, and obstacles such as the torso, head and pinna affecting sound transmission. Sound is delayed in arrival time as it travels to the ear furthest from the sound source, and for higher frequencies is reduced in level by the head shadow effect (Blauert 1997; Yost and Dye 1997). It is the brain's segregation or "streaming" of acoustic signals based on ITD and IID cues that enables the listener to attend to a sound source of interest. This process is aided if sounds arise from different locations (i.e. when they are spatially separated) (Bronkhorst and Plomp 1988; Goupell and Hartmann 2007; Cameron and Dillon 2008; Ching et al. 2011).

Spatial listening is dependent on the accurate processing of binaural cues by the central auditory nervous system. Both timing and intensity cues are initially transferred to the cochlear nucleus (CN) from the ipsilateral auditory nerve, before input from both ears is received by the superior olivary complex (SOC) (Brugge and Geisler 1978). Given timing cues arise predominantly from low frequency stimuli (mostly because of greater ease in which phase can be tracked within the longer periods of low frequency sounds), processing of these occurs in the medial superior olive, which has a discharge rate favourable towards low frequencies (Guinan, Norris, and Guinan et al. 1972). Conversely, given that intensity cues arise predominantly from high frequency stimuli (mostly resulting from the head shadow effect) processing of these cues occurs in the lateral superior olive (Guinan, Norris, and Guinan 1972). Following on from the SOC, integration and processing of binaural cues occurs in the inferior colliculus (IC) (Lau et al. 2013). Input to the IC is both excitatory and inhibitory, with the particular activation pattern of neurons determining how interaural cues are eventually interpreted by the auditory cortex (Zatorre and Penhune 2001). See Joris and Yin (1995) and Middlebrooks and Green (1991) for further explanation regarding the physiological processes behind cue binaural processing.

Spatial listening is achieved when binaural differences cues are used to attend to the location of a target signal while actively suppressing sound sources arising from other locations. A reduced ability to utilise these spatial cues is referred to as spatial processing disorder (SPD) (Cameron and Dillon 2008), a disorder that can have a detrimental effect on the ability to detect speech in noise. Children with SPD present with speech reception thresholds within the normal range when speech and noise are co-located (i.e. arise from the same location), but require significantly higher signal-to-noise ratios (SNRs) than typically developing peers when speech and noise arise from different locations (i.e. spatially separated). Spatial listening ability can be measured, and SPD can be diagnosed in a clinical setting under headphones with the Listening in Spatialised Noise Sentence test (LiSN-S) (Cameron and Dillon 2007). The presence of SPD is thought to result from an inability to distinguish subtle timing and intensity differences between the two ears (Cameron, Glyde, and Dillon 2012). Recent studies have confirmed a link between early disruptions to binaural auditory cues as a result of a history of conductive hearing loss with otitis media and SPD (Tomlin

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and Rance 2014; Graydon et al. 2017). Links are hypothesised to be a result of interruptions to normal binaural input to the central auditory nervous system during key developmental years. Animal models have shown a clear link between these early disruptions and changes within the central auditory nervous system, with these changes thought to affect how cues are interpreted and managed longer-term (Knudsen et al. 1994; Ihlefeld et al. 2016). The underlying physiological mechanisms that lead to difficulties processing spatial cues (i.e. spatial processing disorder) are yet to be fully understood.

Electrophysiological measures may provide insight into neural networks underlying binaural processing and have the potential to indicate when the auditory pathway is disrupted (Furst et al. 1990), in cases of SPD. Evidence of binaural interaction, measurable at a physiological level, comes from the presence of a binaural interaction component (BIC) within an evoked potential. The BIC is the difference between the sum of monaurally evoked potentials compared to the binaurally evoked potential (Dobie and Berlin 1979), with the amplitude of the binaurally evoked condition typically being smaller when compared to the sum of the monaurally evoked potentials (Dobie and Norton 1980; McPherson and Starr 1993). The BIC is evidence of merging neural outputs from both ears (i.e. binaural interaction), with the smaller evoked potential amplitude in the binaural condition thought to be a result of inhibition as binaural cues converge (Furst et al. 1985; Pratt et al. 1997; Brantberg et al. 1999; Junius et al. 2007). Further evidence of binaural processing using evoked potentials comes from studies that have varied interaural cues (Dobie and Norton 1980; Kevanishvili and Lagidze 1987; McEvoy et al. 1990; Picton et al. 1991; McPherson and Starr 1993). The observed reduction in evoked potential amplitude is thought to reflect the summation or cancellation of the response in the presence of binaural differences cues (Clinard, Hodgson, and Scherer 2017). To date, most studies in this area have relied on transient stimuli to elicit evoked potentials, stimuli that may not be reflective of real-world binaural cue processing (Wilson and Krishnan 2005). Evoked potentials that are able to reflect the processing of speech-like cues may be better candidates if wanting to assess real-world binaural processing rather than processing of transient stimuli (Haywood et al. 2015).

The frequency-following response (FFR) is an evoked potential that phase-locks to the stimulus with the capacity to represent the neural processing of a periodic sound such as speech (Aiken and Picton 2008). The FFR's ability to maintain the integrity of target speech, even in the presence of noise (Du et al. 2011) indicates its potential to reflect binaural cue processing indicative of real-world listening (Wilson and Krishnan 2005). The response is predominantly generated from brainstem nuclei (Smith et al. 1975; Glaser et al. 1976), although there is evidence to suggest cortical contributions also (Coffey et al. 2016). According to lesion studies, the FFR's primary site of origin is the inferior colliculus (IC) (Sohmer, Pratt, and Kinarti 1977), with ancillary contributions from the lateral lemniscus (LL) and cochlear nucleus (CN) (Chandrasekaran and Kraus 2010). Early binaural cue processing occurs at the level of the brainstem (Bushara et al. 1999), with animal studies able to demonstrate improved signal representation in response to binaural configurations at the level of the IC (Du et al. 2011). This binaural unmasking, which is necessary for improved signal detection in noise, has also been shown present in the human brainstem (i.e. the neural generators of the FFR) in response to interaural difference cues (Clark et al. 1995; Krishnan and McDaniel 1998; Ballachanda and Moushegian 2000).

If the FFR is to be an electrophysiological correlate of binaural processing and spatial listening abilities, then its relationship to these abilities needs to be established. Previous studies have focussed on the FFRs ability to preserve processing related to the binaural masking level difference (BMLD) test (Wilson and Krishnan 2005; Clinard, Hodgson, and Scherer 2017). The BMLD is a perceptual measure where the listener is able to better detect the signal in noise when presented out-of-phase between the two ears (Hirsh 1948). In normal hearing adults, Wilson and Krishnan (2005) were able to demonstrate a similar release from masking within the FFR, with larger amplitudes (in the form of amplitude recovery) in conditions when binaural difference cues were available. Clinard, Hodgson, and Scherer 2017 reported a similar effect, with reduction in FFR amplitude when the signal was opposite in phase at each ear, again related to binaural interaction. They also found a relationship between FFR amplitude differences in phasic versus antiphasic conditions with the behavioural BMLD, with smaller amplitude differences predictive of poorer behavioural BMLDs and vice versa. The authors suggest the main reason for the association between the behavioural and physiological response was likely due to the similar stimuli used in both conditions. These reported links between the FFR and BMLDs show potential for using the FFR as an electrophysiological measure of binaural processing and spatial listening abilities. To fully explore this potential, however, further research is needed that uses stimuli and behavioural measures that better reflect binaural processing and spatial listening in real-world conditions.

The FFR has potential as an objective measure of binaural processing and spatial listening abilities. To further investigate this potential, the present study aimed to: 1) evaluate the frequency-following response (FFR) as a measure of binaural processing and spatial listening in the brainstem, and 2) investigate the relationship between the FFR and a behavioural measure of binaural processing and spatial listening, the LiSN-S test.

Materials and methods

Ethics

This study was approved by the Ethics Committee of the Royal Victorian Eye and Ear Hospital (13/1117H). All testing conformed to the tenets of the Declaration of Helsinki (2013) and informed consent was obtained from all participants after explanation of the research design including the nature, purpose and expected outcomes of the study.

Participants

Thirty-two children aged 6.0 to 13.1 years participated in the study (mean age 8.2 ± 1.2 years; 12 girls). Children were either conveniently sampled from a clinical population from The University of Melbourne Audiology Clinic with known spatial processing ability or sampled from the local school-aged community. The sampling was that of convenience. A parent/caregiver for each participating child reported that the child spoke English as his or her first language, and had no speech and/or language delay at the time of assessment.

Procedure

Audiometric testing, the Listening in Spatialised Noise Sentence task (LiSN-S) and the Frequency-Following Response (FFR) recording were administered on all children. Testing took approximately 1.5 hours to complete per participant.

Measures

Audiometric testing. Participants were assessed in a sound proof booth using TDH 39 headphones (Telephonics, Farmingdale, NY, USA) with the Affinity 2.0 AC 440 module (Interacoustics, Middelfart, Denmark) audiometer. Pure tone thresholds were assessed using standard audiometric procedures (Carhart and Jerger 1959), and normal hearing acuity (defined as hearing thresholds of 20 dB HL or better at octave frequencies from 500 Hz to 8000 Hz) was established prior to proceeding. All participants were shown to have normal middle-ear pressure and compliance at the time of assessment (Jerger type A tympanograms (Jerger 1970)), defined as a peak compliance within 0.2–1.6 mmhos, and peak pressure within −100 to +20 dPa.

LiSN-S. The LiSN-S was presented through Sennheiser HD 215 headphones (Old Lyme, CT, USA) connected to a Dell PC (Dell, Round Rock, TX, USA) via a Buddy 6 G USB (InSync Speed Technologies) soundcard. The LiSN-S task measured the ability to utilise spatial cues in order to differentiate target sentences (presented at 0° azimuth) from competing background speech. The subject was required to repeat the target sentence in four different listening conditions where the background speech varies in location (co-located [0°] versus separated [90°]) and voice characteristics (same voice [SV] or different voice [DV]). In the four listening conditions (SV0, SV90, DV0, and DV90) the speech reception threshold (SRT) was established by adjusting the signal-to-noise ratio until the listener understood 50% of the target sentence. Target sentences were initially presented at 62 dB SPL with the competing speech at 55 dB SPL. Advantage scores were then generated based on the SRTs. The spatial advantage score was calculated by the LiSN-S programme as the improvement in SRT when spatial cues were present versus absent (i.e., when the target sentence and noise were separated by 90° azimuth versus when the target sentence and noise were located at 0° azimuth) (Cameron, Glyde, and Dillon 2012). The LiSN-S task was conducted according to the recommended test order DV90, SV90, DV0 and SV0 (Cameron and Dillon 2008).

FFR Stimuli. Stimuli were created and delivered using MATLAB R2013b software (Mathworks, Natick. MA, USA) through a multichannel Fireface UC soundcard (RME, Haimhausen, Germany) and presented binaurally through electromagnetically shielded ER3A insert phones (Etymotic Research, Elk Grove Village, IL, USA). The stimuli were based on the Listening in Spatialised Noise Tonal (LiSN-T) test which intends to provide a non-language option for the LiSN-S (Buchholz, Dillon, and Cameron 2013). The stimuli were composed of 220 concatenated blocks, with every 1560-ms block containing 26 segments, each 60 ms long (Figure 1). The first 13 segments contained one 30 ms target each. All 26 segments had 2 distractors each. Hence, one block contained 52 distractors and 13 targets in total. Each 30 ms target had 5 ms cosine-shaped onsets and offsets, a fundamental frequency of 225 Hz, harmonics up to 6000 Hz, and onset times at $60^*(i-1)\ +15$ ms ($i = 1, \ldots, 13$) after the start of each block. The 30-ms targets evoked the FFR. The distractors matched the targets' length and shape, with randomised fundamental frequencies between 100 and 350 Hz (centred around 225 Hz), and randomised onset times at $60^*\ (i-1) + j$ ms ($i = 1, \ldots, 26$; $0 \leq j \leq 30$).

From a real-world perspective, LiSN-T stimuli were designed to have considerable ecological validity. These stimuli mimicked real-world speech stimuli through the use of a fundamental frequency and its harmonics, as well as spatial cues to maximise spatial advantage (as targets and distractors are extremely similar), minimise stimulus interval lengths (important for clinical applications), and to maximise measurement reliability (Buchholz, Dillon, and Cameron 2013).

Target and distractors were spatialised with non-individualised Head-Related Transfer Functions (HRTFs) to create spatial conditions under headphones. The HRTFs were created and measured at the National Acoustic Laboratories (NAL, Sydney, Australia) on a Knowles Electronics Manikin for Acoustic Research (KEMAR) (Knowles, Itasca, USA). Two different spatial conditions were presented, co-located (C) and separated (S). In the co-located condition, targets and the two sets of distractors were presented at the front (0° azimuth). In the separated condition, the target was presented at the front, and one set of distractors was presented from the left (−90°), and the other set from the right (+90°). Stimuli were calibrated at 60 dB SPL using an IEC126 HA2 2-cc coupler, incorporating a 1-inch 4144 microphone, a 1-to-1/2-inch DB0375 adaptor and a 30-second averaging time window on a Brüel and Kjaer 2231 sound level metre (Brüel and Kjaer, Naeum, Denmark). The target was presented at 60 dB SPL, with the target to distractor signal-to-noise ratio (SNR) being 5 dB. If both distractors were presented simultaneously with the target, this amounts to 2 dB SNR.

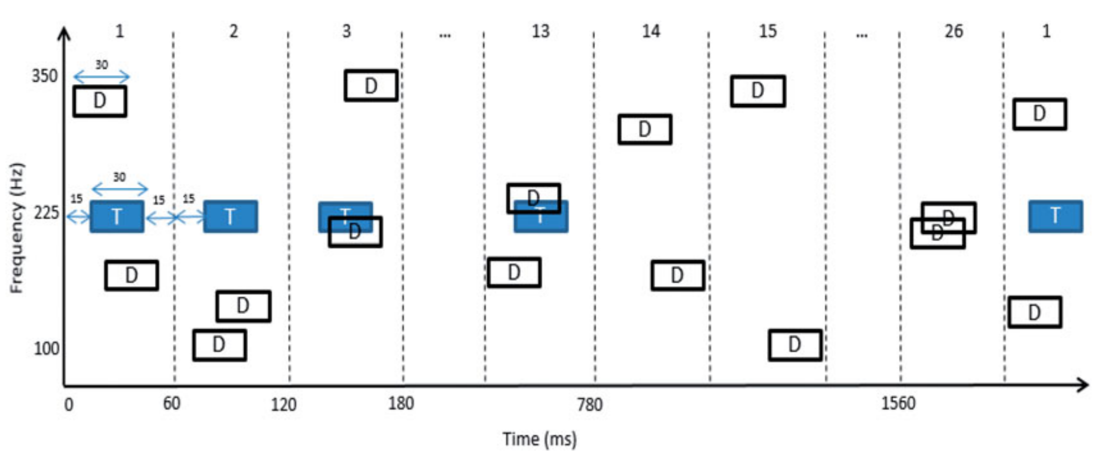

Figure 1. Representation of stimuli used to elicit FFRs. Each recording consists of 220 blocks with every block containing 26 segments. Each segment is made up of 13 target stimuli (T) and 52 distractors (D).

Recordings. Single channel FFRs were recorded using a Biologic Navigator 210 Pro Auditory Evoked Potential (AEP) system and software (Natus, Pleasanton, CA, USA). The non-inverting electrode was placed on the upper forehead and the inverting electrode on the right or left mastoid in a balanced order (sixteen right mastoid). The ground electrode was placed on the lower forehead. Ambu Neuroline Electrodes (Ambu, Copenhagen, Denmark) were used and electrode impedances were <5 kohms in all cases. The channel amplifier gain was 100,000 with bandpass filtering between 70 and 500 Hz, and an artefact rejection level of 30 µV. Recording epochs were 810.67 ms long. The sampling rate was 1263.16 Hz. Only averaged data were made available by the recording system. The order of testing was randomised between subjects with either the co-located condition or the separated condition first. A third, inaudible (I) condition was included with the co-located stimuli presented through the insert phones but not placed in the subject's ear. The inaudible condition provided a baseline measure of the ambient electrical noise in the room and the participant's electrical activity, as well as serving as a control for electrical stimulus artefacts. Each condition took approximately seven minutes to complete. Once all three conditions were measured (C1, S1 and I), both C and S were repeated in order to assess test-retest reliability (C2 and S2). The recording was conducted in a sound proof booth. Children sat quietly while playing on an iPad throughout the recording.

Data analysis

All recordings (C1, C2, S1, S2 and I) were analysed using MATLAB. The averaged FFR epoch was first digitally high pass filtered at 150 Hz using a 100th order filter to reduce 50 Hz contamination. It was then divided in 13 portions of 50 ms with the start of each portion matching the onset of a target stimulus. The final FFR waveform was derived by averaging the 13 portions into a single grand average, which contained 2860 repetitions (220 blocks*13 portions per block). No compensation of the insert phone tube delay was required given the recording system automatically compensated for the 0.9 ms delay. The frequency spectrum of the FFR was calculated on the region from 5.1 to 40.0 ms using a Fast Fourier Transform (FFT) with a bin width of 5 Hz. The amplitude of the FFR corresponding to the fundamental frequency (225 Hz) of the target stimulus was determined as the amplitude (in nV) of the FFT bin corresponding to 225 Hz. It was acknowledged that the energy in the 225 Hz bin did not originate from the target stimuli alone. Other identified sources were 1) the distractor stimuli overlapping temporally and spectrally, without being time-locked, with the target stimuli; 2) non-biological (i.e. electrical) target stimulus artefact; and 3) any other noise sources not related to the biological response to the target stimulus. For this reason, the inaudible condition was recorded with FFR amplitudes (in nV) of the 225 Hz bin taken as the estimate of the contribution of other sources at that specific frequency. It was assumed that this contribution was constant across each appointment given each participant did not move extensively during and in between recordings, and the distractor stimuli were identical for both co-located and separated spatial conditions.

Statistical analysis

To account for slight variability in the recordings, the C1 and C2 traces were averaged (C) and the S1 and S2 traces were averaged (S). In five participants, C2 and S2 were unable to be established as the child did not sit still long enough to complete testing. In these cases, C1 and S1 were used.

Parametric comparisons were applied for all analyses as amplitudes for the FFR measures were found to generally follow normal distributions as determined by histograms. The LiSN-S programme automatically derives z-scores for all measures and conditions (DV90, SV0 and spatial advantage) to compare across age groups. Due to potential effects of age on FFR amplitudes (Johnson et al. 2008), comparisons between the evoked potential measures and LiSN-S were made using the raw speech reception threshold (SRT) rather than the z-score.

Results

Figure 2 shows the FFR results in the co-located, separated and inaudible stimulus conditions. Recordings of four participants were excluded because of excessive noise (>10 nV) in the 225 Hz bin of the inaudible condition. In the remaining 28 participants, average noise in the 225 Hz bin of the inaudible condition was equal to 4.31 nV (SD = 1.80 nV; range: 1.37–8.19 nV). A further two participants were excluded from the results analysis as they were considered outliers (using scatterplots) in the test/retest co-located condition.

FFR test/retest analysis

To establish the relationship between the test and retest measures a Pearson correlation was performed. In the remaining 26 participants, a significant correlation was found between the test and retest FFR amplitude for the co-located stimulus condition ($r = 0.57$, $p = 0.007$) and the separated stimulus condition ($r = 0.50$, $p = 0.021$).

Co-located versus separated

Comparisons were made for each child between the three recording conditions in order to establish whether amplitude differences exist. Figure 2 shows individual recordings and grand average traces for the FFR waveforms in co-located, separated and inaudible conditions for all subjects.

Paired t-test analyses showed significant differences between the average FFR amplitude in the co-located stimulus condition (C) versus the separated condition (S) [$t(26) = 3.14$, $p \leq 0.005$] the co-located stimulus condition (C) versus the inaudible condition (I) [$t(26) = 4.07$, $p \leq 0.001$], and the separated stimulus condition (S) versus the inaudible stimulus condition (I) [$t(26) = 4.99$. $p \leq 0.001$]. These results are displayed in Table 1.

Correlation with behavioural results

LiSN-S and FFR

Pearson correlation analyses showed no significant correlations between FFR amplitude measures in the co-located (C) or separated (S) stimulus conditions and the LiSN-S SRT measures. These results are displayed in Table 2.

A Pearson correlation was also performed between an FFR amplitude difference measure (separated minus co-located (S-C)) and LiSN-S measures. No correlation was observed between the S-C amplitude and the LiSN-S measures ($p > 0.05$ for SV90, DV0 and DV90 as well as spatial advantage) except in the SV0 condition ($r = 0.44$, $p = 0.02$).

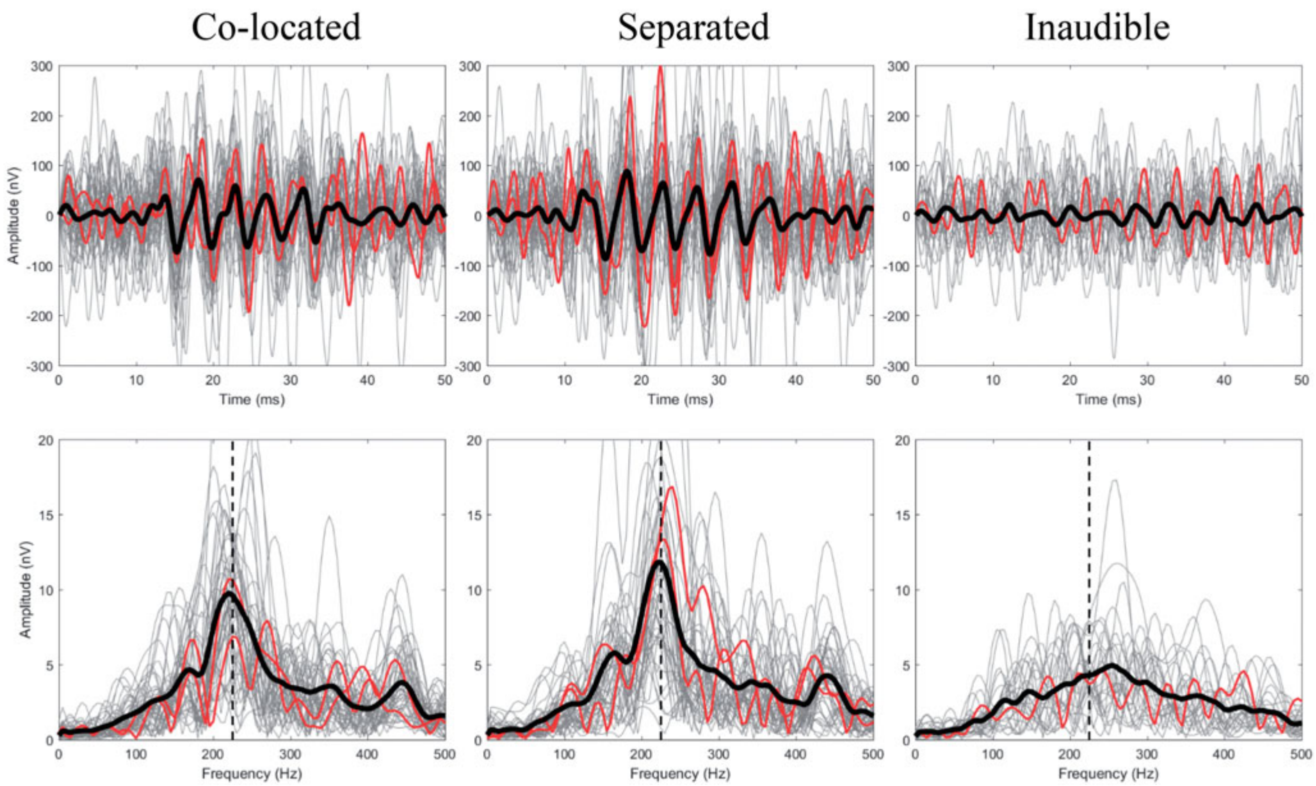

Figure 2. FFR traces for 26 subjects. The 225 Hz bin is indicated by the vertically dashed line. Dark grey: test and retest traces of subject 2.

Table 1. FFR comparisons for the three different recording conditions and 26 subjects. SD: standard deviation. SEM: standard error of the mean. CI: confidence interval.

	Co-located (C) vs Inaudible (I)		Separated (S) vs Inaudible (I)		Separated (S) vs Co-located (C)	
	C	I	S	I	S	C
Mean (nV)	10.32	4.27	12.40	4.27	12.40	10.32
SD (nV)	7.61	1.81	8.40	1.81	8.40	7.61
SEM (nV)	1.49	0.36	1.65	0.36	1.65	1.49
95% CI for mean difference (nV)	(2.99, 9.11) T value = 4.07 p value = 0.000		(4.78, 11.49) T value = 4.99 p value = 0.000		(0.72, 3.45) T value = 3.14 p value = 0.004	

Table 2. Correlations between LiSN-S measures and FFR amplitudes (co-located and separated).

	Co-located		Separated	
FFR	r	p	r	p
SV0	−0.006	0.975	0.173	0.397
SV90	−0.155	0.451	−0.072	0.726
DV0	−0.304	0.132	−0.320	0.111
DV90	−0.048	0.815	−0.010	0.960
Spatial advantage	0.152	0.459	0.156	0.448

Discussion

This study's findings suggest the FFR is able to reflect binaural difference cues important for spatial listening, but could be measuring different processes to those measured by the LiSN-S.

The ability of the FFR to reflect the processing of binaural difference cues in speech-like stimuli was seen in the larger FFR amplitudes to the separated (S) versus the co-located (C) stimuli. In this regard, the FFR was seen to reflect the spatial advantage present in the separated stimuli condition. The significant spatial advantage for FFR amplitude observed in the current study is assumed a result of the cross-correlation that occurs within neural networks in response to interaural difference cues (Freyman et al. 1999). That is, in the co-located condition, neurons are activated in response to the frontal distractor, with the presence of the target only resulting in a small FFR amplitude increase. In contrast, in the separated condition, the introduction of a spatially separated target results in an enhanced amplitude relative to the co-located condition. This is due to the simultaneous suppression of the distractor (i.e. a release from masking) that occurs in response to the spatially separated target. Excitation, as well as suppression driven by the contralateral pathway, is the likely reason for the observed binaural unmasking and the larger observed amplitude in the separated recording condition. Findings from the current study are in agreement with those reported by Wilson and Krishnan (2005) who demonstrated an FFR amplitude recovery with the introduction of binaural cues (i.e. physiological unmasking). Results from the current study support the notion that the binaural processing of complex speech-like stimuli is measurable at the level of the brainstem, the primary site of origin of the FFR (Sohmer, Pratt, and Kinarti 1977; Chandrasekaran and

Kraus 2010). These findings are in agreement with others, who demonstrated in both animals and humans, the FFRs resistance to presence of noise (Li and Jeng 2011; Russo et al. 2005). To the authors knowledge, the current study is the first to measure this phenomenon at the level of the FFR using speech-like binaural difference cues.

Direct comparisons were made between the FFR and a behavioural correlate (LiSN-S) to determine the ability of the FFR to reflect spatial processing ability. The lack of correlation between the FFR amplitudes and the LiSN-S results suggests the spatial processing measured by the FFR differs from that measured by the LiSN-S. The absence of a relationship between the activity at the level of the FFR and behavioural measures would support the notion that lower brainstem structures are responsible for transfer of binaural information, but the activity at the brainstem does not define behavioural processing. While it is possible the FFR was not sensitive enough to identify processing at the level of the brainstem responsible for spatial listening, it is also feasible that spatial processing is defined by activity at higher levels within the central auditory nervous system (Fowler and Mikami 1996; Fowler 2017). Given the reliance of the LiSN-S on spatial streaming (Middlebrooks et al. 2002; Cameron and Dillon 2008), it is conceivable that spatial processing ability incorporates more centrally mediated processes and is defined by activity measurable at higher level centres including the auditory cortex (Fowler and Mikami 1996; Fowler 2017). Therefore, even though spatial cues appear to be managed at the level of the brainstem (FFR), this activity may be a necessary, but not essential condition for the behavioural tasks of the LiSN-S.

Limitations

Although the current study found a group data effect, the results suggests the described method is not suitable on an individual basis. The current study was set-up to be conducted in a clinical environment using equipment designed for clinical use. Modification of the current recording paradigm is therefore required before future investigations are undertaken at an individual level.

Conclusions

The present study's results suggest the FFR has the potential to reflect binaural difference cues important for binaural processing and spatial listening, but could be measuring different processes to those measured by the LiSN-S. Further investigation is still required into the neural mechanisms underlying spatial processing ability. Future research involving comparisons in children with confirmed auditory deficits (including spatial processing disorder) before and after auditory training may add to these findings.

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Disclosure statement

The author is not aware of any conflicts of interest.

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References

Aiken, S. J., and T. W. Picton. 2008. "Envelope and Spectral Frequency-following Responses to Vowel Sounds." *Hearing Research* 245 (1–2):35–47. doi:10.1016/j.heares.2008.08.004.

Ballachanda, B. B., and G. Moushegian. 2000. "Frequency-Following Response: Effects of Interaural Time and Intensity Differences." *Journal of the American Academy of Audiology* 11 (1):1–11.

Blauert, J. 1997. *Spatial Hearing: The Psychophysics of Human Sound Localization*. London (UK): MIT Press.

Brantberg, K., H. Hansson, P.-A. Fransson, and U. Rosenhall. 1999. "The Binaural Interaction Component in Human ABR Is Stable within the 0-to 1-ms Range of Interaural Time Differences." *Audiology and Neuro-Otology* 4 (2):88–94. doi:10.1159/000013825.

Bronkhorst, A., and R. Plomp. 1988. "The Effect of Head-induced Interaural Time and Level differences on speech intelligibility in noise." *The Journal of the Acoustical Society of America* 83 (4):1508–1516. doi:10.1121/1.395906

Bushara, K. O., A. Weeks, K. Ishii, J. Catalan, B. Tian, J. Rauschecker, and M. Hallett. 1999. "Modality-Specific Frontal and Parietal Areas for Auditory and Visual Spatial Localisation in Humans." *Nature Neuroscience* 2 (8):759–766. doi:10.1038/11239.

Brugge, J. F., and C. D. Geisler. 1978. "Auditory Mechanisms of the Lower Brainstem." *Annual Review of Neuroscience* 1:363–394. doi:10.1146/annurev.ne.01.030178.002051.

Buchholz, J. M., H. Dillon, and S. Cameron. 2013. "Towards a Listening in Spatialized Noise Test using Complex Tones." In Proceedings of Meetings on Acoustics ICA2013 19 (1):050047. ASA.

Cameron, S., and H. Dillon. 2007. "Development of the Listening in Spatialized Noise-Sentences Test (LiSN-S)." *Ear and Hearing* 28 (2):196–211. doi:10.1097/AUD.0b013e318031267f.

Cameron, S., and H. Dillon. 2008. "The Listening in Spatialized Noise-Sentences test (LISN-S): Comparison to the Prototype LISN and results from Children with Either a Suspected (central) auditory processing disorder or a confirmed language disorder." *Journal of the American Academy of Audiology* 19 (5):377–391. doi:10.3766/jaaa.19.5.2

Cameron, S., H. Glyde, and H. Dillon. 2012. "Efficacy of the LiSN & Learn Auditory Training Software: Randomized Blinded Controlled Study." *Audiology Research*, 2:86–93. doi:10.4081/audiores.2012.e15.

Carhart, R., and J. Jerger. 1959. "Preferred Method for Clinical Determination of Pure-Tone Thresholds." *Journal of Speech and Hearing Disorders* 24:330–345. doi:10.1044/jshd.2404.330.

Chandrasekaran, B., and N. Kraus. 2010. "The Scalp-recorded Brainstem Response to Speech: Neural Origins and Plasticity ." *Psychophysiology* 47 (2):236–246. doi:10.1111/j.1469-8986.2009.00928.x.

Ching, T. Y., E. van Wanrooy, H. Dillon, and L. Carter. 2011. "Spatial Release from Masking in Normal-Hearing Children and Children Who Use Hearing Aids." *The Journal of the Acoustical Society of America* 129 (1):368–375. doi:10.1121/1.3523295.

Clark, J. L., G. Moushegian, and A. L. Rupert. 1995. *Interaural Time Effects on the Frequency-following Response*. Doctoral dissertation, University of Texas at Dallas.

Clinard, C. G., S. L. Hodgson, and M. E. Scherer. 2017. "Neural Correlates of the Binaural Masking Level Difference in Human Frequency-Following Responses." *Journal of the Association for Research in Otolaryngology*: *Jaro* 18 (2):355–369. doi:10.1007/s10162-016-0603-7.

Coffey, E. B., S. C. Herholz, A. M. Chepesiuk, S. Baillet, and R. J. Zatorre. 2016. "Cortical Contributions to the Auditory Frequency-following Response Revealed by MEG." *Nature Communications* 7:1–11. doi:10.1038/ncomms11070.

Dobie, R., and S. Norton. 1980. "Binaural Interaction in Human Auditory Evoked Potentials." *Electroencephalography and Clinical Neurophysiology* 49 (3–4):303–313. doi:10.1016/0013-4694(80)90224-2

Dobie, R. A., and C. I. Berlin. 1979. "Binaural Interaction in Brainstem-Evoked Responses." *Archives of Otolaryngology* (*Chicago, Ill*: *1960)* 105 (7):391–398. doi:10.1001/archotol.1979.00790190017004

Du, Y., L. Kong, Q. Wang, X. Wu, and L. Li. 2011. "Auditory Frequency-following Response: A Neurophysiological Measure for Studying the "Cocktail-Party Problem"" *Neuroscience and Biobehavioral Reviews* 35 (10):2046–2057. doi:10.1016/j.neubiorev.2011.05.008.

Fowler, C. G. 2017. "Electrophysiological Evidence for the Sources of the Masking Level Difference." *Journal of Speech, Language, and Hearing Research*: *JSLHR* 60 (8):2364–2374. doi:10.1044/2017_JSLHR-H-16-0251.

Fowler, C. G., and C. Mikami. 1996. "Phase Effects on the Middle and Late Auditory Evoked Potentials." *Journal of the American Academy of Audiology* 7 (1):23–30.

Freyman, R. L., K. S. Helfer, D. D. McCall, and R. K. Clifton. 1999. "The Role of Perceived Spatial Separation in the Unmasking of Speech." *The Journal of the Acoustical Society of America* 106 (6):3578–3588. doi: 10.1121/1.428211

Furst, M., S. Eyal, and A. D. Korczyn. 1990. "Prediction of Binaural Click Lateralization by Brainstem Auditory Evoked Potentials." *Hearing Research* 49 (1–3):347–359. doi:10.1016/0378-5955(90)90113-4

Furst, M., R. A. Levine, and P. M. McGaffigan. 1985. "Click Lateralization is Related to the Beta Component of the Dichotic Brainstem Auditory Evoked Potentials of Human Subjects." *The Journal of the Acoustical Society of America* 78 (5):1644–1651. doi:10.1121/1.392802

Glaser, E., C. Suter, R. Dasheiff, and A. Goldberg. 1976. "The Human Frequency-following Response: its Behavior during Continuous Tone and Tone Burst Stimulation." *Electroencephalography and Clinical Neurophysiology* 40 (1):25–32. doi:10.1016/0013-4694(76)90176-0

Goupell, M. J., and W. M. Hartmann. 2007. "Interaural Fluctuations and the Detection of Interaural Incoherence. III. Narrowband Experiments and Binaural Models." *The Journal of the Acoustical Society of America* 122 (2):1029–1045. doi:10.1121/1.2734489.

Graydon, K., G. Rance, R. Dowell, and B. Van Dun. 2017. "Consequences of Early Conductive Hearing Loss on Long-Term Binaural Processing." *Ear and Hearing* 38 (5):621–627. doi:10.1097/AUD.0000000000000431.

Guinan, J. J., B. E. Norris, and S. S. Guinan. 1972. "Single Auditory Units in the Superior Olivary Complex: II: Locations of Unit Categories and Tonotopic Organization." *International Journal of Neuroscience* 4 (4):147–166. doi:10.3109/00207457209164756.

Haywood, N. R., J. A. Undurraga, T. Marquardt, and D. McAlpine. 2015. "A Comparions of Two Objective Measures of Binaural Processing: The Interaural Phase Modulation following Response and the Binaural Interaction Component." *Trends in Hearing* 19:1–17. doi:10.1177/2331216515619039.

Hirsh, I. 1948. "Binaural Summation and Interaural Inhibition as a Function of the Level of Masking Noise." *The American Journal of Psychology* 61 (2):205–213. doi:10.2307/1416966

Ihlefeld, A., W. Chen, and D. Sanes. 2016. "Developmental Conductive Hearing Loss Reduces Moduation Masking Release." *Trends in Hearing* 20:1–14. doi:10.1177/2331216516676255.

Jerger, J. (1970). Clinical experience with impedance audiometry. Archives of otolaryngology, 92(4):311–324.

Johnson, K. L., T. Nicol, S. G. Zecker, and N. Kraus. 2008. "Developmental Plasticity in the Human Auditory Brainstem." The *Journal of Neuroscience*: *The Official Journal of the Society for Neuroscience* 28 (15):4000–4007. doi:10.1523/JNEUROSCI.0012-08.2008.

Joris, P. X., and T. Yin. 1995. "Envelope Coding in the Lateral Superior Olive. I. Sensitivity to Interaural Time Differences." *Journal of Neurophysiology* 73 (3):1043–1062. doi:10.1152/jn.1995.73.3.1043.

Junius, D., H. Riedel, and B. Kollmeier. 2007. "The Influence of Externalization and Spatial Cues on the Generation of Auditory Brainstem Responses and Middle Latency Responses." *Hearing Research* 225 (1–2): 91–104. doi:10.1016/j.heares.2006.12.008.

Kevanishvili, Z., and Z. Lagidze. 1987. "Masking Level Difference: An Electrophysiological Approach." *Scandinavian Audiology* 16 (1):3–11. doi:10.3109/14992028709042149.

Knudsen, E., S. Esterly, and J. Olsen. 1994. "Adaptive Plasticity of the Auditory Space Map in the Optic Tectum of Adult and Baby Barn Owls in Response to External Ear Modification." *Journal of Neurophysiology* 71 (1):79–94. doi:10.1152/jn.1994.71.1.79.

Krishnan, A., and S. S. McDaniel. 1998. "Binaural Interaction in the Human Frequency-following Response: Effects of Interaural Intensity Difference." *Audiology & Neuro-Otology* 3 (5):291–299. doi:10.1159/000013801.

Lau, C., J. W. Zhang, J. S. Cheng, I. Y. Zhou, M. M. Cheung, and E. X. Wu. 2013. "Noninvasive fMRI Investigation of Interaural Level Difference Processing in the Rat Auditory Subcortex." *PLoS One* 8 (8):e70706 doi:10.1371/journal.pone.0070706.

Li, X., and F. C. Jeng. 2011. "Noise Tolerance in Human Frequency-following Responses to Voice Pitch." *The Journal of the Acoustical Society of America* 129 (1):21–26. doi:10.1121/1.3528775.

McEvoy, L. K., T. W. Picton, S. C. Champagne, A. J. Kellett, and J. B. Kelly. 1990. "Human Evoked Potentials to Shifts in the Lateralization of a noise." *Audiology*: *Official Organ of the International Society of Audiology* 29 (3): 163–180. doi:10.3109/00206099009072848

McPherson, D. L., and A. Starr. 1993. "Binaural Interaction in Auditory Evoked Potentials: Brainstem, Middle- and Long-latency Components." *Hearing Research* 66 (1):91–98. doi:10.1016/0378-5955(93)90263-Z

Middlebrooks, J. C., and D. M. Green. 1991. "Sound Localization by Human Listeners." *Annual Review of Psychology* 42:135–159. doi:10.1146/annurev.ps.42.020191.001031.

Middlebrooks, J. C., L. Xu, S. Furukawa, and B. J. Mickey. 2002. "Location signaling by cortical neurons.". In *Integrative Functions in the Mammalian Auditory Pathway*, edited by R.R. Fay, D. Oertel, A.N. Popper, 319–357. New York (NY): Springer.

Picton, T. W., L. K. McEvoy, and S. C. Champagne. 1991. "Human Evoked Potentials and the Lateralization of a Sound." *Acta Oto-Laryngologica* 111 (sup491):139–144. doi:10.3109/00016489109136791.

Pratt, H., A. Polyakov, and L. Kontorovich. 1997. "Evidence for Separate Processing in the Human Brainstem of Interaural Intensity and Temporal Disparities for Sound Lateralization." *Hearing Research* 108 (1–2):1–8. doi: 10.1016/S0378-5955(97)00033-6.

Russo, N. M., T. G. Nicol, S. G. Zecker, E. A. Hayes, and N. Kraus. 2005. "Auditory Training Improves Neural Timing in the Human Brainstem." *Behavioural Brain Research* 156 (1):95–103. doi:10.1016/j.bbr.2004.05.012.

Smith, J. C., J. T. Marsh, and W. S. Brown. 1975. "Far-Field Recorded Frequency-following Responses: Evidence for the Locus of Brainstem Sources." *Electroencephalography and Clinical Neurophysiology* 39 (5):465–472. doi:10.1016/0013-4694(75)90047-4

Sohmer, H., H. Pratt, and R. Kinarti. 1977. "Sources of Frequency following Responses (FFR) in Man." *Electroencephalography and Clinical Neurophysiology* 42 (5):656–664. doi:10.1016/0013-4694(77)90282-6

Tomlin, D., and G. Rance. 2014. "Long-Term Hearing Deficits after Childhood Middle Ear Disease." *Ear and Hearing* 35 (6):e233–e242. doi:10.1097/AUD.0000000000000065.

Wilson, J. R., and A. Krishnan. 2005. "Human Frequency-following Responses to Binaural Masking Level Difference Stimuli." *Journal of the American Academy of Audiology* 16 (3):184–195. doi:10.3766/jaaa.16.3.6

Yost, W. A., and R. H. Dye. 1997. "Fundamentals of Directional Hearing." *Seminars in Hearing* 18 (04):321–344. doi:10.1055/s-0028-1083035.

Zatorre, R. J., and V. B. Penhune. 2001. "Spatial Localization after Excision of Human Auditory Cortex." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 21 (16):6321–6328. doi:10.1523/JNEUROSCI.21-16-06321.2001.