

# USING THE AUDITORY BRAINSTEM RESPONSE ELICITED BY WITHIN-CHANNEL GAPS TO MEASURE TEMPORAL RESOLUTION

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## Résumé

Les potentiels auditifs du tronc cérébral (PÉATC) peuvent être utilisés pour mesurer l'activité temporelle précoce du système auditif. Des PÉATC des bruits intermittents ont été développés pour mesurer la réponse électrophysiologique à la stimulation auditive sans l'attention active. Dans la présente étude, des jeunes adultes ont écouté passivement des stimuli avec les périodes de silence de différentes largeurs dans des séquences séparées. Pendant une seule séquence, deux bruits à bande étroite identiques de 15 ms, avec une fréquence centrale de 750 ou 3750 Hz, ont été présentés avec une période de silence (durée de 2, 5, 10, 20, 30, 40 ou 50 ms) avec un deuxième bruit suivi par un intervalle interstimulus de 50 ms ou plus. Des PÉATC ont été enregistrés à l'activation du premier bruit avant et au début du deuxième bruit (à la fin de la période silencieuse). L'amplitude de l'onde V après l'intervalle augmentait avec la durée plus longue de la période silencieuse. Ceci contrastait avec la vague V avant l'intervalle, le contrôle, qui restait relativement constant. Une différence significative a été constatée entre l'amplitude de la vague V évoquée avant et après l'intervalle, pour des durées d'intervalle égales ou inférieures à 20 ms et à 5 ms, pour 750 et 3750 Hz, respectivement. Les PÉATC évoqués par le bruit intermittent peuvent fournir des informations spécifiques à la fréquence pour l'étude de la résolution temporelle chez les populations avec divers problèmes auditifs.

**Mots clefs :** PÉATC, électrophysiologie, résolution temporelle, discrimination temporelle

## Abstract

The Auditory Brainstem Response (ABR) can be used to measure the early temporal activity of the auditory system. A gap-in-noise ABR has been developed to measure the electrophysiological response to auditory stimulation without attending to the task. In the present study, young adults passively listened to stimuli of various gap widths in separate sequences. In a single sequence, two identical 15 ms filtered noise bursts, with a center frequency of either 750 or 3750 Hz, were presented separated by a gap (2, 5, 10, 20, 30, 40 or 50 ms in duration), with the second noise burst followed by an interstimulus interval of no less than 50 ms. An ABR was recorded at the onset of the first noise burst, before the gap (pre-gap), and at onset of the second noise burst, after the gap (post-gap). The gap duration had a suppressive effect on the amplitude of wave V for the noise burst following the gap. In contrast, wave V amplitude before the gap (i.e. the control) remained relatively constant. A significant difference was found between the amplitude of wave V elicited before and after the gap for gap durations equal to and below 20 and 5 ms, for 750 and 3750 Hz, respectively. The gap-in-noise ABR can potentially provide frequency-specific information for the study of temporal resolution in populations with a variety of hearing disorders.

**Keywords:** ABR, electrophysiology, temporal resolution, gap detection

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## 1 Introduction

Temporal resolution refers to the ability to detect changes in the envelope of a sound over time [1]. It is used for comprehension of speech by detecting the separation between words. The mechanism of temporal resolution is modelled in Moore (1995) in 4 phases: 1) bandpass filtering, 2) compressive nonlinearity, 3) a sliding temporal integrator, and 4) a decision device. As a stimulus enters the cochlea, it engages a specific location of the basilar membrane that is most sensitive to the stimulus frequency.

The basilar membrane then displaces in response to the stimulus and triggers a nerve spike [2]. The neural spikes are then processed in a sliding temporal integrator where the window builds when the stimulus is turned on and decays when it is turned off. It is believed this process occurs after the auditory nerve [1], possibly linking the peripheral temporal information to cortical rules that determine if the input originating from the temporal integrator is qualified as a "gap". Indeed, studies where the auditory cortex was ablated bilaterally in rats showed elevated gap detection thresholds [3].

Behavioural gap detection thresholds are often used to investigate temporal processing. Gap detection methodologies determine the threshold of detecting a gap, or a just-noticeable silent interval, within a sound by altering

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the length of the interval [4-6]. These studies, using broadband noises, determined normal hearing participants could detect gaps as small as 2 to 3 ms in length [4], however its perceptibility can vary with changes to intensity [4, 5] and stimulus bandwidth [7-9]. In addition to this, performance is affected by the level of attention, concentration, motivation, and the response criteria used [10, 11]. It is thus of interest to use alternative measures that are more objective to mitigate the potential effects of performance on the detection of gaps.

Objective measures such as auditory event-related potentials have been demonstrated as an alternative method of measuring neural gap detection [12-19]. The advantage of such neural measures is that they are often elicited passively, in the absence of attention, while a participant is reading a book or watching a film.

The auditory brainstem responses (ABR) have been used clinically to assess the summed activity of auditory nerve [20]. The ABR is an acoustically stimulated electrophysiological response that represents synchronized activity that appears as a five-peak waveform generated less than 10 ms following the onset of a stimulus [21]. These voltage changes are recorded using 3 to 4 electrodes placed on the scalp of the head. One of the advantages of the ABR is that it is inexpensive, non-invasive and routinely used in clinical practice.

ABRs using gapped stimuli have been explored to measure temporal discrimination in animal models, pediatric populations, and the elderly [22-24]. The ABR elicited by gaps was investigated using two identical noise bursts separated by a silent interval. The ABR to the first noise represents a typical response that would be similar to a non-gapped ABR. The ABR to the second noise is an altered response that is reflective of the length of the silent interval. Boettcher et al. (1996) used Mongolian gerbils to identify latencies of waves I, II, III and IV for the second noise occurring 1.4 to 2.0, 2 to 3, and 4 to 7 ms, respectively, following the offset of the gap. The amplitudes were measured from the peak of wave II to the trough following wave III, and the peak of wave IV to the trough following wave V. The amplitudes for the second noise burst were generally smallest for the narrowest gaps and grew as the gap size widened. The latency changes after the gap were small but consistently shorter as gap duration increased, particularly for gerbil wave IV. Both Werner et al., (2001) and Poth et al. (2001), showed the amplitude of human wave V, occurring at a similar latency following the gap as in gerbils, increased with widening gap size. Werner et al. (2001) found measureable differences in wave V amplitude for gap sizes as small as 4 ms. It was demonstrated that when the ABR is used as a measure of gap detection threshold in humans, the results correspond well with established psychophysical measures [22].

We are interested in further exploring the early impairments that may be responsible for impaired gap detection by differentiating the ABR gap-in-noise elicited by higher and lower frequency filtered stimuli. The gap-elicited ABR has been investigated using broadband noise bursts, which does not provide information on the effects of

varying the spectral characteristics of the carrier stimulus. Behavioural responses to large gaps do not change with the carrier frequency [25], however increasing the center frequency can decrease the gap detection threshold [26, 27]. Shailer and Moore (1987) interpreted this effect as the result of inherent fluctuations in the low frequency noise that resemble the embedded gap, making detection of the gap more difficult. It is unclear whether this confusion occurs at the level of auditory bandpass filters or later in the higher-order decision device.

The present experiment aims to investigate the use of the ABR gap in noise paradigm in normal hearing participants, as a means of validating the methodology for use with frequency-specific stimuli. Noise burst center frequency and gap duration will be varied and ABR wave V amplitudes will be measured and compared before and after the gap similar to Poth et al. (2001), and Werner et al. (2001). We hypothesize that the amplitude of the ABR wave V following increasing gap lengths will show similar recovery for both center frequency stimuli as previous reported for wave V elicited by the post-gap stimulus.

## 2 Method

### 2.1 Participants

Fifteen normal hearing participants ages 18-30 years old (7 males and 8 females, mean age=21.1) were recruited for this study. All participants completed a questionnaire on their auditory health and noise history to ensure that none of the participants were exposed to more than 3 hours of noise per week. Based on these questionnaires, none of the participants reported any known hearing difficulties. Participant hearing thresholds were measured using an audiometer (AC40, Interacoustics) and with supra-auricular headphones (TDH39P, Telephonics). All participants had auditory thresholds of 15 dB HL or lower at 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz. All procedures and testing were approved by the University of Ottawa Research Ethics Board and written and verbal consent was given by the participants prior to the testing.

### 2.2 Electrophysiology

#### Preparation

Participants were tested while resting in an inclined armchair in a sound isolated Faraday cage. The ABR was acquired from a one-channel montage of high forehead to ipsilateral mastoid. The contralateral mastoid served as a ground using an Amplitrode™ (Vivosonic). All electrodes were disposable pre-gelled adhesive electrodes (Neuroline 720, Ambu) and each surface was prepared using an abrasive gel (NuPrep, Weaver and Company) and an alcohol wipe to ensure optimal electrode contact. Prior to recording, the electrical impedance of each electrode was below 5 k $\Omega$ .

#### Stimulus

In a single sequence, two identical 15 ms filtered Gaussian noise bursts were presented, separated by a gap, with the

second noise burst followed by an interstimulus interval of no less than 50 ms. Each noise burst was filtered using a 2<sup>nd</sup> order Butterworth filter with a 1 ms Blackman ramp on and off (within the 15 ms noise). The filters were set from 500 to 1200 Hz, for the low frequency condition, and 3500 to 4000 Hz, for the high frequency condition. Stimuli were presented at 100 dB pe SPL through an insert tube earphone (Etymotics, ER-3) placed in the right ear. Each test session ran multiple gap lengths:  $\Delta t = 2, 5, 10, 20, 30, 40$  and 50 ms, presented in descending order. The stimulus rate was held constant at 12.2 Hz, causing the interstimulus interval (ISI) to range from 50 ms (for a gap of 50 ms) to 100 ms (for a gap of 2 ms).

### Recordings

ABR waveforms were recorded using the Vivosonic Integrity system which includes the Vivolink V500 (VN0266, Vivosonic) which communicates via Bluetooth connection to a laptop with the Vivosonic Integrity V500 software (version 8.3, Vivosonic). The system was calibrated according to manufacturer recommendations. Filter settings were 30 to 1500 Hz with a 12 dB/oct high pass and a 24 dB/oct low pass filter roll off. Polarity was set to rarefaction. For each subject and each test condition (gap/noise frequency), two ABRs were recorded: one corresponding to the onset of the first noise burst before the gap (pre-gap) and one corresponding to the onset of the second noise burst (i.e. post-gap). This was called the ‘two-stimulus trial’. For 10 subjects, the pre-gap average was also recorded without the synchronization of the post-gap, a ‘one-stimulus trial’, in order to compare the pre-gap ABR with a control ABR. All recordings were conducted when the patient was at rest and the raw EEG was relatively flat. Kalman weighting was used in conjunction with the Amptrode™ for artifact rejection [28].

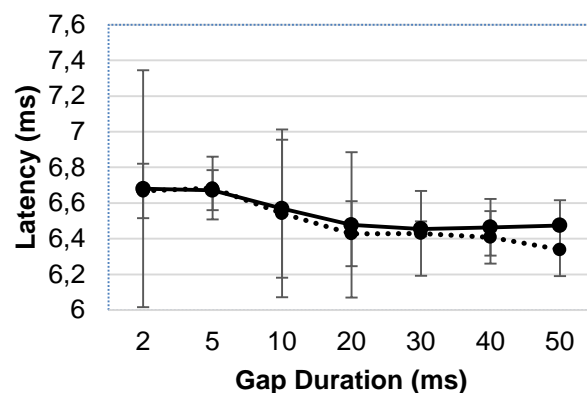
Responses were sequentially replicated for the first five participants up to 2000 sweeps for each gap width and frequency to ensure replicability of results. In other words, the trial was repeated a second time to ensure that the waveforms were not significantly different. For the remaining 10 participants, two buffer channels were used to separate the data into two grand average waveforms. The two buffers were compared to measure the replicability of the waves. After 1200 sweeps were collected, if the two buffers were correlated by 0.7 or higher, the recording was retained for further analysis. For correlations below 0.7, testing continued until the residual noise was below 0.035  $\mu\text{V}$  or 2500 sweeps. A t-test determined this method had higher correlations and lower residual noise than the initial sequential method.

### Data analysis

Waveforms before and after the gap were subjectively marked based on the average known latency of wave V as previously reported [22]. Two experienced judges decided on the presence or absence of the wave V. A response for the presence of wave V was retained if both judges agreed.

The latency and amplitude of wave V was then computed using the Vivosonic Integrity software.

The latency was determined according to the local maximum of the expected latency range for waves I and V as reported in Boettcher et al. (1996) (see introduction).



**Figure 1:** Latency of wave V following the gap for various gap durations. The solid line represents the latencies for wave V elicited by a 750 Hz stimulus. The dotted line shows the latencies for the ABR elicited by the 3750 Hz condition. Standard deviation is indicated by brackets.

The amplitude of wave V was measured as the amplitude difference between the peak to the following trough. A 3-way repeated measures ANOVA was performed on the amplitude of wave V using the measure of gap size (2, 5, 10, 20, 30, 40 and 50 ms), position (pre or post-gap), and frequency (750 or 3750 Hz). A post-hoc analysis using a pairwise t-test was applied to compare the amplitude before and after each gap. A one-tailed p-value was chosen as only positive amplitudes were considered valid wave V deviations. The two and one-stimulus trials were compared in a repeated measures ANOVA on frequency, stimulus (one or two-stimulus) and gap width.

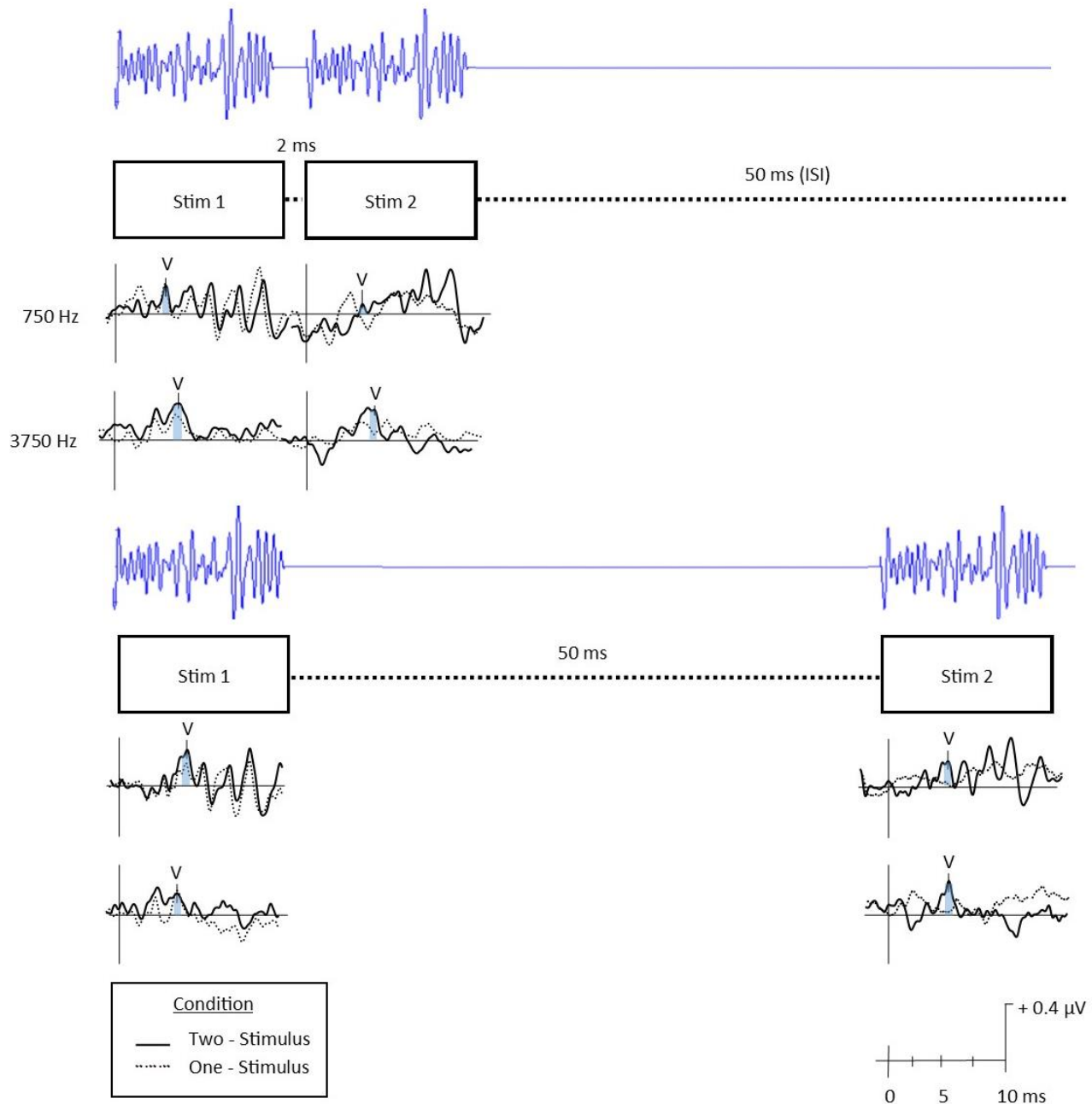
## 3 Results

### 3.1 Effect of stimulus frequency on the ABR latency

The latency of the auditory brainstem response at wave V was consistent for both before the gap and following the gap. Figure 1 shows the latency responses were not significantly different between the two frequency conditions. The latency also did not significantly change with the increase of gap duration, however a slight decreasing trend is observed.

### 3.2 Effect of stimulus frequency on the ABR amplitude

The auditory brainstem response was analyzed using a peak-to-peak measure of the maximum (peak) of wave V to the immediate trough. In other words, the maximum positive deflection to the preceding negative deflection at the latency range reported in previous studies [22, 23].



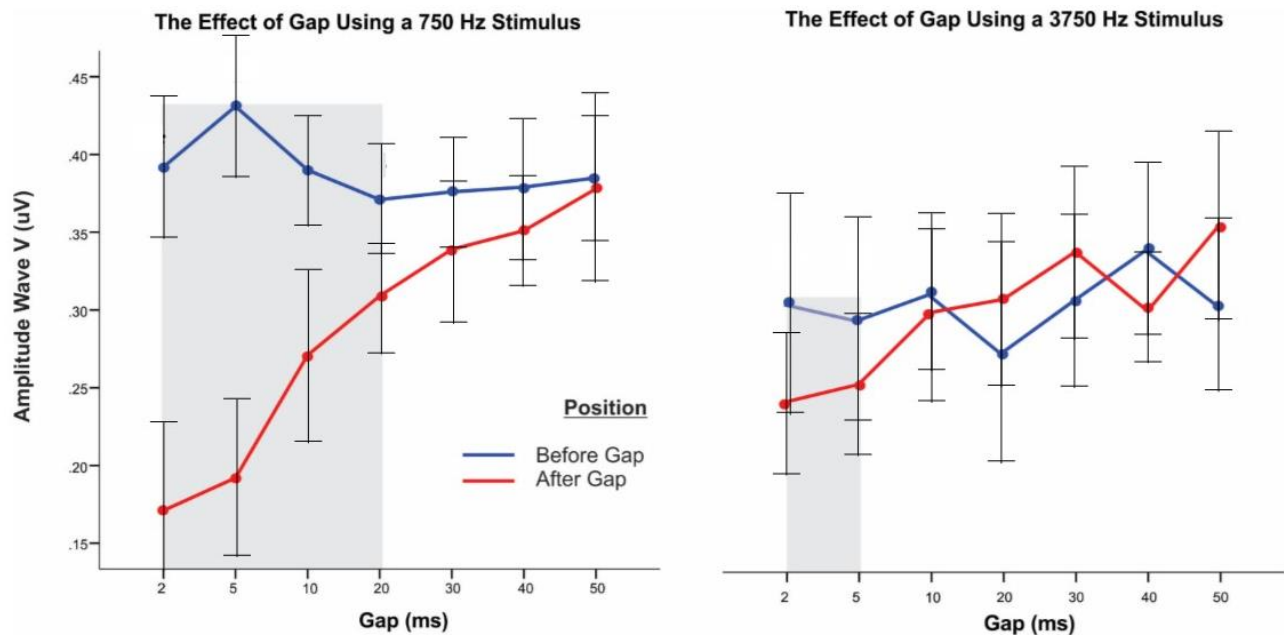
**Figure 2:** The two-stimulus design gaps of various widths separating stimulus 1 and 2. The stimulus rate was kept at a constant of 7.6 Hz and the ISI varied based on the length of the gap from a maximum of 100 ms (for the 2-ms gaps) to a minimum of 50 ms (for the 50-ms gaps). The ABR, shown for a single participant (subject 6), was elicited by the onset of stimulus 1 and the onset of stimulus 2 after the gap, shown with the solid lines. The dotted lines represent the ABR elicited by only stimulus 1 in the absence of stimulus 2 (i.e one-stimulus condition). The amplitude was measured peak-to-peak from the local maximum of wave V to the subsequent trough, therefore the baseline was set to the trough of wave V, or when the wave V was absent, to the trough where wave V is seen in the two-stimulus condition. For stimuli at 750 and 3750 Hz, there was a decrease in the amplitude of the post-gap wave V for 2-ms gaps, however when the gap was large as in the 50-ms gaps, the post-gap wave V amplitude were similar to pre-gap values.

This peak-to-peak measure was determined for both the onset of the stimulus before the gap and following the gap as shown in Figure 2.

A three-way repeated measures ANOVA revealed a three-way interaction between gap width, position, and frequency,  $F(6.54)=2.78$ ,  $MSE=.16$ ,  $p=.02$ . Larger amplitudes were recorded for wave V elicited by the low

frequency stimulus (750 Hz) compared to the high frequency stimulus (3750 Hz),  $F(1,9)=2.78$ ,  $MSE=0.16$ ,  $p=.002$ . This can be seen in the average amplitude shown in figure 3.

However, the low-frequency condition showed smaller amplitudes for the smaller gap durations than the high frequency condition.



**Figure 3:** Mean peak-to-peak amplitude of wave V before and after a silent gap between two noise bursts (n=10) for the 750 Hz stimulus and the 3750 Hz stimulus. As indicated in the shaded grey area, the wave V amplitude before the gap (blue) is significantly larger than post-gap (red) for gap widths below 20 ms and 5 ms, for the 750 and 3750 Hz stimuli, respectively (one-tailed t-test,  $p < 0.05$ ). Brackets indicate standard deviation.

### 3.3 Effect of gap width on the ABR amplitude

Figure 3 and Table 1 show the post-gap amplitudes of wave V at lower gap widths were significantly smaller than the amplitudes for larger gap widths in both the high and low frequencies.

At 750 Hz, the post-gap amplitude was significantly smaller at and below 20 ms ( $t(9) < 2.3$ ,  $p < 0.026$ ). While at 3750 Hz, only gap widths under 5 ms showed significant amplitude differences ( $t(9) < 2.8$ ,  $p < 0.05$ ).

### 3.4 Effect of single and double stimulus averaging

The ABR was elicited with either a single stimulus, stimulus 1, or with two stimuli, stimulus 1 and 2. As seen depicted in Figure 2, the second stimulus elicits a change on the amplitude of the post-gap ABR, however there was no effect of the post-gap averaging on the pre-gap.

When the ABR amplitude was measured before the gap using either a single or two stimulus averaging within a recording, there was no significant difference to the amplitude of the pre-gap ABR,  $F(1,9) = 1.13$ ,  $MSE = .012$ ,  $p = .32$ . There was also no interaction between gap duration and stimulus condition.

## 4 Discussion

Our results demonstrate the feasibility of using the ABR recordings to a gapped stimulus among normal hearing participants using a high and low-frequency noise carrier. The results show a significant suppression of the post-gap amplitude of wave V for small gap durations for low and high frequencies. For large gap durations wave V shows an unsuppressed amplitude that is not significantly different from the pre-gap ABR.

**Table 1:** Mean wave V amplitude before and after the onset of the gap at various widths for the 750 and 3750 Hz conditions. Standard deviation between parentheses. (\*one-tailed t-test,  $p < 0.05$ )

Gap	Pre/Post-gap	Mean amplitude, $\mu V$ (SD)	
		750 Hz	3750 Hz
2 ms	Pre	.39 (.09)	.31(.14)
	Post	.17 (.11)*	.24(.09)*
5 ms	Pre	.43 (.09)	.30(.13)
	Post	.19 (.10)*	.25(.09)*
10 ms	Pre	.39 (.07)	.31(.10)
	Post	.27 (.11)*	.30(.11)
20 ms	Pre	.37 (.07)	.28(.14)
	Post	.31 (.07)*	.31(.11)
30 ms	Pre	.38(.07)	.31(.11)
	Post	.34(.09)	.34(.11)
40 ms	Pre	.38(.09)	.34(.11)
	Post	.35(.07)	.35(.07)
50 ms	Pre	.39(.08)	.31(.11)
	Post	.38(.12)	.36(.12)

Previous studies on the ABR and gap detection have shown that the onset of the stimulus before a gap elicits a clear ABR with a latency that is similar to a regular click stimulus [22, 23]. This is similar to the findings in this study, which showed an average wave V latency across the 750 and 3750 Hz conditions of 6.0 to 7.3 ms post-gap. This is a more narrow range of latencies than the wave V latency post-gap to a broadband click of 6.0 to 8.4 ms [23]. All latencies before and after the gap were not significantly different which is supported by previous studies [22, 23]. In Poth et al. (2001), gaps of 4, 8, 32 and 64 ms were inserted

within a 100-ms broadband click. When testing young subjects, a measurable wave V amplitude decreased post-gap with decreasing gap duration similar to the results of this study. In Werner et al. (2001), ABR gap detection was measured using gaps inserted in 30-ms, 7 kHz low-pass filtered noises. They determined an electrophysiological gap detection threshold of 2.4 ms which was the smallest gap length that elicited a detectable post-gap wave V. This implies the post-gap wave V amplitude also decreased with decreasing gap width similar to Poth et al. (2001) and the amplitudes reported in this study.

Suppression of the ABR following the gap may be related to the temporal representation of the early auditory system. Reliable neuronal phase locking is known to occur for frequencies less than 2000 Hz and not for higher frequencies [2], which may be the reason for fewer gap widths with significant post-gap wave V suppression than the lower frequency condition.

In other words, the afferent neurons that lock themselves to the phase of higher frequency sounds may not be able to discharge with enough efficiency as the lower frequency sounds. This has been discussed in previous literature regarding the encoding of the auditory nerve fibers using temporal fine structures and the slower temporal envelope information [29]. At higher frequencies, the auditory nerve fibers do not phase lock to the temporal fine structures, which means that auditory nerve fibers are unable to discharge at a rate that corresponds to the timing of the sinusoidal band-pass carrier fluctuations. It is thus possible that cortical processing uses the changes in discharge, as represented by the wave V amplitude suppression, as an indicator that there is no gap in the stimulus.

Studies on behavioural gap detection show roughly constant gap thresholds of 6-8 ms for frequencies 400 to 2000 Hz at intensity levels above 55 dB SPL [30]. This suggests that gap sizes that are undetected behaviourally (i.e. below the gap thresholds) may correspond with a greater suppression of the post-gap amplitude. If this were the case, then the higher frequencies where the amplitude suppression occurs for only 2 of the 7 gaps shows better gap detectability. Improved gap detection with narrower stimulus bandwidth has been reported [30]. Behavioural gap detection intra-subject variability increases with larger signal bandwidth [7]. As mentioned earlier, the low frequency stimulus in this study elicited significant post-gap suppression for larger gap widths, up to 20 ms, whereas it occurs for smaller gaps, up to 5 ms, for the high frequency stimulus. This suggests that the ABR suppression occurs for a smaller range of gap widths with a high-frequency carrier (10-50ms) than the low-frequency carrier (30-50ms). Unlike the behavioural gap detection, the variability of the ABR amplitude was roughly stable for the high and low frequency conditions.

## 5 Conclusion

This study demonstrates the utility of the ABR as a measure of the early, short-latency response to gaps within a high

and a low carrier frequency stimulus. Several previous studies indicate that the wave V is an appropriate biomarker of post-gap amplitude changes that are related to psychophysical gap detection. This study demonstrates that the suppression of the post-gap wave V amplitude may be an indicator of the afferent information that allows the central system to determine the presence of a gap. The results from this study suggest that the ABR gap detection is different for low frequencies compared to high frequencies. Further studies comparing the amplitude changes to behavioural results using similar carrier frequencies may elucidate whether such ABR suppression is related to perceptual temporal resolution.

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**NOISE**

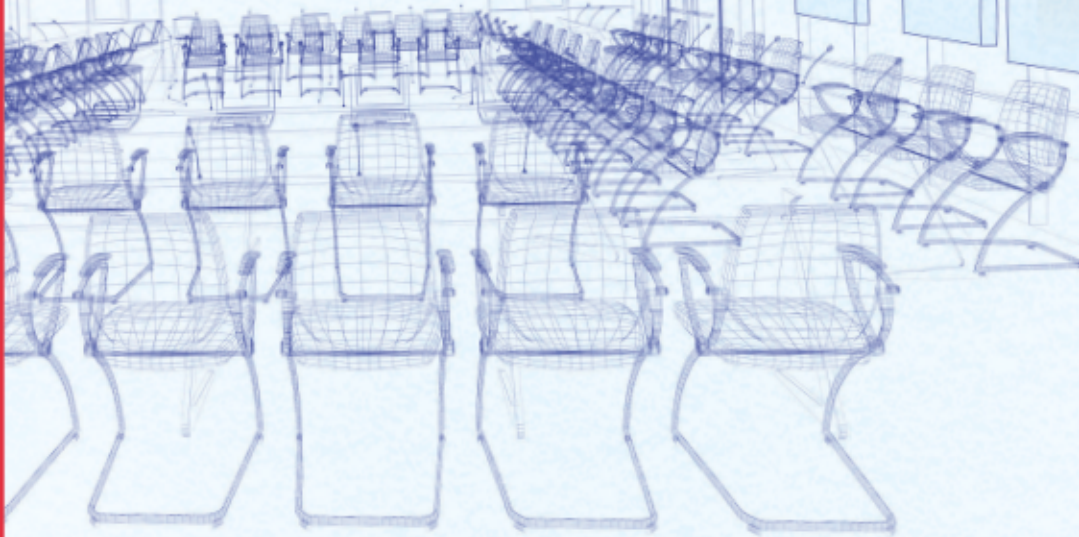
**VIBRATION**

- > Noise & Vibration Control in Land-use Planning
- > Noise & Vibration Studies: Residential and Commercial
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