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THE BINAURAL INTERACTION COMPONENT IS ENHANCED WITH CHIRPS RELATIVE TO CLICKS AND PRODUCES BETTER BEHAVIORAL LATERALIZATION

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ABSTRACT

The binaural interaction component (BIC) of the auditory brainstem response (ABR) is obtained by subtracting a binaurally-evoked ABR from the sum of monaural left and right ear ABRs. BIC amplitude is modulated by interaural time differences (ITDs) and has been proposed as a biomarker of binaural hearing ability. Traditionally, clicks are used to evoke ABRs; however, chirps are recommended to compensate for the cochlear traveling wave and enhance wave V. Whether chirps improve BIC measurements has not been systematically examined. Here, ABRs and BICs were measured in subjects (n = 6; 21-29 years) for three stimuli; 1) 100-µsec clicks, 2) level-independent CE chirps, and 3) Level-Specific (LS) chirps at four intensities ranging from 65-40 dB nHL. Subjects also completed behavioral testing measuring ITD discrimination thresholds. Compared to clicks, chirps generally elicited larger monaural and binaural wave V and larger BIC amplitudes, particularly at lower intensities. Subjects also exhibited lower ITD thresholds for chirps than clicks, mainly at lower stimulus levels. Chirps may provide an enhancement to ABR wave V and BIC, improving signal-to-noise ratio and reliability. The improved behavioral sensitivity to ITDs with chirps supports the hypothesis that BIC arises from binaural brainstem nuclei that are important for binaural hearing.

Keywords: *auditory brainstem response, binaural interaction component, binaural hearing, interaural time difference*

1. INTRODUCTION

The auditory brainstem response (ABR) is an electrophysiological measure widely used both clinically and in research to investigate the integrity of the auditory system pathway. A binaural interaction component (BIC) can be obtained by subtracting a binaurally evoked ABR from the sum of the monaural right and left ear ABRs [1]. If there were two independent monaural pathways, the resulting difference waveform would be zero (minus any measurement artifact or noise); However, a small negative component appears at approximately the latency of ABR wave V or its roll-off slope in human subjects. This indicates a different amount of synchronous neural activity occurring in the brainstem during binaural stimulation than during monaural. In the literature, this most prominent BIC component has been called “DN1” [2-6].

The ABR BIC has been measured in a number of animal models [2], [7], [8], as well as in normal-hearing human subjects [6], [9-16]. The BIC has been reported to be abnormal in the elderly [17], in persons with multiple sclerosis [18], in specific language disorder [19], and in children diagnosed with CAPD [20], [21]. The ABR BIC is thought to be generated at the level of the lateral superior

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olive of the brainstem ([1], [8], [22]), an area that has been associated with neural processing of interaural sound cues.

The BIC has received increasing attention as a non-invasive biomarker of binaural processing. For example, researchers have observed systematic changes in the amplitude and latency of the BIC DN1 component when interaural cues that control perceptual lateralization are varied in normal hearing adults. Specifically, latency of DN1 systematically alters with increasing interaural level difference (ILD) and/or interaural time difference (ITD) cues [3], [6], [12], [23], [24], [25]. In addition, BIC amplitude has been found to correspond with a behaviorally measured ability to lateralize sound as a function of ITD and ILD and its presence is assumed to indicate fusion of binaural stimuli [12], [23], [26]. Recently, Brown et al. [27] and Sammeth et al. [16] reported that BIC amplitude also varies systematically with interaural frequency mismatch and corresponds to ITD sensitivity measured behaviorally.

Unfortunately, however, the ABR BIC has not proven to date to be useful as a potential clinical diagnostic indicator for suprathreshold hearing ability because it is not always obtained reliably in human subjects. While the BIC is readily obtained in sedated animals, it is time consuming and difficult to obtain a clear, replicable response in awake human subjects [6], [28]. This is mostly due to its very small size relative to the size of myogenic (muscle) and other noise artifacts in the waveform, and also because the larger head size in humans than in animal models (such as rodents) results in a surface electrode measurement that is farther away from the neural generators for the BIC [8]. In ongoing efforts to find a means to more reliably obtain the ABR BIC, members of our research lab recently showed that the use of an alternative to a standard ABR click stimulus, namely, a rising frequency "chirp" stimulus, optimizes recordings of the BIC in chinchillas [29]. The current experiment was designed to determine if this stimulus advantage is also seen in human subjects.

The stimuli typically used for measurement of ABRs and BIC is the acoustic click. However, some researchers have suggested that this might not always be the best stimulus choice to obtain a robust auditory electrophysiologic response [30], [31], [32], [33], [34]. This is because the traveling wave on the basilar membrane elicits an auditory system response first from high frequencies, then from progressively lower frequencies [35]. Cochlear tonotopicity reduces temporal response synchrony to a click stimulus, resulting in reduced ABR amplitude. Therefore, chirp stimuli have been developed that compensate for the dispersion of the traveling wave by presenting low frequencies first, then progressively higher frequencies in an upward sweep, and that have been found to produce larger ABR wave V amplitude at least at a moderately/high stimulus level ([24], [31], [33], [34], [36]. As BIC DN1 arises at a similar latency as ABR wave V, we hypothesize that chirps might produce a larger BIC response.

Chirps are now widely used clinically in ABR measurements, but to our knowledge only one publication has directly explored the use of chirps versus clicks to measure BIC DN1 in humans. Reidel and Kollmeier [24] reported that, compared to clicks, chirps designed to enhance monaural ABR wave V also produced larger BIC at low to moderate sound levels, although the enhancement was not as great as seen for wave V.

A chirp stimulus now commonly used in clinical auditory evoked potential measurement equipment that was empirically derived is the "CE-Chirp®" [33], [34]. Because derivation of the standard CE-Chirp is based only on the cochlear traveling wave delay at a moderate/high stimulation level (~60 dB nHL), it is considered a "level-independent" chirp [37]. However, it has been found that the frequency sweep rate of chirps should vary by stimulation level for optimal results [36], [38], [39]. As a consequence, so-called level-dependent chirps, or "Level-Specific (LS) CE-Chirps®", which compensate for this level effect were developed [39], [40].

Of note is that both standard CE-Chirps and LS-Chirps were designed to optimize ABRs measured monaurally, while BIC is derived from binaural versus monaural stimulation. In our study, Owrusky et al. [29] considered that a chirp stimulus specifically derived from BIC DN1 latency for different frequencies of stimulation might be optimal to enhance BIC response amplitude. In their results, however, no additional DN1 amplitude enhancement was found for the DN1 latency-derived chirps compared to LS-Chirps, and therefore in the current study we chose here to only use the standard CE-Chirp and LS-Chirps.

Specifically, the current study compared the ABR BIC measured in normal-hearing young adults across multiple stimulation levels for three stimuli: 1) a standard click, 2) the level-independent CE-Chirp, and 3) the level-dependent LS-Chirps. The purpose was to build on the work of Reidel and Kollmeier [24] and Owrusky et al. [29] to evaluate our hypothesis that LS-Chirps will generate significantly higher response amplitude for the ABR BIC in human subjects across stimulus levels than will either the standard CE-Chirp or a click. In this short paper, our main objectives were to investigate if 1) chirps improve BIC measurement in humans, and if 2) chirps alters ITD sensitivity compared to traditional click stimuli.

2. METHODS

Approval was obtained from the Colorado Multiple Institutional Review Board for human subjects. All subjects had bilateral hearing thresholds < 10 dB HL at frequencies from 250 Hz to 4000 Hz and < 15 dB HL for extended high frequencies of 6000 to 16000 Hz, with symmetrical hearing thresholds between the ears (< 10 dB difference at a given audiometric frequency). None of the subjects had a history of otologic or neurological disorder. Subjects were paid for participation in the study. Subjects were 6 normal hearing adults (4 females) aged 21 to 30 years.

2.1 ABR measurements

ABR measurements were completed across six, 2-hour sessions for each subject, completed on different days. Two sessions were used for each of the three stimulus types. For example, in the first session, measurements were obtained at four stimulus levels, and in the second session, the measurements were replicated.

ABR waveform acquisition was accomplished using the commercially available International Hearing System (IHS) Duet AEP measurement system with research module. EEG was amplified by 100,000 and were bandpass filtered 100-3000 Hz. Artifact rejection threshold was set to ± 20 µV. Three different stimuli were used: 1) 100-µs clicks, 2) CE chirp, and 3) Level Specific (LS) chirp. ABRs and BICs were measured with each stimulus at stimulus levels of 65, 60, 50 and 40 dB HL. For each ABR, 4000 total sweeps were averaged across two runs. The BIC was calculated post-hoc as the binaurally stimulated ABR minus the sum of the right and left ear monaural ABRs. Two complete BIC measurements were completed for each stimulus at each level, to confirm replicability of the DN1.

Stimulus level was calibrated via a 2cc coupler attached to a Larson-Davis sound level meter and Tektronix oscilloscope for determination of peak equivalent SPL of the stimuli compared to a 1000 Hz calibration tone. The stimulus repetition rate was ~11.1 per second and was presented in rarefaction. Stimuli were presented via ER-2 insert earphones. ABRs were recorded from Ambu Neuroline 720 disposable surface electrodes (Ambu Inc., Columbia, MD).

Following skin preparation, electrodes were placed according to the International 10-20 Electrode System [41] using a midline montage: Fz (high forehead) was referenced to the nape of the neck (just above the 7th cervical vertebra), with Fpz (low forehead) as the ground. Electrode impedances were < 5 kΩ (typically 2-3 kΩ) and balanced between electrode pairs within 1 kΩ. Subjects were seated comfortably with a neck pillow in a slightly reclining chair in a darkened room and asked to close their eyes, relax, and sit quietly or sleep during measurements.

2.1.1 Marking of the Waveforms

Marked and labeled peaks (Fig. 1) were initially placed on the waveforms by the first author, who is an experienced audiologist who did all the electrophysiological testing for this study, but were then reviewed by the second author, who is also an audiologist experienced in these

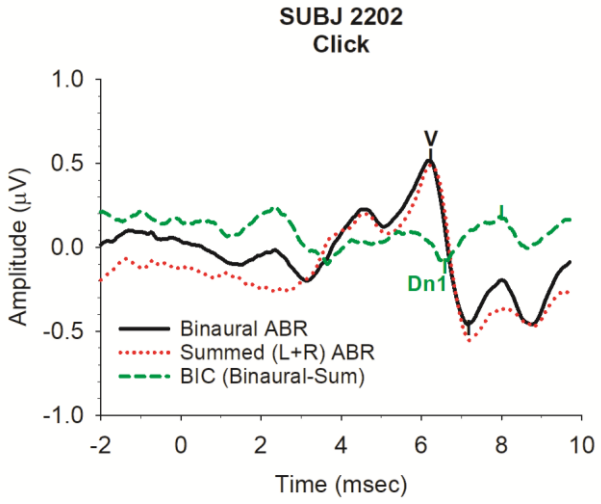

Figure 1. Example Binaural/Summed ABR and calculated BIC using clicks. Wave V was marked from the peak to following trough. BIC DN1 was marked as the most prominent trough and following peak occurring near ABR Wave V.

measures. In all cases, markings were agreed upon by both authors. All identifiable latencies and peak-to-trough amplitudes of waves I through VI of the monaural and binaural ABR waveforms were first marked, to aid in identification of the DN1 component of the BIC in the difference traces. The DN1 component of the BIC was identified as the most prominent negative peak in the temporal region of the difference waveform that corresponded to wave V and its roll-off slope and was only accepted as a valid response if it was replicable across both BIC traces for a given stimulus type and level. DN1 was marked both for latency of the negative trough, and for relative amplitude (negative peak to the

following positive peak) amplitude. When the positive peak following BIC was equivocal (e.g., as sometimes occurred in the presence of multiple fluctuations or a shallow rising slope), it was marked as the most prominent positive point occurring prior to the latency of an identifiable wave VI peak.

2.2 Behavioral ITD discrimination task

Behavioral measurements were completed across multiple sessions. The task measured both ITD discrimination threshold and subjective lateralization of each of the stimuli at four levels, 10, 20, 40 and 60 dB HL. The method was based on that used by Brown and Tollin [42], [43]. This task was implemented in a separate MATLAB program, with stimuli delivered via the playback system and insert earphones described above.

During testing, subjects sat at a desk in a lighted sound booth and responded using a large touch screen monitor (Fig. 2). On the screen was a schematic illustration of a head, with horizontal bars indicating the right and left sides of the head. Each trial consisted of presentations of two sequential sets of tone pips. A train of 5 stimuli (e.g, the CE chirp) at 14/sec was first presented simultaneously to each ear (ITD=0 µs) and this was followed by a train of 5 stimuli with a non-zero ITD. Left-favoring ITDs were imposed by delaying the stimulus to the right ear, and right-favoring ITDs imposed by delaying the stimulus to the left. The subject's task was to discriminate whether the second stimulus (target) fell perceptually to the left or the right of the first stimulus (reference). If the target set was perceived as falling to the right of the reference, the subject was instructed to touch the bar that was on the right side of the screen, and vice versa. Further, subjects were asked to indicate on the bar how far to the right or to the left the target appeared relative to the reference, i.e., a subjective lateralization task. Subjects received immediate feedback regarding the left/right discrimination response, via a green asterisk flashing on the bar if their response was correct, and a red asterisk flashing if their response was incorrect (these colors were readily discriminable by all subjects).

Each run started with the ITD for the second binaural stimulus train at 800 µs. ITD was then changed adaptively depending on the subject's response. A 3-down, 1-up procedure was used, i.e., three consecutive correct responses were required for the ITD to decrease, but one incorrect response resulted in an increase in the ITD, targeting a 79.4% correct threshold (Levitt, 1971). Step size was initially large but then rapidly decreased over a run, so that the task became increasingly difficult. Specifically, a log step size adjustment was used (1/100.2, then 1/10.05); i.e., the adjustment magnitude was a fixed percentage of the ITD magnitude so that step size decreased as subjects approached threshold. Within a run, two separate 3-down 1-up tracks were initialized and run simultaneously. Testing continued until 8 reversals were observed. The first 4 reversals were discarded, and the geometric mean of the last 6 reversals averaged to determine the ITD discrimination threshold for that condition.

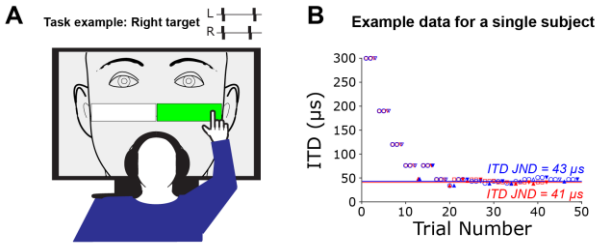

Figure 2. A) Subjects responded using a touch screen monitor and received feedback regarding the left/right response. B) A 3-down, 1-up procedure was used. Testing continued until 10 reversals were observed and the last 6 averaged to determine the ITD discrimination threshold (i.e,. ITD JND).

Practice runs were completed to familiarize and train subjects on the task. Subsequently, three runs were completed for each of the four stimulus levels, randomly ordered, and the average of the ITD discrimination thresholds for the three runs per frequency condition and stimulus level was used for final analysis.

3. RESULTS

3.1 ABR measurements

ABR measurements, and subsequent BIC, were obtained in 5 subjects in response to 1) click, 2) CE Chirp, and 3) LS Chirp stimuli presented at 65, 60, 50, 40 dB nHL. Replicable BIC detection rates ranged from 100% (50 dB CE Chirp) to 20% (65 dB LS Chirp) (Fig. 3).

As ABR BIC is derived from ABR wave V, peak-to-peak amplitudes of binaural and summed ABRs were examined to characterize enhancements to wave V, and subsequent DN1, due to differing stimuli (Fig. 4). Statistical analyses using paired t-tests revealed significantly larger binaural and summed wave V amplitudes to CE Chirp stimuli at 40 dB nHL compared to LS Chirp and Click stimuli ($p<0.05$). For summed monaural waveforms, wave V amplitude to CE Chirp stimuli at 50 dB nHL was also significantly larger than wave V evoked from LS Chirp

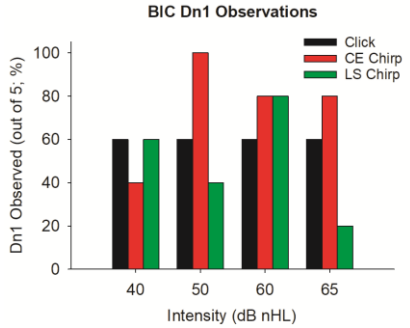

Figure 3. Percentage of replicable BIC DN1 observed from 5 subjects for each test condition.

stimuli ($p<0.05$). All other conditions did not reveal significant wave V amplitude differences between stimulus type. DN1 amplitudes also were not statistically different across all stimulus types ($p>0.05$ for all).

3.2 Behavioral ITD discrimination task

Behavioral testing was completed by 6 subjects using the same stimulus type as ABR with additional high-pass filtered stimuli at 2 kHz and a reverse chirp stimulus (Fig. 5). The high-pass condition was completed to remove the dominance of low frequency fine structure ITD cues [44]. Intensity levels included 60, 40, 20, and 10 dB nHL. Paired t-tests revealed enhanced ITD discrimination to unfiltered LS Chirp stimuli compared to Click at 10 dB nHL ($p<0.0001$) and CE Chirp ($p<0.05$). ITD discrimination was similar across stimulus types at higher intensities. With regards to filtered stimuli, high-pass at 2 kHz to remove low-frequency fine structure cues, similar statistical differences were observed as ITD discrimination was significantly better to LS Chirp at 20 dB nHL compared to click at 20 dB nHL ($p<0.0001$) and CE Chirp compared to click at 10 dB nHL ($p<0.001$).

4. CONCLUSIONS

Overall, a replicable BIC was observed in all participants for at least one stimulus type, however, the use of chirp had variable effects on BIC producibility. As expected, use of chirps generally enhanced ABR wave V, specifically at lower intensities, however, this difference was not observed for both chirp types. With regards to behavioral data, clicks yielded poorest performance compared to chirps at lower intensities. As high pass filtering eliminated an ITD

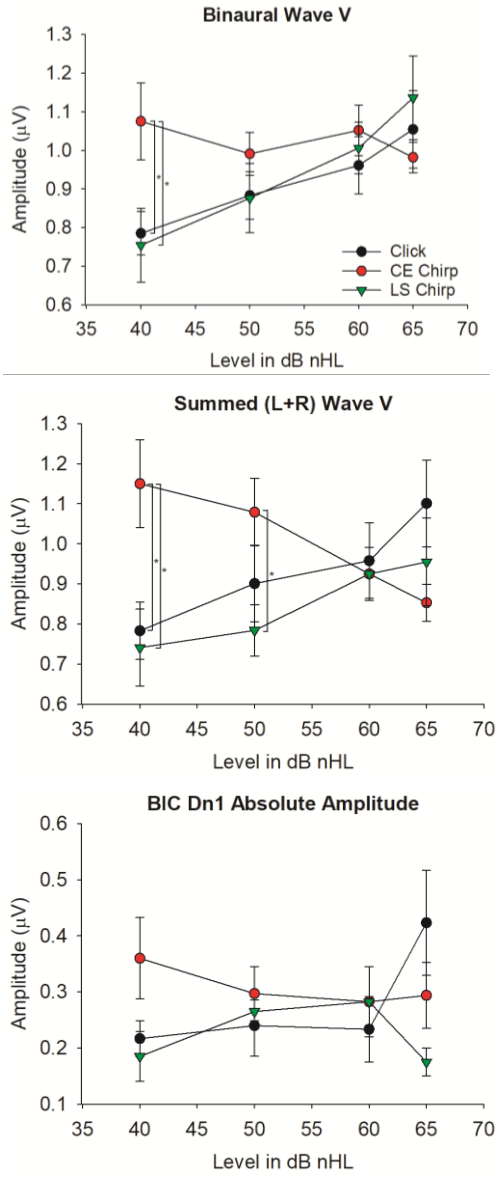

Figure 4. Average Wave V (Top, Middle) and DN1 (bottom) peak-to-peak Amplitude +/- 1 SE as a function of intensity for each stimulus. Statistics: t-tests:*$p<0.05$. Top)

dominant region (around 750 Hz;), we see significant differences between chirp and click extend to both 10 and 20 dB nHL conditions. However, no difference was observed between chirp types for filtered conditions. Across both electrophysiological and behavioral experiments, a chirp advantage over traditional click stimuli occurs at

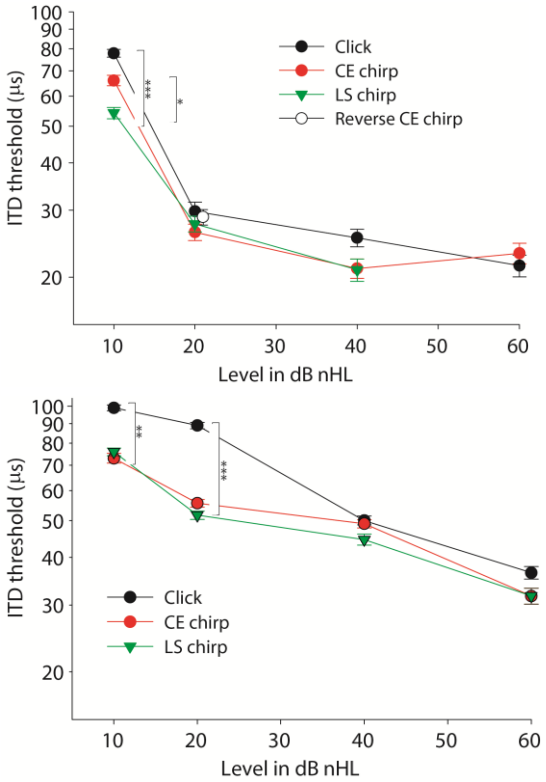

Figure 5. ITD thresholds as a function of intensity for each stimulus. Top) unfiltered stimuli. Bottom) 2 kHz High pass filtered stimuli. Paired t-tests: * $p < 0.05$; ** $p < 0.001$ and *** $p < 0.0001$

lower intensities improving perceptual lateralization and wave V characteristics. These finding support the use of chirp stimuli particularly at lower, near-threshold intensities for binaural hearing assays. To date, 5 subjects have completed both electrophysiological and behavioral measurements and future research will examine relationships between measured outcomes to investigate the utility of BIC as a marker of binaural hearing.

5. ACKNOWLEDGMENTS

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