A Sound Foundation Through Early Amplification

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CE-Chirp® stimuli for pediatric electrophysiology

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Abstract

Early identification of hearing loss relies heavily on electrophysiologic measures of hearing. The speed and accuracy of auditory brainstem response (ABR) and auditory steady state response (ASSR) measures can be dramatically improved through the implementation of technological advances in clinical systems. The CE-Chirp® and Narrow Band (NB) CE Chirps® are carefully engineered stimuli that counteract the phase cancellation effects of the cochlear traveling wave. The result is dramatic increases in response amplitude over traditional stimuli of the same spectra and level. The lead scientist on the development of these stimuli was Claus Elberling, thus the CE in the names. Replacing traditional stimuli with narrowband CE Chirps® for both ABR and ASSR yields larger responses, reduces test time, and improves the accuracy of threshold prediction (Ferm, Lightfoot & Stevens, 2013; Ferm & Lightfoot, 2015; Stürzebecher, Cebulla, Elberling, & Berger, 2006; Cebulla, Stürzebecher, Elberling, & Müller, 2007). The NB CE-Chirps® stimuli have been integrated with improvements in automated response detection for ASSR. This has resulted in a completely objective, automated tool that can estimate audiometric thresholds in a fraction of the time needed for current technologies (Cebulla, Stürzebecher, & Elberling, 2006). "Next generation" ASSR has the added advantage of providing statistical evidence of response presence or absence, thereby improving accuracy as well as adding objectivity to audiometric assessment of infants and toddlers. These exciting advancements in clinical electrophysiology will change and dramatically improve the way in which electrophysiologic assessments of infants and toddlers are carried out in the future.

PHONAK
life is on

Introduction

Rarely are substantial technological advances developed that can have a significant impact on clinical practice. This has certainly been the case for clinical auditory electrophysiology as it is applied to pediatric hearing assessment. With the advent of newborn hearing screening programs worldwide, the need for fast, accurate, and reliable measures of hearing thresholds for infants has snowballed. Any advances that can provide faster audiogram predictions could have dramatic implications on the Early Hearing Detection and Intervention (EHDI) system.

Accurate assessment of hearing in infants must be accomplished while they sleep. For babies under 6 months of age, natural sleep is best for testing but the test time is generally limited to an hour and often less. Increasing test speed even slightly could increase the number of single visit assessments or conversely reduce the number of multiple appointments for estimating thresholds. This could lead to earlier identification of hearing loss and fitting of amplification, which in turn can lead to better communication outcomes. Sininger, Grimes and Christensen (2010) found that the age of child at hearing aid fitting was the most important factor they studied for predicting good outcomes on speech perception, speech production, and language development in infants and toddlers with hearing loss.

Faster assessments and fewer overall appointments allow audiology clinics to see more children and reduce wait times, reduces the number of infants lost to follow-up between multiple visits, reduces parental anxiety (particularly for the significant number of children with normal hearing who fail screenings), reduces the number of cases requiring sedation, and reduces health care costs. In short, small improvements in clinical efficiency can have dramatic results overall.

For decades, clinical and research-based auditory electrophysiology has relied on the broadband click stimulus for a variety of reasons. The traditional click is a short pulse, usually 100 μsec, that results in a stimulus with a broad, flat spectrum when presented through traditional transducers. The main advantages of this stimulus are the ease of presentation and the broad spectrum. By activating a wide area of the basilar membrane and the corresponding auditory neurons, the amplitude produced by the click is substantial. This is especially important for human clinical work in which recordings are obtained from far-field electrodes and the resulting electrical potentials are quite small, requiring signal averaging from hundreds to thousands of stimuli.

The traditional click stimulus produces a wide range of frequencies simultaneously. However, the mechanics of the cochlea are such that the basilar membrane and the attached hair cells and auditory neurons are activated in a sequential fashion from high frequencies to low. This sequential activation is known as the "traveling wave". The consequent dispersion of neural activity over time leads to phase cancellations in the surface recorded potential.

This concept is well illustrated by the work of Don and colleagues (1994) using a technique described as the "stacked ABR" (Don, Ponton, Eggermont & Masuda, 1994). Employing a method that records click-evoked ABRs with simultaneous high-pass, filtered noise, they derived ABRs that represented responses from frequency regions or bands. These bands when summed are equivalent to the click response as shown on the left side of Figure 1. The time delays imposed by the cochlea create shifts in the latency of wave V in the bands with progressively longer delays as the frequency lowers. The addition of out-of-phase components cause the response amplitude to be reduced when the summed response is averaged. Don and colleagues (1994) demonstrated that if the phase of wave V is aligned in the frequency bands artificially (as shown on the right side of Figure 1) the summed response is considerably larger because the phase cancellations are eliminated.
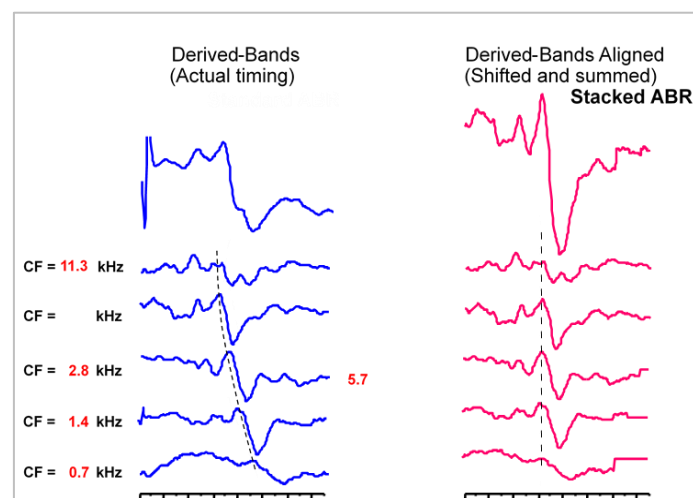

Figure 1. From M. Don. Derived-band ABRs with actual latencies (left) and after alignment of Wave V in all bands (right). The summed response is shown for both at the top. The increased amplitude of the shifted or "stacked" ABR comes from the elimination of phase cancellations found with the original derived-band ABRs.

Don et al. (1994) achieved a larger response by artificially manipulating the output of the cochlea, the evoked neural potential. The concept of the "chirp" is to achieve the same result (i.e., greater response amplitude) by manipulating the input to the cochlea -- the stimulus. Such a stimulus is a rising-frequency chirp. This is a broadband stimulus in which the low frequency components precede the highs in a smooth transition. An example of a chirp can be found in Figure 2. If

the timing of the frequency transitions corresponds to the cochlear traveling wave delay, the cochlear delay is eliminated or, more correctly, compensated. An appropriate analogy can be found in a foot race. If the goal of a race is to have all runners cross the finish line at the same time (to have all neurons fire at the same time) one would start the slowest runners (lowest frequencies) first and stagger the others based on their speed or, in the case of the chirp, based on the traveling wave delay for that frequency component. The subsequent synchronous neural firing will produce a larger response even though the spectrum and overall energy in the chirp is the same as in the click.
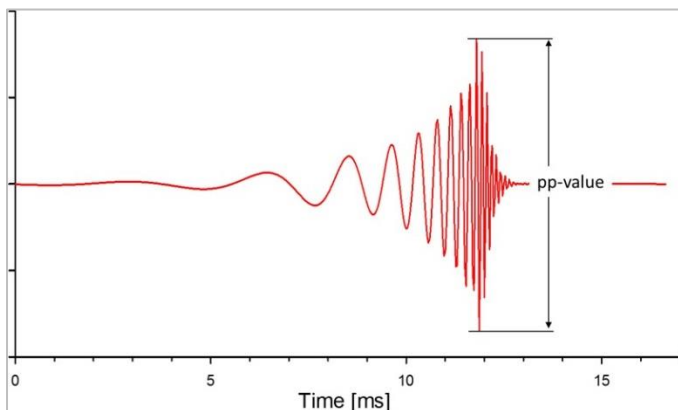

Figure 2. A time waveform of a typical low-frequency leading chirp. Note the slow onset of low frequencies followed by progressively higher frequency components.

Lütkenhöner, Kauffmann, Pantev and Ross (1990) and later Dau, Wegner, Mellert and Kollmeier (2000) were the first to apply the rising-frequency chirp to the recording of the ABR. Lütkenhöner's group (1990) used ABR latencies to frequency-specific stimuli for the basis of their delay model for a chirp and Dau and colleagues (2000) based their delay model on the work of de Boer (1980). Both groups found that the chirp produced a significant increase in ABR amplitude as compared to the click.

More recently, scientists have developed and tested sophisticated chirp stimuli that combine a series of cosigns, each with phase compensation, to adjust the onset of the frequency components in a manner appropriate for traveling wave compensation (Stürzebecher et al., 2006). The desired modulation rate is created by the frequency spacing of the individual cosigns. Several delay models have been tested originally based on derived-band ABR latencies from the work of Don and colleagues (1994). It soon became apparent that the appropriate delay model needed to be specified as a function of the level of the broadband chirp to account for the level-specific influence of the upward spread of masking and changes in the cochlear delay (Elberling, Callø & Don, 2010). The development of the final delay model for the level-specific (LS) CE-Chirp® is described by Elberling and

Don (2008). The LS CE-Chirp® results were verified when the resulting ABR amplitudes were compared to non-level-specific chirps and to clicks at a range of levels (Kristensen & Elberling, 2012). The LS CE-Chirp® maintained a significant amplitude advantage at all levels from 20 to 80 dB nHL.

Although the wide-band CE-Chirp® is a significant innovation, clinical auditory electrophysiology requires narrow band stimuli to predict audiometric thresholds. The traditional stimulus for ABR is a narrowband tone burst (a ramped, short duration tone), and the traditional stimulus for ASSR is a pure tone with amplitude modulation and generally also with frequency modulation that broadens the spectrum and renders the subsequent response larger and easier to detect. As with clicks, tone bursts (also known as tone pips) and traditional ASSR stimuli suffer from the same amplitude reduction due to phase cancellations brought on by the cochlear traveling wave delay. While time delays for narrowband stimuli are clearly shorter than seen for broadband, the amplitude decrease that is induced by cochlear delay is still apparent. This is particularly true for 500 Hz where traveling wave velocity is particularly slow. Estimates of hearing threshold at 500 Hz have been difficult, elevated or absent relative to behavioral thresholds, particularly for ASSR (see Stürzebecher et al., 2006 for review).

The scientists applied the same logic as used for CE-Chirp® development to create narrowband (NB) CE-Chirps® (Stürzebecher et al., 2006) with center frequencies near 500, 1000, 2000 and 4000 Hz. Each NB CE-Chirp® is composed of a series of cosigns with frequency spacing corresponding to the desired modulation frequency and phase adjustments in each cosign appropriate for compensation for the traveling wave delay. Figure 3 displays the time waveforms and spectra of the four NB CE-Chirps®. Composition with cosigns creates a smooth spectrum that is free from side lobes. In addition, these stimuli were further modified to separate the cosign components from the harmonics of the modulation of each stimulus to avoid detection of electrical artifacts with the ASSR paradigm.
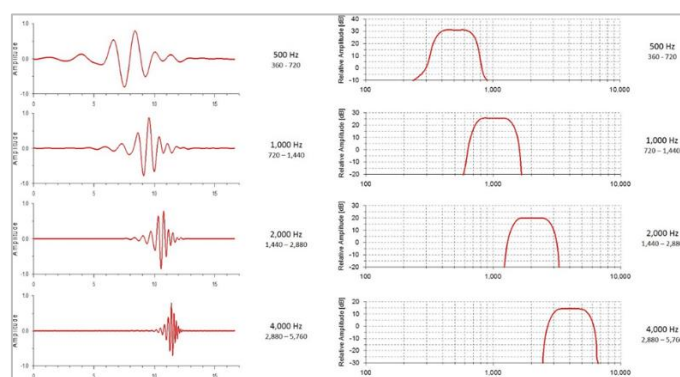

Figure 3. Time waveforms (left) and corresponding spectra of octave-band CE-Chirps® with center frequencies at 500, 1000, 2000 and 4000 Hz.

Perhaps the most brilliant application of the NB CE-Chirp® to clinical auditory electrophysiology has been to the ASSR paradigm. What I call the "next generation" ASSR, utilizes an advanced detection algorithm that seeks to identify activity not only at the ASSR modulation frequency, as found in previous ASSR systems, but at many multiples of the modulation rate which will also carry information regarding the presence of a response (Cebulla et al.,, 2006). Older systems utilized a one-sample test while the newer test uses a q-sample test with q being the number of harmonics of the modulation frequency evaluated. The number of harmonics that may be used is limited only by the number that provides additional information to the detection process. The present generation of the Interacoustics Eclipse tests at least 12 harmonics. In addition to evaluating multiple harmonics, the "next generation" ASSR uses both phase and amplitude information in detection of harmonic components while some of the previous systems used phase alone. The addition of these features to the detection of the ASSR was systematically shown to improve detection of small responses and to reduce the test time to do so (Cebulla et al., 2006).

Evidence for the clinical advantages of the CE-Chirp®: ABR

The most direct demonstration of the value of the NB CE-Chirp® is to compare the actual recordings of the ABR in response to chirps and to standard tone bursts in individual infants and toddlers. This was accomplished by Ferm and colleagues from the United Kingdom. The first study (Ferm et al., 2013) compared responses to traditional and CE-Chirp® narrowband stimuli with center frequencies of 1 and 4 kHz and the second study (Ferm & Lightfoot, 2015) used 0.5 and 2 kHz narrowband stimuli. Subjects were newborns, under 11 weeks of age, who had passed the British newborn hearing screening program and were assumed to have normal hearing. Threshold searches using 10 dB steps were conducted using both sets of stimuli below 50 dB nHL.

These studies had three consistent findings for all four frequency stimuli. First, they found an amplitude advantage for the chirps that ranged from 31% to 70%. The second consistent finding was the average Fmp value associated with each ABR ranged from 1.8 to 3.0 times larger in the chirp-elicited responses (the Fmp is a metric generated during the averaging process that is an indicator of response quality and is associated with the signal-to-noise ratio). Finally, the studies found that the thresholds obtained using the chirps were lower than those from standard stimuli, on average by 5.2 to 6.2 dB. Based on these results, the authors recommended lowering the nHL to eHL correction factors for all four frequencies when using NB CE-Chirps® by 5 dB and endorsed the use of the NB CE-Chirp® stimuli for audiologic

follow-up to newborn hearing screening in the UK (Ferm et al., 2013; Ferm & Lightfoot, 2015) .

Although it was not measured explicitly because of the design of the study, the authors pointed out that the increase in response amplitude translates to a reduction in the amount of averaging that is needed to achieve the same signal to noise ratio. If the amplitude is increased by 40%, as in most of the examples given, the test time (averaging) could theoretically be halved.

A second study with a similar design was conducted by Rodrigues, Ramos and Lewis (2013). Subjects included 40 normal hearing infants evaluated with NB CE-Chirps® and standard tone bursts at the same four clinical frequencies as above. Testing was conducted with stimuli of 80 to 20 dB nHL in 20 dB steps and two recordings were conducted at each level, stopping when the averaged background noise reached 40 nV. ABRs in response to NB CE-Chirps® were statistically larger than for tone bursts for all stimuli at the 20 and 40 dB nHL levels and for three of the four frequencies at 60 dB nHL. It must be noted that the level-specific (LS) stimuli had not been implemented at that time. The LS stimuli have been shown to extend the ABR amplitude advantage to 80 dB in adults and should be expected to do the same in infants.

Clinical advantages of NB CE-Chirps® for ASSR

The enhanced amplitude of the neural response to the NB CE-Chirp® can also be appreciated in an ASSR paradigm. Cosign components of the stimuli are spaced by a frequency appropriate for modulation (around 90 Hz for sleeping children, 40 Hz for awake adults). In addition to the improved stimuli, the advanced detection algorithms used by the next generation of ASSR are far more sensitive than those used in the original ASSR systems (Cebulla et al., 2007).

These two factors, chirp stimuli that elicit a larger electrophysiologic response and q-sample statistical detection that can find smaller electrophysiologic responses, have combined to dramatically improve the speed and accuracy of threshold detection with ASSR (Cebulla et al., 2006; Cebulla et al., 2007). The additional unique ability of the ASSR test to evaluate four frequencies in each ear simultaneously makes this technology the optimal test battery for rapid, accurate and objective assessment of hearing in children. Normative data have been published for adults with normal hearing and full-term infants with robust OAEs (Rodrigues & Lewis, 2014). These thresholds are in close agreement with previous similar studies using ABR (Sininger, Abdala & Cone-Wesson, 1997).

Excellent prediction of behavioral thresholds has been demonstrated using this technology with infants and toddlers. Venail, Artaud, Blanchet, Uziel and Mondain (2015) conducted a prospective study of 32 infants with a mean age of 7.4 months who were referred for audiologic evaluation. The study utilized the Eclipse ASSR with simultaneous measurement of responses to NB CE-Chirps® with nominal frequencies of 500, 1000, 2000 and 4000 Hz in each ear. The mean duration of testing for ASSR was 22.9 minutes. All infants were later evaluated by behavioral tests blinded to the ASSR results. The ASSR thresholds were highly correlated to the behavioral responses with a range of R2 from 0.84 to 0.92. In addition, they reported that 90.7% of ASSR thresholds were within 10 dB of behavioral thresholds. These results far exceed any that have been presented for similar studies using ABR and tone bursts as predictors of behavioral thresholds. The landmark study of Stapells, Gravel and Martin (1995) compared ABR tone-burst thresholds to behavioral thresholds (500, 2000 and 4000 Hz) in infants & young children with hearing levels ranging from normal to profound. In that study, 80% of the threshold comparisons were within 15 dB. The excellent predictions of behavioral thresholds by ASSR in this study can be attributed to the two main changes in the "next generation" ASSR that are the use of the NB CE-Chirp® and the advanced detection algorithm.

Conclusion

After many years of discussion on the potential advantages of a low-frequency leading chirp stimulus for clinical electrophysiology, a broad band and four narrowband chirps have been developed by Elberling and his colleagues (CE-Chirps®) and are now available for use in the audiology clinic. Preliminary data using these stimuli for estimating hearing thresholds in children is excellent. When used with ABR, the NB CE-Chirps® produce larger responses and lower thresholds than traditional tone bursts (pips). The increased response amplitude theoretically will allow a reduction in averaging time to reach a threshold response. Perhaps most exciting is the application of the NB CE-Chirps® with ASSR technology. When combined with advanced statistical detection algorithms, the "next generation" ASSR technology has been shown to be extremely fast and accurate as a predictor of behavioral thresholds for infants and children requiring an electrophysiologic evaluation. The additional objectivity of the ASSR technique will reduce testing errors. It seems clear that the CE-Chirp driven ASSR will be the accuracy increasing and time reducing "shot in the arm" that has been needed in pediatric clinical audiology.

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