cABR: A neural probe of speech-in-noise processing

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Understanding speech in noise (SIN) is a highly complex task affected by reciprocal sensory-cognitive interactions in the brain. The auditory brainstem response to complex stimuli (cABR) provides an objective index of the neural transcription of features (e.g. temporal, spectral) that are important for speech understanding. Influenced by cognitive factors such as attention and memory, measures of subcortical processing can further our knowledge of the biological mechanisms associated with deficits in SIN perception in clinical populations, such as children with learning impairments, older adults, and individuals with hearing impairment. Further, subcortical processing is modifiable through long-term experience and short-term training, making cABR a highly reliable probe for delineating the effects of training on neural speech processing.

INTRODUCTION

Understanding speech in background noise is hard for everyone, but especially so for children with language-based learning impairments, individuals with hearing loss, and older adults. Older adults frequently complain that they can hear what is said, but cannot understand the meaning, especially in background noise. They have particular difficulty understanding rapid speech, especially the rapidly-changing parts of speech contained in consonant-vowel transitions (Gordon-Salant *et al*., 2006). These difficulties occur in individuals with hearing loss and those who have audiologically normal hearing (Souza, 2007). Older adults are known to have slower neural processing. This neural slowing has been attributed to temporal jitter (Pichora-Fuller *et al*., 2007), delayed neural firing (Walton *et al*., 1998), and decreased inhibition (Caspary *et al*., 2008). We asked whether correlates of this neural slowing are found in the auditory brainstem response to complex sounds (cABR), and whether age-related deficits in subcortical spectrotemporal speech encoding are related to speech-in-noise (SIN) perception. We are currently investigating the efficacy of training for reversing age-related deficits in neural processing and SIN perception.

APPROACH

The cABR is well suited for assessing aging effects on neural processing of speech. Its fidelity to the stimulus can be seen in representation of timing features (onsets, offsets, envelope), pitch (encoding of the fundamental frequency (F_0) of the stimulus), and timbre (representation of formants above the F_0) through cycle-by-cycle neural phase-locking (Skoe and Kraus, 2010a). Given this fidelity and high reliability, the cABR has

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provided an effective means of relating subcortical processing features to everyday listening skills (as reviewed in Anderson and Kraus, 2010; Anderson *et al*., 2011; Song *et al*., 2010).

Analyses of the cABR include traditional measures in the time (root mean square magnitude (RMS) and latency and amplitude of individual peaks in the waveform) and frequency (magnitude of the fundamental frequency (F_0) and individual harmonics) domains. Cross-correlations quantify the similarity between the response and the stimulus. Cross-correlations can also be performed between responses obtained in two conditions (e.g. quiet and noise) to determine the extent to which noise degrades the response. The "phaseogram" is a precision measure of timing differences between two signals, providing a means for analysis of the response in the time-frequency domain (Skoe *et al*., 2011). The phase difference between two waveforms, in radians, is converted to timing differences using the following equation:

$$[(x*(1/50)) / (2\pi)] * 1000 = y$$

x= radians $\quad$ y = ms $\quad$ (Eq.1)

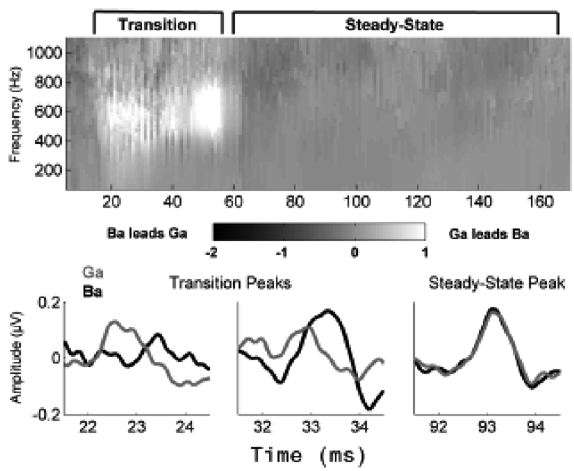

Fig. 1: Top: Cross-phaseogram differences in grand-average responses to the syllables [ga] and [ba] in a group of normal-hearing 40 children, ages 8 to 12. The pattern of [ga] phase leading [ba] is evident during the formant transition region of the response. Bottom: In a representative individual response, the pattern of earlier timing in [ga] versus [ba] (corresponding to the tonotopicity of the basilar membrane), is present in the two transition peaks (centered at 23 and 33 ms), but is not evident in the steady-state peak (centered at 93 ms). Adapted from Skoe *et al*., *Journal of Neuroscience Methods,* 2010.

Phase differences can be represented by either color or shading differences to illustrate how the phase relationship evolves in time. For example, the phase difference between the response waveforms to the syllables [ba] and [ga] is represented in the regions of the response corresponding to the consonant-vowel transition (20-60 ms), during which the formants change over time, but not during the steady-state region (60-170 ms), corresponding to the shared vowel between the two syllables (Fig. 1).

BIOLOGICAL BASES OF HEARING IN NOISE

Effects of aging

SIN perception difficulties in older adults cannot be fully accounted for by peripheral hearing loss. To better understand these problems, attention has focused on perceptual and neurophysiological demonstrations of central auditory deficits both in humans and in animals. Age-related changes in temporal (Ross *et al*., 2010; Tremblay *et al*., 2002; Vander Werff and Burns, 2011; Walton, 2010) and spectral (Clinard *et al*., 2010; Harris *et al*., 2008) processing are present at subcortical and cortical levels of the auditory pathway. Decreased levels of inhibitory neurotransmitters, found in aging rats (Caspary *et al*., 2005; Hughes *et al*., 2010) may account for some of these deficits, as balanced inhibition is required for the sharpened fine tuning of neural responses to fast-changing stimuli (Caspary *et al*., 2008; Wehr and Zador, 2003). Accurate auditory processing of the temporal and spectral aspects of sound is important for the discrimination of complex stimuli, such as speech (Divenyi and Haupt, 1997; Phillips *et al*., 2000; Snell *et al*., 2002).

Neural timing delays are noted as early as middle age. In the cABR normal hearing older adults (ages 45 to 67, mean: 57) have timing delays in the region of the response corresponding to the consonant-vowel transition in the speech syllable [da] compared to young adults (Parbery-Clark *et al*., 2011b). Importantly, these timing delays are not found in the steady-state region of the responses, which would be expected if the delays were driven by differences in hearing. Timing delays in the transition likely contribute to SIN perception difficulties in older adults, as the transition is perceptually vulnerable in noise (Hedrick and Younger, 2007) .

Neural correlates of speech-in-noise perception

The identification of neural factors associated with better SIN ability may lead to improvements in assessment and management services for older individuals reporting hearing-in-noise difficulties. For example, larger prefrontal cortex volume relates to better SIN perception in older adults, suggesting that this population may benefit from strategies aimed at improving cognitive function (Wong *et al*., 2009).

Relationships among factors in the cABR and SIN performance have also been found. In two groups of age- and hearing-matched older adults who differ in performance on the Hearing in Noise Test (HINT; Nilsson *et al*., 1994), we found that the cABR had larger overall magnitudes and greater representation of the F_0 than the bottom SIN group (Anderson *et al*., 2011), and that greater representation of the F_0 relates to better SIN perception (Fig. 2). Using cross-correlations between the response to the syllable

[da] in quiet and in noise, the top group had higher correlation values than the bottom group, indicating a more robust representation in the top group. The cABR is a highly reliable response (Song *et al*., 2010), unaffected by cognitive state (Irimajiri *et al*., 2005), and may therefore provide useful information to assist in assessment and management of SIN perception difficulties in a clinical setting.

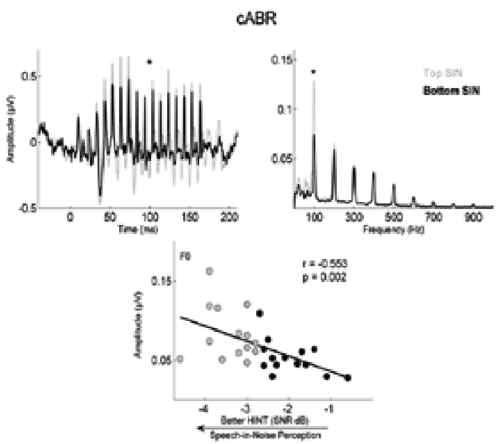

Fig. 2: Top left: A significant difference in RMS amplitude was noted between top (gray) and bottom (black) SIN perception groups in average responses to the syllable [da] (**p* = 0.039). Top right: Average frequency spectra calculated over the entire response range (5 to 190 ms) demonstrate a significant difference for the F_0 between the top and bottom SIN groups (**p* = 0.01). Bottom: Amplitude of the F_0 relates to SIN performance as assessed by the HINT. Adapted from Anderson *et al*., *Ear and Hearing,* 2011.

EFFECTS OF TRAINING

The concept of experience-dependent plasticity is not new. Decades of research have demonstrated auditory plasticity in behavioral, cortical, subcortical, and cochlear studies. The importance of the corticofugal system is evident in the extensive system of descending fibers synapsing all along the auditory pathway, including the outer hair cells of the cochlea (Gao and Suga, 2000). The brainstem has been traditionally viewed as a passive system, the function of which was to relay information from the cochlea to the cortex. There is now a growing body of work demonstrating the importance of the brainstem in experience-dependent plasticity, including a recent finding that a functioning corticocollicular pathway is necessary for auditory learning (Bajo *et al*., 2010). Here we focus on evidence of plasticity in the cABR. The effects of training can be viewed on a continuum from on-line stimulus-related changes (Skoe and Kraus, 2010b), to short-term training of days or weeks (Carcagno and Plack, 2010; Song *et al*.,

2011; Song *et al*., 2008), or long-term changes associated with life-long experiences (Kraus and Chandrasekaran, 2010; Zatorre and Gandour, 2008). We will review recent studies that have investigated the effects of short-term training and life-long experiences.

Life-long experience

Life-long engagement with language or music can enhance processing of relevant features in speech or music (Bidelman and Krishnan, 2010; Kraus and Chandrasekaran, 2010; Krishnan *et al*., 2005; Strait *et al*., 2009; Wong *et al*., 2007). Musicians spend countless hours practicing their instruments, becoming adept at extracting relevant signals from a complex soundscape. Does this skill transfer to the ability to selectively attend to one voice from a group of voices? Patel (2011) recently proposed the OPERA hypothesis, suggesting that experience-dependent plasticity in speech processing occurs under a set of circumstances, including Overlap, Precision, Emotion, Repetition, and Attention. These five conditions are invoked during musical activities. Evidence of transfer from music to non-music domains was found in a study of young adult musicians and nonmusicians (Parbery-Clark *et al*., 2009b). A musician advantage was found for both SIN perception and auditory working memory, a cognitive skill that is highly related to SIN perception. A neural basis for this musician advantage was demonstrated in the subcortical encoding of speech in noise (Parbery-Clark *et al*., 2009a). Young musicians and nonmusicians have similar brainstem responses in quiet, but noise has a greater degradative effect on the nonmusicians' responses, as noted by earlier neural timing and better morphology of the response waveforms of the musicians.

Does this hearing-in-noise advantage extend to older adults? Similar to young musicians, older musicians demonstrate better SIN performance and better auditory working memory than nonmusicians (Parbery-Clark *et al*., 2011b). They also demonstrate enhanced auditory temporal acuity through lower backward masking thresholds, indicating that musicianship may offset age-related declines in the precise temporal processing required for understanding speech in noise (Fig. 3).

In fact, earlier neural timing was found in the transition region of the response in older musicians compared to nonmusicians, the same region that shows enhanced temporal processing in young musicians (Parbery-Clark *et al*., 2011a).

Short-term auditory training

A recent study demonstrated changes in the cABR in young adults following four weeks of training (Song *et al*., 2011). These participants underwent pre-testing, including perceptual measures ((HINT and Quick Speech-in-Noise test (QuickSIN; Killion *et al*., 2004)) and electrophysiology (brainstem responses to [da] presented in quiet and in noise). The experimental group participated in the Listening and Communication Enhancement program (LACE; Neurotone, Inc., Redwood City, CA), which consisted of thirty minutes of computer-based auditory training, five times a week for four weeks. The control group received no training. The pre-tests were

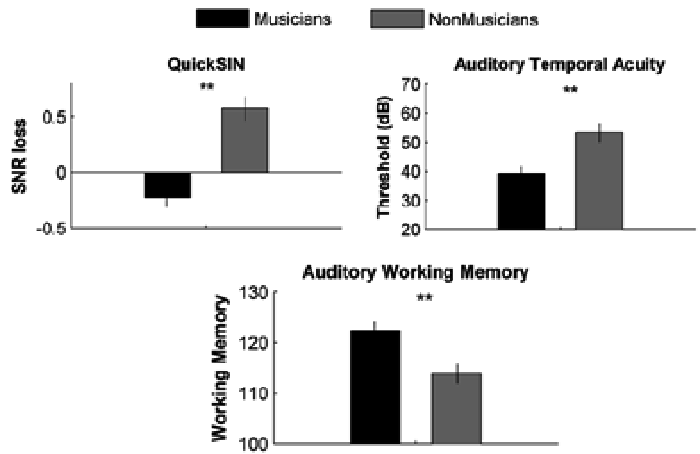

Fig. 3: Compared to nonmusicians, older musicians have better performance on QuickSIN, lower backward masking thresholds (better auditory temporal acuity), and higher auditory working memory. *$p < 0.05$. Adapted from Parbery-Clark *et al*., *PLoS ONE,* 2011.

repeated approximately eight weeks later in both groups. The encoding of pitch-related cues (the F_0 and the second harmonic (H_2)) in the noise condition increased significantly in the experimental group (Fig. 4), and these enhancements were retained at a six-month follow-up session. No changes were noted in the untrained group.

Significant improvements were noted for both QuickSIN and HINT for the experimental but not the treatment group ($F_{4,55} = 7.065$, $p < 0.001$). These changes in SIN performance were related to the strength of the F_0 and H_2 at pre-test, suggesting that the cABR might be used a predictive measure for benefits of training (Fig. 5).

Can training similarly improve SIN performance and neurophysiologic responses in older adults? Plasticity is possible in older adults, but may require more intense training or smaller increments than in younger adults (Linkenhoker and Knudsen, 2002). Behavioral improvements were noted in older rats after a short course (27 to 35 1-hr sessions) of oddball auditory detection training, although their rate of learning was slower and did not achieve the accuracy of the younger rats even at the end of the training period (de Villers-Sidani *et al*., 2010). These behavioral improvements were accompanied by neurophysiological evidence of enhanced temporal coding in the older rats, reversing the age differences in reliability of temporal coding and synchrony of cortical firing. In addition, the density of inhibitory interneurons (parvelbumin and myelin basic protein), which play an important role in cortical synchronization and precise neural timing, increased following training.

Reports of cognitive training effects in older adults have had mixed results, with varying degrees of personal engagement affecting treatment outcomes (Bielak, 2010). Age-related reductions in sensory processing may contribute to cognitive decline (Pichora-Fuller, 2003). It can be reasoned, therefore, that enhanced sensory processing

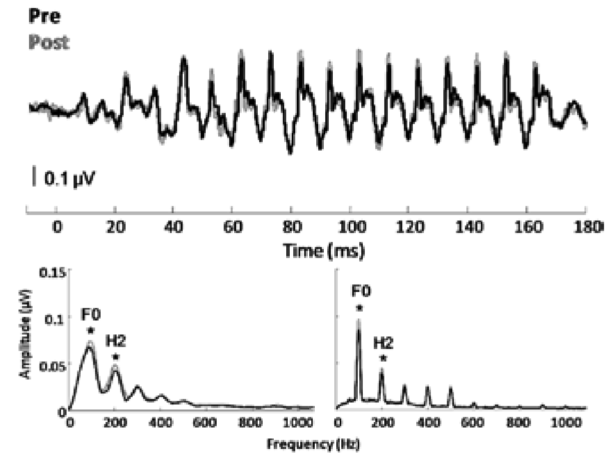

Fig. 4: Top: The training group shows an enhancement of the F_0 in larger amplitudes of the periodic peaks repeating every 10 ms in the frequency following response in six-talker babble in the post data. Bottom: An F_0 and H_2 enhancement is also seen in the fast Fourier transform (FFT) calculated over the transition region (left, 20-60ms) and the steady-state region (right, 60-170 ms) of the experimental group but not the control group ($F_{1,58} = 6.498$, $p = 0.013$). Adapted from Song *et al*., Cerebral Cortex, 2011.

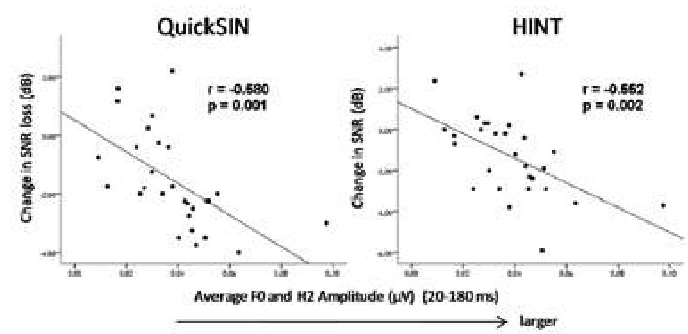

Fig. 5: The strength of pitch encoding measures (F_0 and H_2) is related to the degree of change in both SIN performance measures (QuickSIN and HINT). Adapted from Song *et al*., *Cerebral Cortex,* 2011.

may offset cognitive decline in older adults. The Kraus lab is currently investigating the effects of a computerized cognitive-based auditory training program in older adults. This in-home training is done for 60 minutes, five times a week for eight weeks. The software uses exaggerated temporal transitions to increase participant engagement, purportedly to drive plastic changes. Preliminary results demonstrate improved SIN performance, memory, and neural timing.

SUMMARY

The cABR is an objective biological probe of auditory function, documenting peripheral and central interactions, and serving as a metric of auditory system plasticity (developmental, experiential, and post-intervention). Future applications may include the investigation of amplification devices to inform device design and settings.

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