Research paper

Inferior colliculus contributions to phase encoding of stop consonants in an animal model

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ABSTRACT

The human auditory brainstem is known to be exquisitely sensitive to fine-grained spectro-temporal differences between speech sound contrasts, and the ability of the brainstem to discriminate between these contrasts is important for speech perception. Recent work has described a novel method for translating brainstem timing differences in response to speech contrasts into frequency-specific phase differentials. Results from this method have shown that the human brainstem response is surprisingly sensitive to phase differences inherent to the stimuli across a wide extent of the spectrum. Here we use an animal model of the auditory brainstem to examine whether the stimulus-specific phase signatures measured in human brainstem responses represent an epiphenomenon associated with far-field (i.e., scalp-recorded) measurement of neural activity, or alternatively whether these specific activity patterns are also evident in auditory nuclei that contribute to the scalp-recorded response, thereby representing a more fundamental temporal processing phenomenon. Responses in anaesthetized guinea pigs to three minimally-contrasting consonant-vowel stimuli were collected simultaneously from the cortical surface vertex and directly from central nucleus of the inferior colliculus (ICc), measuring volume conducted neural activity and multiunit, near-field activity, respectively. Guinea pig surface responses were similar to human scalp-recorded responses to identical stimuli in gross morphology as well as phase characteristics. Moreover, surface-recorded potentials shared many phase characteristics with near-field ICc activity. Response phase differences were prominent during formant transition periods, reflecting spectro-temporal differences between syllables, and showed more subtle differences during the identical steady state periods. ICc encoded stimulus distinctions over a broader frequency range, with differences apparent in the highest frequency ranges analyzed, up to 3000 Hz. Based on the similarity of phase encoding across sites, and the consistency and sensitivity of response phase measured within ICc, results suggest that a general property of the auditory system is a high degree of sensitivity to fine-grained phase information inherent to complex acoustical stimuli. Furthermore, results suggest that temporal encoding in ICc contributes to temporal features measured in speech-evoked scalp-recorded responses.

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1. Introduction

Brainstem encoding of complex sounds provides a unique window into the human auditory system and its function. Studies investigating brainstem responses to speech have informed our understanding of normal and impaired auditory systems (Akhoun et al., 2008; King et al., 2002; Krishnan, 2002; Song et al., 2008), the plasticity of auditory processes (Kraus and Banai, 2007), auditory system development (Johnson et al., 2008a; Vander Werff et al., 2011), and how lifelong experiences with language and music mold the auditory system (Krishnan et al., 2005;

Musacchia et al., 2007). Despite the wealth of information that these studies have provided, an inherent limitation of human studies is their inability to provide detailed information about the underlying neural mechanisms contributing to scalp-evoked potentials during the processing of speech, music, and other biologically-important acoustical signals. A method that has been successful in informing our understanding of the origins of scalp-recorded activity in humans is probing near-field auditory function in an animal model of the auditory system using identical acoustical stimuli as those used in human studies (See Cunningham et al., 2002 for a review; King et al., 1999; Kraus et al., 1985, 1988, 1992, 1994a, 1994b). For example, this approach has yielded a deeper understanding of speech processing in the presence of background noise (Cunningham et al., 2002), auditory-based asymmetries (King et al., 1999), and the cortical basis of speech discrimination (McGee et al., 1996). Here, we use this approach to better understand the exquisite timing of the human brainstem in response to speech sounds by examining the temporal dynamics of neural activity measured in the guinea pig inferior colliculus, a brain structure known to contribute to the scalp-recorded response (Chandrasekaran and Kraus, 2010; Marsh et al., 1974; Smith et al., 1975).

Recent work has focused on how the fine spectro-temporal differences distinguishing stop consonants are encoded as timing differences in the human brainstem response (Johnson et al., 2008b; Skoe et al., 2011). The submillisecond timing differences that differentiate brainstem responses to various stop consonants are clinically relevant as slight brainstem timing deficits are associated with behavioral impairments for speech and language (Banai et al., 2009; Hornickel et al., 2009b; King et al., 2002). As a means of further refining these methods for quantifying brainstem temporal processing, Skoe and colleagues recently introduced an analysis that translates these small timing differences into phase differentials between responses to various stimuli (2011). They analyzed brainstem responses to three consonant-vowel (CV) speech syllables that differed by a single formant trajectory during the consonant-vowel transition period. The "cross-phase" method revealed that responses to the CVs with a higher second formant frequency ($F2$) "phase-lead" responses to those with a lower $F2$. The phase differences were most prominent during time regions corresponding to the contrasting frequency modulations in the syllable stimuli, and were limited during the steady state portion of the response which was identical across stimuli. While it is acknowledged that phase information in this context may not contribute significantly to auditory system or behavioral differentiation of these speech sounds, the cross-phase approach reveals meaningful information regarding subtle and reliable timing differences in the brainstem's representation of consonant-vowel stimuli.

An important question is whether the stimulus-specific phase signatures measured at the scalp represent an epiphenomenon associated with far-field (i.e., scalp-recorded) measurement of neural activity, or alternatively whether these specific activity patterns are also evident in auditory nuclei that contribute to potentials measured at the scalp, thereby representing a more fundamental temporal processing phenomenon. Classical studies investigating the frequency-following response (FFR) indirectly addressed this question using pure tone stimuli. In previous work, near-field inferior colliculus (IC) responses showed an extremely similar phase relationship with the surface-recorded FFR in response to a range of pure tone stimuli (Marsh et al., 1974; Smith et al., 1975). Given the non-linear nature of the ascending auditory system, however, phase relationships between the IC and scalp in response to more complex auditory stimuli cannot be predicted by results using simple (i.e., pure tone) stimuli.

To more thoroughly investigate the processing of spectro-temporal patterns embedded in complex stimuli in the scalp-recorded response, as well as its relation to activity in nuclei which contribute to this response, the current study evaluates speech-evoked responses to consonant-vowel stimuli/ba/,/da/, and /ga/. Near-field responses recorded directly from the central nucleus of the inferior colliculus are compared to far-field responses that serve as an analogue to the human surface-recorded response. Phase differentials are used to quantify small timing differences between responses to the three stimuli using the cross-phase method (Skoe et al., 2011). Similarities between the two recording sites will inform the extent to which patterns of phase differences recorded from the scalp reflect a more general auditory processing mechanism evident in nuclei in the ascending auditory system. We made two general predictions. First, we predicted the far-field guinea pig surface responses would strongly resemble the scalp-recorded responses in humans presented with the same stimuli. Second, assuming a contribution of the inferior colliculus to the scalp-recorded responses (Chandrasekaran and Kraus, 2010; Marsh et al., 1974; Smith et al., 1975), we expected the near-field responses to contain response patterns similar to those seen at the surface.

2. Material and methods

The research protocol was approved by the Animal Care and Use Committee of Northwestern University, and all US ethical guidelines for laboratory animal welfare were followed (assurance number A3283-01).

2.1. Animal preparation

The experimental materials and procedures were similar to those reported previously (Abrams et al., 2011; Cunningham et al., 2002; McGee et al., 1996). Ten pigmented guinea pigs (7 female) between 346 and 803 g (average 549 g), were used as subjects. Animals were initially anesthetized with ketamine hydrochloride (100 mg/kg) and xylazine (8 mg/kg). Smaller supplemental doses (25 mg/kg ketamine; 4 mg/kg xylazine) were administered hourly or as needed throughout the rest of the experiment. Following the induction of anesthesia, the animal was mounted in a stereotaxic device, located in a sound-treated booth (IAC), for the duration of the experiment. Body temperature was maintained at 37.5 °C by using a thermistor-controlled heating pad (Harvard) on the guinea pig's abdomen. Prior to surgery, normal hearing sensitivity was confirmed by auditory brainstem response (ABR). ABRs were elicited by a click stimulus at 70 and 40 dB, referenced to previously-established lab-internal guinea pig click ABR threshold norms. Electromyographic needle electrodes were inserted into skin midway between ears, on snout midway between eyes and nose, and into loose skin at neck, for non-inverting, inverting, and ground, respectively. Following confirmation of normal hearing, a rostro-caudal incision was made along the scalp surface and the tissue was retracted to expose the skull. Holes were drilled in the skull under an operating microscope. The dura was removed with a cautery to prevent damage to the recording electrode, and the cortical surface was coated with mineral oil.

2.2. Stimuli

The stop consonants /ba/,/da/and/ga/ were synthesized using a Klatt speech synthesizer according to previously published specifications (Klatt, 1980; Skoe et al., 2011). Briefly, stimuli were constructed to be identical except for the trajectory of the second formant ($F2$) during the 50 ms formant transition portion