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Research paper

Timing is everything: Temporal processing deficits in the aged auditory brainstem

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ABSTRACT

This summary article reviews the literature on neural correlates of age-related changes in temporal processing in the auditory brainstem. Two types of temporal processing dimensions are considered, (i) static, which can be measured using a gap detection or forward masking paradigms, and (ii) dynamic, which can be measured using amplitude and frequency modulation. Corresponding data from physiological studies comparing neural responses from young and old animals using acoustic stimuli as silent gaps-in-noise, amplitude modulation, and frequency modulation are considered in relation to speech perception. Evidence from numerous investigations indicates an age-related decline in encoding of temporal sound features which may be a contributing factor to the deficits observed in speech recognition in many elderly listeners.

1. Introduction

The ability to precisely encode complex temporal features inherent in species-specific vocalizations and environmental sounds is critical for survival in mammals. This capacity requires high resolution temporal processing, often on the order of fractions of a millisecond. The fine-tuned temporal processing demands of the auditory system are met through morphological and physiological adaptations, which serve to counteract the temporal variability inherent in chemical neurotransmission by neurons across multiple synapses (Trussell, 2002). Age-related changes in this complex neuromachinery can result in altered neural timing which may be partly responsible for deficits in speech recognition observed in aged listeners (Gordon-Salant and Fitzgibbons, 1993).

Speech comprehension difficulties observed in aged human listeners has motivated research efforts to identify age-related changes in more central processes affecting speech comprehension. In contrast to age-related changes in audibility, which are the direct consequence of sensory receptor pathology, age-related deficits in speech perception are thought to be related to alteration in coding of sounds in both the peripheral and central auditory system. Central effects have been attributed most often when listeners are processing signals in difficult listening situations (Gordon-Salant and Fitzgibbons, 1995; Snell and Frisina, 2000). These findings have led clinicians to infer a central aging component, which has been substantiated by recent psychoacoustic investigations in which poor speech recognition performance in old listeners is degraded, as compared to young listeners matched for peripheral sensitivity (Fitzgibbons and Gordon-Salant, 1996; Fozard and Gordon-Salant, 2001; Frisina et al., 2001; Dubno et al., 2003). Similarly, impaired temporal acuity in elderly subjects with and without hearing loss has been reported using several different temporal resolution paradigms, such as gap detection or sinusoidal amplitude modulation (Glasberg et al., 1987; Moore and Glasberg, 1988; Moore et al., 1992; Schneider et al., 1994; Snell and Frisina, 2000). In aged listeners, including those with normal hearing, degraded temporal processing has been directly linked to speech identification difficulties (Fitzgibbons and Gordon-Salant, 1996; Snell, 1997; Frisina et al., 2001; Snell and Frisina, 2000). The relative importance of temporal cues is supported by the demonstration of good speech recognition in the absence of spectral cues (Rosen, 1992; Shannon et al., 1995) as well as by the capability of single channel cochlear implants to restore spoken language comprehension (Green et al., 2004).

Typically, two types of stimuli have been used to assess age-related changes in neural correlates of temporal acuity. Static temporal acuity can be measured using the gap detection task and dynamic temporal acuity by measuring the response to amplitude modulation. The gap detection paradigm is probably the most

Abbreviations: AM, amplitude modulation; AVCN, anterior-ventral cochlear nucleus; B, buildup; BMF, best modulation frequency; BF, best frequency; CN, cochlear nucleus; DCN, dorsal cochlear nucleus; FC, fusiform cell; FM, frequency modulation; IC, inferior colliculus; MGB, medial geniculate body; MGT, minimal gap threshold; MTF, modulation transfer function; PB, pauser-buildup; PVCN, posterior-ventral cochlear nucleus; rMTF, rate modulation transfer function; SAM, sinusoidal amplitude modulation; tMTF, temporal modulation transfer function; WC, wide-band chopper

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common method used to measure static temporal resolution in animal models (Salvi and Arehole, 1985; Klump and Gleich, 1991; Walton et al., 1997). It consists of placing a silent gap in between two carriers and models similar types of silent intervals found in the speech signal, for example in the perception of voice onset time. After a series of various gap durations are presented, the shortest detectable gap, or gap threshold, is obtained. Also, inherent in most species-specific vocalizations are intensity fluctuations in the temporal envelope, commonly referred to as amplitude modulation (AM). AM features in speech are known to provide important cues for discrimination of specific phonemic features, such as voicing or vowel perception. In addition, certain parameters of amplitude-modulated speech have been implicated in auditory scene analysis, or a listener's ability to segregate one speaker from many (Grimault et al., 2002). Typically, a range of amplitude-modulated signals is presented using tone or noise carriers whose range of modulation frequencies extends over several octaves, e.g., from 10 to 1000 Hz.

The neural response to sinusoidal AM (SAM) is typically measured in three ways: (i) by measuring the magnitude of the driven rate; (ii) by measuring the degree of synchronization, or phase-locking, of the neural response to each cycle of the envelope and (iii) by quantifying response gain. Rate measures are simply a metric of the number of spikes elicited by the AM signal. Phase-locking can be described using the synchronization index or vector strength which can vary from 0.0 to 1.0, with a value of 1.0 indicating perfect synchrony. Response gain (in dB) is another measure of synchronization to AM, and is calculated by dividing the percent modulation in the response by the percent modulation in the stimulus (Frisina et al., 1990). These measures of AM encoding are used to derive two types of modulation transfer functions (MTFs), the rate MTF (rMTF) which plots driven rate as a function of modulation frequency and the temporal MTF (tMTF) which plots either vector strength or dB gain by modulation frequency. The MTF characterizes the temporal filter properties of the auditory neuron under study.

The neural encoding of AM signals in the auditory nerve and caudal brainstem suggest that the temporal envelope is represented in the phase-locked response of auditory neurons, rather than changes in driven rate (Frisina et al., 1990). However, as one ascends the auditory system the temporal code for AM becomes degraded and appears to be replaced by a rate code (Langner and Schreiner, 1988; Joris et al., 2004). Auditory midbrain neurons show a wide variety of temporal filter properties which can be represented as changes in response rate or phase-locking depending on the modulation frequency. Many neurons display tuning, or have a best modulation frequency (BMF) where a peak is present in both the rMTF and tMTF. These neurons are referred to as band-pass, where other units, showing no such preference for a given modulation frequency are referred to as all-pass. Band-pass type units show tuning for both narrow (tones) and broadband (broadband noise) carrier signals. It is also the case that a unit's BMF for rate is also near the BMF for phase-locking (Langner and Schreiner, 1988; Schreiner and Langner, 1988; Krishna and Semple, 2000). Age-related changes in neural coding of AM in the auditory brainstem have been reported in only the cochlear nucleus and inferior colliculus (IC).

1.1. Age-related temporal processing deficits in the cochlear nucleus

The diversity in anatomical and connectional architecture of the cochlear nucleus (CN) is mirrored in the diversity of different types of response properties to simple sounds found in each of the subnuclei. Two stimulus coding pathways are postulated to have their origin in response properties of CN neurons. The "what" pathway is comprised of the anteroventral (AVCN) and posterior-ventral (PVCN) nuclei where neurons perform simple and complex analysis of sound features, such as frequency, intensity, duration, and envelope periodicity. While the "where" pathway originates in the AVCN and dorsal nuclei (DCN) (Frisina, 2001; Sutherland et al., 1998). Spherical and globular bushy cells of the AVCN are involved in processing localization cues in the horizontal plane, while the principle neurons, or fusiform cells of the DCN have been implicated in the processing of elevation cues important for sound localization (Davis, 2002; Davis et al., 2007). Furthermore, fusiform cells (FCs) show evidence of enhancement of SAM stimuli as compared to auditory nerve fibers by restricting the modulation frequencies they respond to. In effect FCs sharpen the temporal filter for coding AM (Joris and Smith, 1998). Unfortunately, there are few neurophysiological studies which have studied the neural correlates of age-related dysfunction in the CN from aged animal models.

Recently, Caspary and colleagues successfully recorded responses to SAM tones from FCs in young adult and old Fisher Brown Norway rats (Schatteman et al., 2008). Neural coding of SAM tones using three modulation depths (20%, 50% and 100%) were presented 30 dB above the neuron's best frequency (BF), and rate and synchronization MTFs were collected. The authors observed an age-related reduction in band-pass tMTF filter types from FCs recorded from old rats (Fig. 1). The most pronounced shift occurs for 100% AM where the proportion of units having band-pass filter shapes declined from approximately 60% in young rats to 30% in old rats. There was a concomitant increase in the number of low-pass and double-peaked filter types with increasing age. The authors also report a significant reduction in the strength of phase-locking with age at the BMF and this occurred for all three types of unit classifications (Fig. 2). Buildup units (B) tended to have the strongest phase-locking, followed by pauser-buildup (PB), then wideband chopper (WC), with 100% modulation depth SAM producing the greatest vector strength. Regardless of the modulation depth, FCs from old rats consistently showed poorer synchronization to SAM BF tones as compared to units from young rats. In contrast to the age-related alterations in tMTFs, filter properties for rate measures of AM coding remained stable age.

The authors conclude that these results are consistent with an age-related change in the manner that excitatory and inhibitory circuits shape responses to AM. Evidence suggests that the inhibitory neurotransmitter glycine plays a crucial role in shaping responses to SAM tones presented at a units BF. When glycinergic receptors are blocked using strychnine, vector strength is reduced in FCs (Backoff et al., 1997). Thus, the present results suggest that an age-related alteration glycinergic neurotransmission may play a role in the etiology of age-related changes in response to SAM stimuli in the DCN (Backoff et al., 1999; Wang et al., 2009).

1.2. Neural correlates of age-related changes in gap encoding in the inferior colliculus

The inferior colliculus integrates auditory input from over 10 different brainstem nuclei and serves a gateway to the thalamus and cortex (Winer and Schreiner, 2005). IC neurons demonstrate a sophisticated level for processing of complex signals, including species-specific vocalizations (Aitkin et al., 1994), amplitude modulation (Langner and Schreiner, 1988; Rees and Sarbaz, 1997), frequency modulation (Pollak and Bodenhamer, 1981; Hage and Ehret, 2003), spatial localization (Semple et al., 1983; Aitkin et al., 1984, 1985), and gap detection (Walton et al., 1997). In addition, there is definitive evidence which points to an age-related decline in inhibitory neurotransmission in the IC of aged rodents (Milbrandt et al., 1994, 1996, 2000; Caspary et al., 1995; Helfert et al., 1999). For these reasons it has been postulated that age-related alterations in inhibitory neurotransmitters and synaptic