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Aging alters envelope representations of speech-like sounds in the inferior colliculus

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ABSTRACT

Hearing impairment in older people is thought to arise from impaired temporal processing in auditory circuits. We used a systems-level (scalp recordings) and a microcircuit-level (extracellular recordings) approach to investigate how aging affects the sensitivity to temporal envelopes of speech-like sounds in rats. Scalp-recorded potentials suggest an age-related increase in sensitivity to temporal regularity along the ascending auditory pathway. The underlying cellular changes in the midbrain were examined using extracellular recordings from inferior colliculus neurons. We observed an age-related increase in sensitivity to the sound's onset and temporal regularity (i.e., periodicity envelope) in the spiking output of inferior colliculus neurons, relative to their synaptic inputs (local field potentials). This relative enhancement for aged animals was most prominent for multi-unit (relative to single-unit) spiking activity. Spontaneous multi-unit, but not single-unit, activity was also enhanced in aged compared with young animals. Our results suggest that aging is associated with altered sensitivity to a sound's temporal regularities, and that these effects may be due to increased gain of neural network activity in the midbrain.

1. Introduction

Older and middle-aged listeners experience difficulties understanding speech, particularly in challenging listening situations such as in the presence of background sounds, competing speakers, or reverberation (Pichora-Fuller and Souza, 2001; Ruggles et al., 2011). Speech perception depends on the sensitivity of the auditory system to temporal regularities in sounds. Temporal regularities in speech may be divided into 3 categories: the slow fluctuations (<50 Hz) of the speech envelope that capture word and syllabic rate; the periodicity envelope (50–500 Hz), which contains the fundamental frequency of the speaker's voice (f0) and is crucial for speaker identification (Bregman, 1990); and the temporal fine structure (>500 Hz), which contains information about formant structure (Rosen, 1992). The sensitivity of the auditory system to temporal regularity in sounds declines with age, with drastic consequences for speech perception (Anderson et al., 2011; Fullgrabe et al., 2015; Walton, 2010), but the neurophysiological changes that underlie this age-related decline are not well understood.

An age-related decline in temporal processing abilities is thought to be primarily neural in origin because it is independent of changes in hearing thresholds due to impaired cochlear function (Frisina and Frisina, 1997; Gordon-Salant and Fitzgibbons, 2001; Pichora-Fuller and Souza, 2001). The neural deficits that may contribute to impaired sensitivity to temporal regularity include cochlear synaptopathy—that is, the degradation of cochlear synapses between inner hair cells and auditory nerve fibers (Sergeyenko et al., 2013)—and a decrease in inhibitory neurotransmitters in the brainstem, midbrain, and cortex (Caspary et al., 2008; Rabang et al., 2012; Takesian et al., 2009). Loss of inhibition may result in increased neural activity in central auditory regions despite diminished inputs from peripheral structures (Hughes et al., 2010; Mohrle et al., 2016; Parthasarathy et al., 2014; Parthasarathy and Kujawa, 2018). However, it is less clear how aging affects sensitivity to temporal regularity in central auditory regions, in particular for complex, speech-like sounds.

Previous work suggests that neurons in the inferior colliculus show altered temporal processing including changes in the sensitivity to the temporal regularities in sounds (Palombi et al., 2001; Rabang et al., 2012; Schatteman et al., 2008; Walton et al., 1998, 2002). These studies focused on neuronal spiking, which reflects the output of neurons. By contrast, local field potentials (LFPs) are thought to reflect the summed synaptic inputs to a neuron or local

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neuronal population to a large degree (but other nonsynaptic activity might additionally contribute [Bullock, 1997; Buzsaki et al., 2012; Logothetis et al., 2001; Logothetis and Wandell, 2004]). Recent recordings of LFPs and spiking activity show that synchronization of spiking activity (output) is abnormally enhanced in the aging inferior colliculus, despite decreased synaptic inputs (input), and that this age-related relative increase in activity (i.e., from a neuron's input to its output) is specific for sounds with modulation rates below 100 Hz (Herrmann et al., 2017). Whether aging also leads to an oversensitivity to temporal regularities in complex, speech-like sounds is unknown.

In the present study, we test the hypothesis that neural synchronization to the periodicity envelope (~100 Hz) of speech is abnormally enhanced in the inferior colliculus of aged animals. We assess peripheral neural function by measuring wave 1 amplitudes of the auditory brainstem responses (ABRs) and show physiological evidence for cochlear synaptopathy in aged animals. Scalp-recorded neural synchronization to the envelope of a speech-like stimulus is increased specifically in more rostral regions in the auditory pathway such as the inferior colliculus compared with more caudal ones such as the auditory nerve. Furthermore, we assess the relation between LFPs (synaptic input) and spiking output in the inferior colliculus using extracellular recordings. Synchronization of LFPs to the envelope of a speech-like sound is decreased in aged animals, whereas synchronization of spiking activity from well isolated units does not differ between age groups. Multi-unit spike synchronization, however, is drastically increased for aged animals, suggesting changes in gain control mechanisms occurring largely at a neural network level.

2. Methods and materials

2.1. Ethical approval

The experimental procedures described in the present investigation were approved by the Institutional Animal Care and Use Committee of Purdue University (PACUC #1111000167). The experiments included in this study comply with the policies and regulations described by (Drummond, 2009). Rats were housed 1 per cage in accredited facilities (Association for the Assessment and Accreditation of Laboratory Animal Care) with food and water provided *ad libitum*. The number of animals used was reduced to the minimum necessary to allow adequate statistical analyses.

2.2. Subject population

The study design is cross-sectional and used male Fischer-344 rats obtained from Charles River Laboratories and Taconic. The aging Fisher-344 rat has been suggested to be a suitable model to study presbycusis in aging animals (Syka, 2010) and has been shown to exhibit high-frequency hearing loss and metabolic presbycusis that are characteristic of human age-related loss of hearing sensitivity (Allen and Eddins, 2010; Dubno et al., 2013). Eleven young (3–6 months, ~300 g) and 12 aged (22–26 months, ~400–500 g) animals were used for scalp recordings, and 11 young (3–6 months, ~300 g) and 9 aged (22–26 months, ~400–500 g) animals were used for extracellular recordings. A subset of the ABR recordings have been reported in previous studies (Parthasarathy and Bartlett, 2012; Parthasarathy et al., 2014).

2.3. Sound stimulation

The stimulus was a natural English syllable, /ba/, which was 260 ms long and spoken by a male speaker of North American English with a fundamental frequency of ~110 Hz. To account for the differences in the hearing range between rats and humans, as well as to increase the number of responsive neurons in the inferior colliculus of rats, this speech token was half-wave rectified, and used to modulate a broadband noise carrier (0.04–40 kHz) (Fig. 1A). This preserved the periodicity envelope as well as the original fine structure of the speech token, both of which served as the modulator for the broadband noise (Fig. 1B and C). This stimulus design was chosen to understand how neurons represent temporal regularities that are important for human speech and to aid comparison with human literature, rather than investigating the representation of conspecific vocalizations that may not generalize to human speech processing.

2.4. Stimulus generation

Sound stimuli were generated using SigGenRP (Tucker-Davis Technologies [TDT]) sampled at a rate of 97.64 kHz (standard TDT sampling rate) and presented through custom-written interfaces in OpenEx software (TDT). Sound waveforms were generated via a multichannel processor (RX6, TDT), amplified (SA1, TDT), and presented free field through a Bowers and Wilkins DM601 speaker. The output from the speaker was calibrated free field, using SigCal (TDT) and a Bruel & Kjaer microphone with a 0.25-in. condenser, pointed at frontal incidence to the speaker, from the same location as the animal's right ear, and was found to be within ±6 dB for the frequency range tested. All recordings took place in an Industrial Acoustics booth lined with 1 inch (35 mm) Sonex foam with ~90% absorption for frequencies ≥1000 Hz, minimizing potential echoes and reverberations. All analyses described below accounted for the travel time of the sound wave from the speaker to the animals' ears.

2.5. Electrophysiological recordings at the scalp

Methods for experimental setup, sound stimulation, and scalp-potential recordings are similar to those described before (Parthasarathy et al., 2014, 2016). The animals were briefly anesthetized using isoflurane (1.5%–2%) for the insertion of subdermal needle electrodes (Ambu) and the intramuscular injection of dexmedetomidine (Dexdomitor, 0.2 mg/kg), an α-adrenergic agonist that acts as a sedative and an analgesic. Recordings commenced

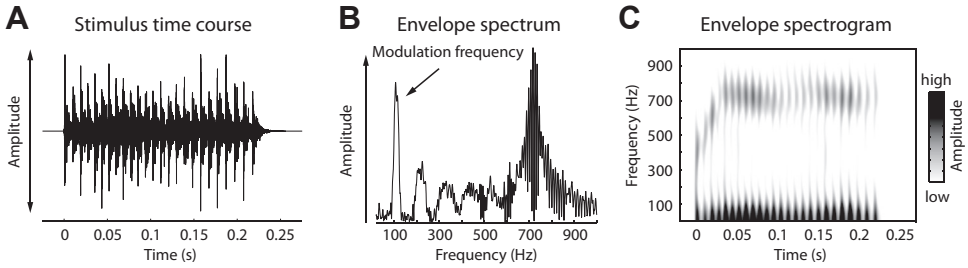

Fig. 1. Speech-like sound used in the present study. (A) Waveform of the speech-like sound. (B) Amplitude spectrum of the envelope of the speech-like sound displayed in panel A. (C) Spectrogram of the envelope of the speech-like sound.