Neuroscience 151 (2008) 868–887

ENCODING OF TEMPORAL FEATURES OF AUDITORY STIMULI IN THE MEDIAL NUCLEUS OF THE TRAPEZOID BODY AND SUPERIOR PARAOLIVARY NUCLEUS OF THE RAT

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Abstract—Neurons in the superior paraolivary nucleus (SPON) of the rat respond to the offset of pure tones with a brief burst of spikes. Medial nucleus of the trapezoid body (MNTB) neurons, which inhibit the SPON, produce a sustained pure tone response followed by an offset response characterized by a period of suppressed spontaneous activity. This MNTB offset response is duration dependent and critical to the formation of SPON offset spikes [Kadner A, Kulesza RJ Jr, Berrebi AS (2006) Neurons in the medial nucleus of the trapezoid body and superior paraolivary nucleus of the rat may play a role in sound duration coding. J Neurophysiol. 95:1499–1508; Kulesza RJ Jr, Kadner A, Berrebi AS (2007) Distinct roles for glycine and GABA in shaping the response properties of neurons in the superior paraolivary nucleus of the rat. J Neurophysiol 97: 1610–1620]. Here we examine the temporal resolution of the rat's MNTB/SPON circuit by assessing its capability to *i*) detect gaps in tones, and *ii*) synchronize to sinusoidally amplitude modulated (SAM) tones. Gap detection was tested by presenting two identical pure tone markers interrupted by gaps ranging from 0 to 25 ms duration. SPON neurons responded to the offset of the leading marker even when the two markers were separated only by their ramps (i.e. a 0 ms gap); longer gap durations elicited progressively larger responses. MNTB neurons produced an offset response at gap durations of 2 ms or longer, with a subset of neurons responding to 0 ms gaps. SAM tone stimuli used the unit's characteristic frequency as a carrier, and modulation rates ranged from 40 to 1160 Hz. MNTB neurons synchronized to modulation rates up to ~1 kHz, whereas spiking of SPON neurons decreased sharply at modulation rates ≥400 Hz. Modulation transfer functions based on spike count were all-pass for MNTB neurons and low-pass for SPON neurons; the modulation transfer functions based on vector strength were low-pass for both nuclei, with a steeper cutoff for SPON neurons. Thus, the MNTB/SPON circuit encodes episodes of low stimulus energy, such as gaps in pure tones and troughs in amplitude modulated tones. The output of this circuit consists of brief SPON spiking episodes; their potential effects on the auditory midbrain and forebrain are discussed.

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Abbreviations: ABR, auditory brainstem response; CF, characteristic frequency; DMPO, dorsal medial periolivary nucleus; FSL, first spike latency; GDT, gap detection threshold; IC, inferior colliculus; MNTB, medial nucleus of the trapezoid body; MR, modulation rate; PSTH, peristimulus spike time histogram; SAM, sinusoidally amplitude modulated; SPON, superior paraolivary nucleus; TDT, Tucker-Davis Technologies.

Key words: superior olivary complex, brainstem, gap detection, amplitude modulation, sound envelopes.

The ability to resolve the fine temporal structure of auditory stimuli is a critical aspect of hearing, and deficits in temporal processing are reportedly related to language impairment (Tallal et al., 1985a,b). Two paradigms commonly used to assess the temporal acuity of auditory circuits are gap detection (reviewed by Phillips, 1999) and coding of sound envelopes (for reviews see Langner, 1992; Frisina, 2001; Joris et al., 2004).

The acuity with which gaps, or silent periods, are detected between closely spaced sounds or components of sounds plays an important role in speech perception (Tyler et al., 1982; Irwin and McAuley, 1987; Glasberg and Moore, 1989; Snell and Frisina, 2000; Snell et al., 2002). Most often, gap detection tasks involve presenting two sounds of equal duration, referred to as leading and trailing markers, with a gap of variable length between them. In humans, the perception in this stimulus paradigm is of two stimuli separated in time when the gap is relatively long. For short gap durations, the perception changes to that of a single discontinuity in an otherwise homogeneous sound (Moore, 1993). Human gap detection thresholds (GDTs) in this paradigm, using noise bursts well above threshold as gap markers, are 2–3 ms (Moore, 1993).

Neural correlates of gap detection have been demonstrated in the frog auditory system (Feng et al., 1994) and various mammalian species including chinchilla (Giraudi et al., 1980; Giraudi-Perry et al., 1982; Salvi and Arehole, 1985), rat (Syka et al., 2002; Rybalko and Syka, 2005), mouse (Barsz et al., 2002; Walton et al., 2002; Allen et al., 2003), gerbil (Wagner et al., 2003), ferret (Kelly et al., 1996), and cat (Eggermont, 1999, 2000) using a variety of behavioral and electrophysiological paradigms. A study comparing behavioral and auditory brainstem response (ABR) GDTs showed the two thresholds to be similar, with the ABR thresholds tending to be lower (Werner et al., 2001). Thus, the information necessary to explain psychophysical performance in a gap detection paradigm appears to be present at the level of the auditory brainstem. To our knowledge however, the neuronal basis for gap detection has not been previously examined in the brainstem.

The envelope of speech signals contains amplitude modulations over a wide range of modulation rates (MRs), ranging from 3 to 4 Hz up to several hundred Hz, and considerable speech information is contained in these amplitude modulations (reviewed by Joris et al., 2004). Audi-

0306-4522/08$32.00+0.00
doi:10.1016/j.neuroscience.2007.11.008

tory neuropathy and aging can degrade temporal processing mechanisms in the auditory system and impair speech comprehension even when hearing thresholds are unchanged (Frisina and Frisina, 1997; Zeng et al., 1999), suggesting that the ability to encode envelope fluctuations is critical to speech processing. Most studies of the responses of superior olivary nuclei to sinusoidally amplitude modulated (SAM) stimuli have focused on mechanisms of directional hearing, describing the interplay of contralateral inhibition and ipsilateral excitation in the lateral superior olive (Joris and Yin, 1995, 1998), and excitatory inputs from both ears in the medial superior olive (Joris and Yin, 1998). Recordings from awake rabbits suggest that while distinct mechanisms underlie the detection of interaural delays between SAM stimuli in the lateral and medial superior olives, both are ultimately based on coincidence detection (Batra et al., 1997a,b).

The medial nucleus of the trapezoid body (MNTB)/ superior paraolivary nucleus (SPON) circuit

Single unit responses from the MNTB and SPON of the rat demonstrate that these two brainstem nuclei form a neural circuit producing duration dependent responses to the offset of pure tones and phase locked responses to SAM stimuli (Kulesza et al., 2003, 2007; Kadner et al., 2006). MNTB neurons display high rates of spontaneous activity and primary-like responses to characteristic frequency (CF) tones (cats: (Guinan et al., 1972a,b; Smith et al., 1998), gerbils: (Kopp-Scheinpflug et al., 2002), mice: (Kopp-Scheinpflug et al., 2003), rats: (Sommer et al., 1993; Paolini et al., 2001; Kulesza et al., 2003; Kadner et al., 2006)). The sustained excitatory response of MNTB units is followed by a period of suppressed spontaneous activity, sometimes lasting several tens of milliseconds, depending on stimulus parameters, that we refer to as the MNTB offset response (Fig. 1A) (Kadner et al., 2006). The MNTB provides a strong glycinergic input to the nearby SPON (Helfert et al., 1989; Banks and Smith, 1992), whose neurons also display offset responses to pure tones; these however take the form of single or brief bursts of action potentials that occur after the stimulus offset (Fig. 1B) (Kulesza et al., 2003, 2007; Kadner et al., 2006). Release from MNTB-derived glycinergic inhibition is critical to the formation of SPON offset responses, as demonstrated by reversible pharmacological blockade of glycine receptors in the SPON (Kulesza et al., 2007). SPON neurons utilize GABA as their neurotransmitter (Kulesza and Berrebi, 2000) and their projection targets include the inferior colliculus (IC) and thalamus (Saldaña and Berrebi, 2000; Jin and Berrebi, 2006). There is also evidence for an extensive system of recurrent axon collaterals within SPON that provide a means for intrinsic GABAergic inhibition of SPON neurons as well as self-inhibition via autapses (Saldaña and Berrebi, 2000; Kulesza et al., 2000).

In contrast to the medial and lateral superior olives, neurons in the rat SPON are monaurally driven and show no evidence of binaural interactions (Kulesza et al., 2003, 2007; Kadner et al., 2006), suggesting that the MNTB/SPON circuit encodes a stimulus feature other than sound source location. Based on current knowledge of its response properties, we hypothesized that this brainstem circuit may be particularly well suited for encoding stimulus features associated with episodes of low or rapidly decreasing sound energy, such as tone offsets and the falling flanks and troughs in SAM stimuli.

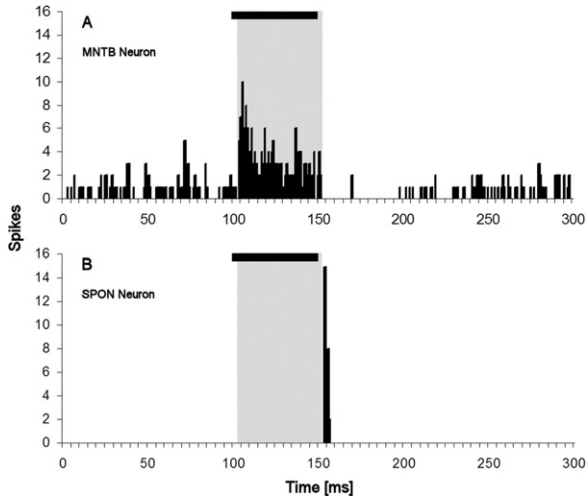

Fig. 1. PSTHs display typical response characteristics of MNTB and SPON neurons to CF tones. (A) MNTB units display high rates of spontaneous activity, and in response to CF tones (20 dB above threshold) display prominent onset and sustained firing during the stimulus presentation. Note the suppression of spontaneous rate following the termination of the stimulus. (B) SPON units have little or no spontaneous activity; in response to CF tones they discharge briefly at the stimulus offset. The black bar at the top of each panel represents the stimulus. The gray shading in both panels denotes the time interval of the excitatory component of the MNTB response.

Hypotheses and experimental paradigms

Because they respond to the stimulus offset, we predicted that SPON neurons would respond to the offset of both the leading and trailing markers in a gap detection paradigm, with the response to the leading marker indicating the presence of a gap. Thus, we expected the SPON to encode gaps by firing brief bursts of action potentials at or near the beginning of the gap. Since the SPON offset response critically depends on the MNTB offset response, we expected that MNTB offset responses would display GDTs similar to those of SPON units. Another indication that MNTB neurons process the leading and trailing markers as separate stimuli would be the appearance of an onset response component to the trailing gap marker. The experimental paradigm used to test these hypotheses was based on the commonly used psychophysical approach described above; we recorded responses of SPON and MNTB neurons to a sequence of two identical CF tones separated by a silent gap of variable duration.

SPON neurons also respond to SAM stimuli with precise synchronization to the stimulus envelope. Our original characterization of SPON neurons suggested that at low MRs their firing coincides with the periodically occurring gaps in MNTB responses to SAM stimuli (Kulesza et al., 2003). Therefore, another aim of the present study was to