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Systematic variation of potassium current amplitudes across the tonotopic axis of the rat medial nucleus of the trapezoid body

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Abstract

Many central auditory nuclei preserve the tonotopic organization of their afferent inputs, generating a frequency "map" across the nucleus. In the medial nucleus of the trapezoid body (MNTB) the most medial neurons receive inputs corresponding to the highest frequency sounds and the most lateral neurons have the lowest characteristic frequencies. Whole-cell patch recording from MNTB principal neurons in rat brainstem slices demonstrates a corresponding tonotopic organization of voltage-gated outward potassium currents. Medial MNTB neurons had larger total outward K^+ current amplitudes than lateral neurons and similar medial to-lateral gradients were observed for two K^+ current subtypes distinguished by their low and high voltage activation thresholds. In contrast, a third K^+ conductance with an intermediate voltage threshold and slower kinetics showed an inverse gradient (being smallest in medial MNTB). The orthogonal axes of MNTB did not exhibit potassium current gradients (dorsal-to-ventral, or rostral-to-caudal). The input resistance was unchanged across the MNTB, but a slow capacitative component was enhanced in lateral neurons. These data demonstrate that the intrinsic properties of rat MNTB neurons are tuned across the tonotopic axis so as to promote shorter action potentials, faster firing and therefore greater accuracy in transmission of auditory information in the high characteristic frequency regions.

Keywords: Potassium; Channel; Capacitance; MNTB; Tonotopic

1. Introduction

A longitudinal gradient in the resonant properties of the basilar membrane maps different sound frequencies along the length of the cochlea, such that basal inner hair cells are stimulated by high frequency sound and apical hair cells by low frequencies. This spatial tonotopic relationship is preserved in the afferent projections through many levels of the central auditory pathway. Intriguingly, expression of voltage-gated K^+ channels mirrors this spatial gradient and is thought to contribute to auditory processing. For example, in turtle and chick, hair cells are

Abbreviations: aCSF, artificial cerebrospinal fluid; aCSF(V), the aCSF used during voltage-clamp experiments; AP, action potential; CF, characteristic frequency; CN, cochlear nucleus; CR, caudal-to-rostral; EPSP, excitatory postsynaptic potential; GBC, globular bushy cell; IID, interaural intensity difference; I_{KHVA}, high-voltage-activated K^+ current; I_{KIVA}, intermediate-voltage-activated K^+ current; I_{KLVA}, low-voltage-activated K^+ current; ITD, interaural time delay; LSO, lateral superior olive; ML, medial-to-lateral; MNTB, medial nucleus of the trapezoid body; MSO, medial superior olivary nucleus; NM, nucleus magnocellularis; PP, prepotential; SBC, spherical bushy cell; SG, spiral ganglion; TEA, tetraethylammonium; VD, ventral-to-dorsal

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electrically tuned to different frequencies along the cochlea, such that basally located cells have the largest amplitudes of rapidly activating and deactivating Ca^{++}-activated K^+ currents (Crawford and Fettiplace, 1981; Pantelias et al., 2001). Though mammalian cochlea hair cells may lack this form of K^+ current-based electrical tuning, a tonotopic gradient has been reported for the firing properties of spiral ganglion (SG) neurons (Adamson et al., 2002) which relay auditory input to the cochlear nucleus (CN). In the same study, immunohistochemistry showed basal SG neurons had stronger expression than apical neurons of K^+ channel subunits Kv1.1 and Kv3.1b, one of two splice variants of Kv3.1 (Adamson et al., 2002).

Kv1.1 and Kv3.1 are also found within brainstem auditory pathways that relay timing and intensity information, including CN bushy cells and their target neurons in the medial nucleus of the trapezoid body, MNTB (Wang et al., 1994; Weiser et al., 1994; Grigg et al., 2000). The functions of channels containing these subunits have been extensively characterized in MNTB neurons. For example, Kv1.1 contributes to the rapidly activating low-voltage-activated K^+ current (I_{KLVA}) which limits MNTB neuron spiking to a single action potential (Brew and Forsythe, 1995; Dodson et al., 2002). I_{KLVA} is thought to improve temporal precision in auditory neurons by decreasing membrane time constants and in some cases limiting temporal summation (Oertel, 1983; Manis and Marx, 1991; Trussell, 1999). Also in MNTB, Kv3.1 subunits contribute to a rapidly activating high-voltage-activated K^+ current (I_{KHVA}) which rapidly repolarizes action potentials (APs) facilitates high frequency firing and hence may aid the high frequency following of synaptic inputs (Brew and Forsythe, 1995; Wang et al., 1998).

Tonotopically organized expression gradients for Kv3.1b have been demonstrated in two brainstem auditory nuclei, the MNTB (Li et al., 2001) and nucleus magnocellularis (NM) whose neurons are the avian equivalents of bushy cells (Parameshwaran et al., 2001). Both studies showed stronger expression in the parts of the nuclei containing neurons with high characteristic frequency (CF).

Two recent reports show that tonotopic gradients for both Kv1.1 expression and firing properties occur in brainstem auditory nuclei, as first demonstrated in SG (see above). In NM the high CF neurons expressed Kv1.1 more strongly, were less likely to fire multiple APs, and exhibited larger increases in firing when subjected to toxin block of their Kv1-type channels (Fukui and Ohmori, 2004). However, in the rat lateral superior olive (LSO, a target nucleus of MNTB) the tonotopic gradient seemed to have opposite slope; it was the low CF neurons which expressed Kv1.1 more strongly, were more likely to fire only a single AP, and had larger I_{KLVA} amplitudes (Barnes-Davies et al., 2004).

Some of these data point to the idea that auditory neurons with higher CF may have stronger expression of rapidly activating K^+ currents. If so, this might correspond with other specializations in higher CF neurons allowing more rapid APs and higher transmission rates (Carr, 1993). For example, tonotopic gradients in dendritic morphology are particularly dramatic within the avian auditory system, with neurons in the higher CF parts of nuclei having fewer dendrites or much shorter dendrites (Smith and Rubel, 1979; Carr and Boudreau, 1993) either of which should minimize membrane capacitance. There also appear to be some gradients in synaptic properties across NM (Fukui and Ohmori, 2004). Gradients in morphology, synaptic properties and K^+ currents could each contribute to optimal encoding of high and low frequency auditory signals.

The MNTB is an ideal nucleus in which to investigate tonotopic variation in K^+ currents and capacitance, because it has a homogenous population of principal neurons (Morest, 1968a) and allows us to build on our previous detailed characterization study of their K^+ currents (Brew and Forsythe, 1995). Also convenient is the orientation of the tonotopic axis of MNTB, running from medial to lateral, high CF to lower CF (Guinan et al., 1972; Sommer et al., 1993). We therefore carried out whole-cell patch clamp recordings from MNTB neurons in transverse slices of rat brainstem, noting their three-dimensional location within MNTB, and recording their K^+ currents, passive properties and firing properties. Parts of this work have been presented in abstract form (Brew and Forsythe, 1994, 1996).

2. Materials and methods

2.1. Slice preparation

Brainstem slices were prepared as described previously (Brew and Forsythe, 1995) and recordings were made from more than 70 visually identified MNTB principal neurons ($n = 28$ rats). The brain was removed from 7–17-day old Lister hooded rats within 10–20 s of their decapitation and placed in ice-cold sucrose-based solution for dissection and slicing. This bicarbonate-buffered solution was continually gassed with a 95% O_2/5% CO_2 mixture, and had contents similar to the standard aCSF (artificial cerebrospinal fluid) described below, except that sucrose was substituted for the sodium chloride. The brainstem was cut away from the forebrain using a straight-edged scalpel, at an angle that transected the inferior colliculus. The cut rostral surface of the brainstem was glued to a vibratome stage (Lancer, Series 1000) and 200 μm slices were cut from the part of the brainstem containing the MNTB. The slices were placed in gassed standard aCSF containing (in mM) NaCl 125, KCl 2.5, $NaHCO_3$ 26, NaH_2PO_4 1.25, Na pyruvate 2, myoinositol 3, glucose 10, $CaCl_2$ 2, $MgCl_2$ 1 and with pH 7.4. After incubating for 1 h at 37 °C, the slices remained