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Review

The effect of monaural middle ear destruction on response properties of neurons in the auditory midbrain of juvenile and adult mice

*Philip Jen**, *Lijing Xu*[1]

Division of Biological Sciences and Interdisciplinary, Neurosciences Program, University of Missouri, Columbia, MO 65211, USA

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ABSTRACT

This article reviews our studies of the effect of monaural middle ear destruction on midbrain auditory response properties of the laboratory mouse, *Mus musculus*. Monaural middle ear destruction was performed on juvenile and adult mice and the auditory sensitivity of neurons in the midbrain inferior colliculus (IC) ipsilateral and contralateral to the intact ear was examined 4 weeks later. When stimulated with sound pulses, IC neurons of the control mice typically had lower minimum threshold, larger dynamic range, and sharper frequency tuning curve than IC neurons of the experimental juvenile and adult mice. In the experimental mice, neurons in the ipsilateral IC had significantly longer latency, higher minimum threshold, and smaller dynamic range than neurons in the contralateral IC. When determined at two sound directions (ipsilateral 40° and contralateral 40° to the recording site), IC neurons of the control mice had higher minimum threshold, sharper frequency tuning curve but smaller dynamic range at I-40° than at C-40°. However, these direction-dependent response properties were not observed for IC neurons of the experimental juvenile and adult mice. Clear tonotopic organization was only observed in the IC of the control mice and experimental adult mice but not in the IC of experimental juvenile mice. These different response properties are discussed in relation to the effect of monaural middle ear destruction.

1. Introduction

In auditory physiology, the processing of auditory signals has traditionally been explained by excitatory and inhibitory interactions of divergent and convergent projections within the auditory system (Suga et al., 1998). For example, in the auditory pathway, the central nucleus of the inferior colliculus (IC) receives and integrates excitatory and inhibitory inputs from many lower auditory nuclei as well as from the auditory cortex (Adams, 1979; Herbert et al., 1991; Huffman and Henson, 1990; Saldana et al., 1996; Winer et al., 1998). The inhibitory inputs to the IC are glycinergic, which originate extrinsically, and GABAergic, which originate extrinsically and intrinsically (Fubara et al., 1996; Oliver and Shneiderman, 1991; Roberts and Ribak, 1987). Many studies have shown that the interplay between excitation and GABAergic and/or glycinergic inhibition shapes auditory response properties and multi-parametric selectivity of IC neurons (e.g. discharge

* *Corresponding author*. Fax: +1 573 884 5020.
E-mail address: jenp@missouri.edu (P. Jen).
[1] Present address: Department of Anatomy and Neurobiology, University of Tennessee, Memphis, TN 38163, USA.

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pattern, duration, frequency, amplitude, direction, etc.) (Casseday et al., 2000; Fuzessery and Hall, 1996; Jen and Feng, 1999; Jen and Zhang, 2000; Jen et al., 2002; Klug et al., 1995; Koch and Grothe, 1998; LeBeau et al., 1996, 2001; Lu and Jen, 2001). Furthermore, two recent studies have shown that inhibitory inputs with stronger intensity and longer duration are more effective in producing inhibition of auditory response of IC neurons than inhibitory inputs with weaker intensity and shorter duration (Lu and Jen, 2001, 2002, 2003).

Previous studies have shown that abnormal auditory stimulation during early postnatal development can be manifested through anatomical and physiological changes that occur in the central auditory system (Rubel and Fritzsch, 2002; Syka, 2002). For example, electrophysiological studies have shown that early monaural plugging, blocking, or occlusion changes the auditory spatial sensitivity of neurons in bats, owls, and guinea pigs (Clements and Kelly, 1978; Jen and Sun, 1990; Knudsen et al., 1984). This monaural auditory deprivation also produces substantial loss of binaural interaction of auditory neurons in rats and cats (Clopton and Silverman, 1977, 1978; Moore and Irvine, 1981; Silverman and Clopton, 1977). As a result, use of binaural time and intensity differences for sound localization is impaired (Erulkar, 1972; Masterton and Imig, 1984). Other studies have shown that unilateral cochlear removal produces a threefold increase in the number of excitatory response neurons in ipsilaterally excited IC recording loci with lower thresholds, wider dynamic ranges, more sustained discharge patterns, and shorter latencies (Batkin et al., 1970; Kitzes, 1984; Kitzes and Semple, 1985; McAlpine et al., 1997; Moore and Kitzes, 1986). Conversely, early stimulation with a specific sound frequency in mice and rats results in most IC neurons tuned to the early exposed sound frequency (Clopton and Winfield, 1976; Poon and Chen, 1992; Poon et al., 1990). Complementary to these observations, anatomical studies showed that cochlear ablation leads to significant reduction in the number and soma size of neurons in the ipsilateral cochlear nucleus (Blatchly et al., 1983; Coleman and O'Connor, 1979; Hashisaki and Rubel, 1989; Powell and Erulkar, 1962; Trune, 1982; Webster and Webster, 1977, 1983), the ipsilateral trapezoid body (Moore, 1992; Pasic et al., 1994), the ipsilateral lateral and medial superior olivary nuclei (Feng and Rogowski, 1980) as well as the contralateral nucleus of the lateral lemniscus (Powell and Erulkar, 1962) and the contralateral IC (Hardie and Shepherd, 1999; Harrison et al., 1998; Nishiyama et al., 2000).

In our laboratory, we have shown that monaural middle ear destruction in the juvenile laboratory mouse, *Mus musculus*, produces significantly smaller size and number of neurons in the IC ipsilateral to the intact ear than in the contralateral IC when examined at adulthood (Xu et al., 2001). In this review article, we present our electrophysiological studies on the effect of monaural middle ear destruction on multi-parametric auditory response properties of neurons in the IC of the same species of mice.

A detailed description of materials and methods can be found in earlier papers (Jen and Xu, 2002; Xu and Jen, 2001). Briefly, monaural middle ear destruction is performed under Nembutal anesthesia (50 mg/kg b.w.). A pair of fine forceps is inserted through the ear canal under the light microscope to remove the tympanic membrane and the ossicular chain. The operated mice are then observed under a heat lamp until they completely recovered from anesthesia. This monaural middle ear destruction represents an acoustic manipulation or conductive modification that severely reduces the sound intensity (by 15 dB with frequency below 20 kHz) transmitted to the inner ear (Suga and Jen, 1975; Tonndorf and Khanna, 1970; Tonndorf et al., 1976). As a result, monaural middle ear destruction produces asymmetrical sound stimulation conditions in which sound intensity to the operated ear is severely attenuated.

In acoustically guided behavior, mice like most mammals move their pinna conjunctively or disjunctively to create interaural time and pressure differences which are the two main cues for sound localization along the horizontal plane (Bergeijk and van, 1962). Our earlier study has shown that the directionality of sound pressure transformation at the pinna of the mouse contributes importantly to the directional sensitivity of the auditory neurons (Chen et al., 1995). Because attenuated sound conduction at the operated ear of the mouse in our studies inevitably altered the two cues and the directionality of sound pressure transformation at the pinna, we also studied the effect of monaural middle ear destruction on responses of ipsilateral IC neurons to sounds delivered at two opposite directions in the frontal auditory field (contralateral 40°, C-40°, and ipsilateral 40°, I-40°, to the recording site).

Studies on the multi-parametric auditory response properties of individually recorded IC neurons were conducted in three groups of mice: (1) Control (recording was made at 6–8 weeks after birth, 18 mice, 9 males and 9 females), (2) Experimental juvenile (monaural middle ear destruction was performed at 2 weeks after birth, recording was made at 4 weeks later, 26 mice, 11 males and 15 females), and (3) Experimental adult (monaural middle ear destruction was performed at 6–7 weeks after birth, recording was made at 4 weeks later, 17 mice, 9 males and 8 females).

2. Discharge patterns, best frequency (BF), minimum threshold (MT), and latency of IC neurons determined with sounds at C-40° to the recording site

The discharge patterns of 437 IC neurons in response to presented sound pulses can be described as phasic responders, phasic bursters, or tonic responders. Phasic responders discharged 1–2 impulses (Fig. 1A) whereas phasic bursters discharged 3–7 impulses to presented sound pulses (Fig. 1B). In contrast, tonic responders discharged impulses throughout or longer than the duration of presented sound pulses (Figs. 1C, D). Most (75–86%) neurons in both ICs of all three groups of mice were either phasic responders or phasic bursters. The remaining (16–25%) neurons were tonic responders. While the percent of tonic neurons was comparable in both ICs of the control mice, the ipsilateral IC of both groups of experimental juvenile and adult mice had relatively fewer (5–11%) tonic responders than the contralateral IC. This observation is likely due to the fact that monaural middle ear destruction produced increased inhibition and thus significantly raised the threshold of neurons in the ipsilateral