Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

Research Report

Auditory nerve synapses persist in ventral cochlear nucleus long after loss of acoustic input in mice with early-onset progressive hearing loss

Brian McGuire[a], *Benjamin Fiorillo*[a], *David K. Ryugo*[b,c], *Amanda M. Lauer*[a,*]

[a]*Center for Hearing and Balance and Department of Otolaryngology-HNS, Johns Hopkins University, Baltimore, MD 21205, USA*

[b]*Hearing Research Unit, Garvan Institute of Medical Research, Darlinghurst 2010, NSW, Australia*

[c]*School of Medical Sciences, University of New South Wales, Kensington 2052, NSW, Australia*

ARTICLE INFO

Article history:
Accepted 6 February 2015
Available online 14 February 2015

Keywords:
Ventral cochlear nucleus
Auditory nerve
Endbulb
Hearing loss
Deafness

ABSTRACT

Perceptual performance in persons with hearing loss, especially those using devices to restore hearing, is not fully predicted by traditional audiometric measurements designed to evaluate the status of peripheral function. The integrity of auditory brainstem synapses may vary with different forms of hearing loss, and differential effects on the auditory nerve–brain interface may have particularly profound consequences for the transfer of sound from ear to brain. Loss of auditory nerve synapses in ventral cochlear nucleus (VCN) has been reported after acoustic trauma, ablation of the organ of Corti, and administration of ototoxic compounds. The effects of gradually acquired forms deafness on these synapses are less well understood. We investigated VCN gross morphology and auditory nerve synapse integrity in DBA/2J mice with early-onset progressive sensorineural hearing loss. Hearing status was confirmed using auditory brainstem response audiometry and acoustic startle responses. We found no change in VCN volume, number of macroneurons, or number of VGLUT1-positive auditory nerve terminals between young adult and older, deaf DBA/2J. Cell-type specific analysis revealed no difference in the number of VGLUT1 puncta contacting bushy and multipolar cell body profiles, but the terminals were smaller in deaf DBA/2J mice. Transmission electron microscopy confirmed the presence of numerous healthy, vesicle-filled auditory nerve synapses in older, deaf DBA/2J mice. The present results suggest that synapses can be preserved over a relatively long time-course in gradually acquired deafness. Elucidating the mechanisms supporting survival of central auditory nerve synapses in models of acquired deafness may reveal new opportunities for therapeutic intervention.

© 2015 Elsevier B.V. All rights reserved.

Abbreviations: ABR, auditory brainstem response; ASR, acoustic startle reflex; SPL, sound pressure level; TEMm, transmission electron microscopy; VCN, ventral cochlear nucleus; VGLUT1, vesicular glutamate transporter 1

*Correspondence to: Center for Hearing and Balance and Department of Otolaryngology-HNS, Johns Hopkins University, 515 Traylor Building, 720 Rutland Ave., Baltimore, MD 21205, USA.
E-mail address: alauer2@jhmi.edu (A.M. Lauer).

http://dx.doi.org/10.1016/j.brainres.2015.02.012
0006-8993/© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Peripheral damage patterns and audibility cannot fully account for performance on complex auditory processing tasks or success with hearing devices. For instance, postlingually deafened patients who receive cochlear implants as adults can show speech discrimination and recognition scores of 0 to 100% (Green et al., 2007; Lazard et al., 2010). Central auditory system factors such as deafness-related synaptic alterations, cortical and subcortical reorganization, and capacity for plasticity likely play a critical role in determining outcomes in hearing device recipients. Studies have demonstrated loss of auditory nerve synapses in the ventral cochlear nucleus (VCN) after acoustic overexposure (Kim et al., 2004), surgical destruction of the cochlea (Fyk-Kolodziej et al., 2011; Gentschev and Sotelo, 1973), and application of ototoxic substances (Yuan et al., 2014; Zeng et al., 2009a), but the effects of other forms of acquired deafness on these synapses are unclear.

Mouse models provide an efficient means of investigating the effects of different forms of acquired hearing loss on the central auditory system including hereditary and environmental determinants of synaptic integrity. The DBA/2J mouse is one such model in which the genetic contributions to accelerated age-related hearing loss (Johnson et al., 2008; Noben-Trauth et al., 2003; Shin et al., 2010; Someya et al., 2007), and the effects of manipulations to the acoustic environment (Turner and Willott, 1998; Willott et al., 2005) have been well characterized. Hearing loss in DBA/2J mice begins at high frequencies around the time of weaning (3–4 weeks) and becomes severe at all but the lowest frequencies by about 4 months of age (Erway et al., 1993; Mikuriya et al., 2008; Someya et al., 2007; Xie and Manis, 2013). The hereditary hearing loss is related to a mutation of cadherin 23, a transmembrane protein involved in cell adhesion (Noben-Trauth et al., 2003), and a variant of fascin-2, a developmentally regulated actin crosslinker in hair-cell stereocilia (Shin et al., 2010).

The DBA/2J cochlea initially contains more cochlear hair cells than other inbred strains (Ding et al., 2001). Progressive base-to-apex damage to hair cells in the base of the cochlea occurs within the first six months of age in this strain (Shin et al., 2010; Someya et al., 2007). Spiral ganglion neurons (SGN) are almost completely lost from the base by 6–8 months of age, with partial SGN loss also occurring in apical regions (Mikuriya et al., 2008; Someya et al., 2007; Willott and Erway, 1998).

Transmission at auditory nerve endbulb synapses in anteroventral cochlear nucleus (AVCN) is altered in young adult DBA/2J mice (Wang and Manis, 2005, 2006). One and a half to two month old DBA/2J mice show slower and smaller mEPSCs, reduced release probability, higher action potential firing thresholds, larger after-hyperpolerizations, reduced entrainment during long stimulus trains, and shorter spike latencies in high frequency regions compared to younger DBA/2Js (Wang and Manis, 2005, 2006). These mice also show abnormal neural responses in the inferior colliculus and cochlear nucleus in young adulthood (Willott, 1981).

We investigated the effects of early-onset progressive hearing loss on the structural integrity of central auditory nerve synapses in deaf DBA/2J mice. We hypothesized that deaf DBA/2J mice would show a reduced complement of auditory nerve synapses in VCN compared to young hearing DBA/2J mice. Surprisingly, we found that auditory nerve synapses in VCN survived in deaf DBA/2J mice, in contrast to what has been described for other forms of acquired deafness.

2. Results

2.1. Hearing screening

2.1.1. Auditory brainstem responses (ABRs)

Individual ABR thresholds for DBA/2J mice ages 1 to 7 months are plotted in Fig. 1. Average thresholds from 4 normal-hearing

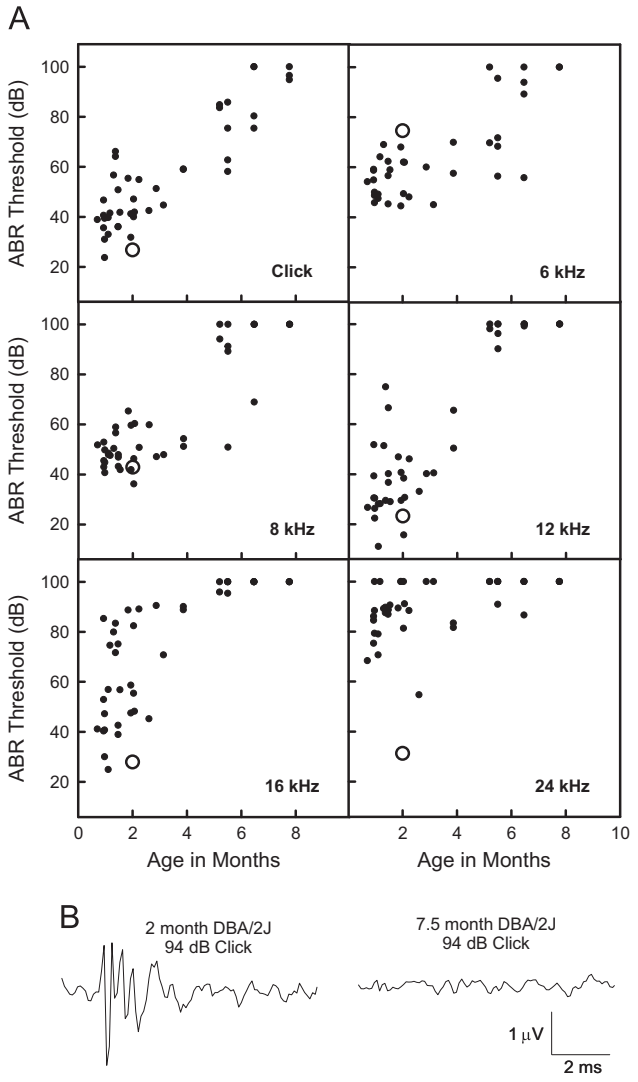

Fig. 1 – Auditory brainstem responses (ABR) thresholds for DBA/2J mice as a function of age. (A) individual DBA/2J mice (filled circles) and average CBA/CaJ thresholds at 2 months of age (large open circles). DBA/2J mice show a profound hearing loss by 5 months of age. Click thresholds are in dB peak equivalent level. Tone thresholds are in dB sound pressure level (SPL). (B) Examples of ABR waveforms from a young, hearing DBA/2J and an older, deaf DBA/2J mouse evoked by broadband clicks.

Download English Version:

https://daneshyari.com/en/article/4323864

Download Persian Version:

https://daneshyari.com/article/4323864

Daneshyari.com