Hearing Research 343 (2017) 92–107

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Crossmodal plasticity in auditory, visual and multisensory cortical areas following noise-induced hearing loss in adulthood

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ARTICLE INFO

Article history:
Received 19 March 2016
Received in revised form
21 June 2016
Accepted 27 June 2016
Available online 4 July 2016

Keywords:
Crossmodal plasticity
Sensory reorganization
Multisensory integration
Extrastriate visual cortex
Extracellular electrophysiology
Rat

ABSTRACT

Complete or partial hearing loss results in an increased responsiveness of neurons in the core auditory cortex of numerous species to visual and/or tactile stimuli (i.e., crossmodal plasticity). At present, however, it remains uncertain how adult-onset partial hearing loss affects higher-order cortical areas that normally integrate audiovisual information. To that end, extracellular electrophysiological recordings were performed under anesthesia in noise-exposed rats two weeks post-exposure (0.8–20 kHz at 120 dB SPL for 2 h) and age-matched controls to characterize the nature and extent of crossmodal plasticity in the dorsal auditory cortex (AuD), an area outside of the auditory core, as well as in the neighboring lateral extrastriate visual cortex (V2L), an area known to contribute to audiovisual processing. Computer-generated auditory (noise burst), visual (light flash) and combined audiovisual stimuli were delivered, and the associated spiking activity was used to determine the response profile of each neuron sampled (i.e., unisensory, subthreshold multisensory or bimodal). In both the AuD cortex and the multisensory zone of the V2L cortex, the maximum firing rates were unchanged following noise exposure, and there was a relative increase in the proportion of neurons responsive to visual stimuli, with a concomitant decrease in the number of neurons that were solely responsive to auditory stimuli despite adjusting the sound intensity to account for each rat's hearing threshold. These neighboring cortical areas differed, however, in how noise-induced hearing loss affected audiovisual processing; the total proportion of multisensory neurons significantly decreased in the V2L cortex (control 38.8 ± 3.3% vs. noise-exposed 27.1 ± 3.4%), and dramatically increased in the AuD cortex (control 23.9 ± 3.3% vs. noise-exposed 49.8 ± 6.1%). Thus, following noise exposure, the cortical area showing the greatest relative degree of multisensory convergence transitioned ventrally, away from the audiovisual area, V2L, toward the predominantly auditory area, AuD. Overall, the collective findings of the present study support the suggestion that crossmodal plasticity induced by adult-onset hearing impairment manifests in higher-order cortical areas as a transition in the functional border of the audiovisual cortex.

1. Introduction

Hearing loss represents a clinically-relevant form of sensory deprivation which can lead to extensive anatomical and physiological changes throughout the central auditory system (for review, see (Chen and Yuan, 2015). The consequences of this experience-dependent neuroplasticity are not restricted to how sound is processed, as crossmodal plasticity can also occur, which is characterized by an increased responsiveness of neurons in the central auditory system to visual and/or tactile stimuli. Functional neuroimaging studies in hearing-impaired humans (for review, see Bavelier et al., 2006; Heimler et al., 2014; Pavani and Roder, 2012) and single-unit recordings in animal models (Allman et al., 2009a; Hunt et al., 2006; Meredith et al., 2012; Meredith and Allman, 2012; Meredith and Lomber, 2011) have identified that the nature and extent of cortical crossmodal plasticity depends on the severity of the hearing loss (e.g., profound deafness versus mild hearing impairment) as well as the age at which the deprivation commenced (e.g., congenital/early-onset versus in adulthood) (Lambertz et al., 2005). For example, studies on humans (Auer et al., 2007; Doucet et al., 2006; Finney et al., 2003, 2001; Vachon et al., 2013), mice (Hunt et al., 2006) and cats (Meredith and Lomber, 2011; but see Kral et al., 2003) have revealed that early-onset profound deafness results in sensory replacement, whereby there

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http://dx.doi.org/10.1016/j.heares.2016.06.017
0378-5955/

is an increased recruitment of the deprived auditory cortex for visual and/or tactile processing. Importantly, such crossmodal plasticity has been shown to underlie the behavioral enhancements that occur in the processing of peripheral visual stimuli and visual motion following congenital deafness (Lomber et al., 2010).

In contrast to profound deafness which fully deprives the brain of auditory cues from the environment, an incomplete lesion of the cochleae spares some degree of residual auditory processing. To date, relatively few studies have investigated cortical crossmodal plasticity in humans with mild-moderate hearing loss (Campbell and Sharma, 2014, 2013; Musacchia et al., 2009), despite being a fairly common occurrence with nearly one in five adults in the USA having a measurable hearing loss (Agrawal et al., 2008; Lin et al., 2011). In ferrets partially-deafened early in life (Meredith and Allman, 2012) or in adulthood (Meredith et al., 2012), single-unit recordings in the core auditory cortex revealed an increased proportion of neurons capable of processing *both* auditory and non-auditory stimuli (i.e., multisensory neurons). The neural and behavioral consequences of this increase in multisensory convergence are poorly understood; however, it is reasonable to predict that higher-order areas downstream of the core auditory cortex would also be affected by partial hearing loss.

In the present study, we sought to characterize the nature and extent of crossmodal plasticity induced by adult-onset partial hearing loss in higher-order cortical areas that normally integrate audiovisual information. To that end, we used extracellular electrophysiological recordings in anesthetized rats at specific stereotaxic coordinates to consistently and comprehensively map neuronal responses to auditory and visual stimuli in the dorsal auditory cortex (AuD), an area outside of the auditory core, as well as in the neighboring region of the lateral extrastriate visual cortex (V2L), an area known to contribute to audiovisual processing (Barth et al., 1995; Hirokawa et al., 2008; Toldi et al., 1986; Wallace et al., 2004; Xu et al., 2014). To induce partial hearing loss, adult rats were bilaterally exposed for two hours to a loud broadband noise. Subsequent electrophysiological testing used auditory stimuli well-above each rat's hearing threshold as assessed with auditory brainstem responses to control for differences in audibility caused by the noise exposure. Single- and multi-unit activity was recorded in response to auditory, visual and combined audiovisual stimuli in rats two weeks after noise exposure and the results were compared to age-matched controls. Similar to previous studies in the core auditory cortex of partially-deafened animals (Meredith et al., 2012; Meredith and Allman, 2012), we investigated whether noise-induced crossmodal plasticity manifested in the AuD and V2L cortices as an increased responsiveness to non-auditory stimuli, thereby changing the relative proportion of multisensory versus unisensory neurons. Related to this, we also examined the prevalence and nature of multisensory integration, a hallmark of multisensory processing in which a multisensory neuron's response to one sensory modality is significantly modulated by stimulation in another modality (for review, see (Stein and Meredith, 1993), as this property could greatly influence residual auditory processing and perception following partial hearing loss (Meredith et al., 2012).

2. Material and methods

2.1. Animals

Fourteen adult male Sprague-Dawley rats (age: 103 ± 3 days; body mass: 425 ± 8 g) were used in this study. All rats were housed in a temperature controlled room on a 12-h light-dark cycle with food and water *ad libitum*. All experimental procedures were approved by the University of Western Ontario Animal Use Subcommittee, and were in accordance with the guidelines established by the Canadian Council on Animal Care.

2.2. Hearing assessment with an auditory brainstem response

Hearing levels were assessed using an auditory brainstem response (ABR) which was performed in a double-walled sound-attenuating chamber. Rats were anesthetized with ketamine (80 mg/kg; i.p.) and xylazine (5 mg/kg; i.p.), and subdermal electrodes (27 gauge; Rochester Electro-Medical, Lutz, FL) were positioned at the vertex (active electrode), over the right mastoid process (reference electrode) and on the mid-back (ground). The animal was not secured in a stereotaxic frame during the ABR testing. Body temperature was maintained at ~37 °C using a homeothermic heating pad (507220F; Harvard Apparatus, Kent, UK).

Sound stimuli were generated by a Tucker-Davis Technologies (TDT, Alachua, FL) RZ6 processing module at 100 kHz sampling rate and delivered by a magnetic speaker (MF1; TDT) positioned 10 cm from the animal's right ear. The left ear was occluded with a custom foam earplug. Sound stimuli for the ABR, noise exposure procedure and electrophysiological recording experiments were calibrated with custom Matlab software (The Mathworks, Natick, MA) using a 1/4-inch microphone (2530; Larson Davis, Depew, NY) and preamplifier (2221; Larson Davis).

The auditory evoked activity was collected using a low-impedance headstage (RA4L1; TDT), preamplified and digitized (RA16SD Medusa preamp; TDT), and sent to a RZ6 processing module via a fiber optic cable. The signal was filtered (300–3000 Hz) and averaged using BioSig software (TDT). Auditory stimuli consisted of a click (0.1 ms) and two tones (4 kHz and 20 kHz; 5 ms duration and 1 ms rise/fall time), which were each presented 1000 times (21 times/second) at decreasing intensities from 90 to 10 dB sound pressure level (SPL) in 10 dB SPL steps. Near threshold, successive steps were decreased to 5 dB SPL, and each sound level was presented twice in order to best determine ABR threshold using the criteria of just noticeable deflection of the averaged electrical activity within the 10-ms window (Popelar et al., 2008).

Rats in the control group (n = 7) underwent an ABR to assess their hearing levels, followed immediately by an electrophysiological recording experiment. Rats in the noise exposure group (n = 7) had their baseline hearing tested with an initial ABR, followed by exposure to a loud broadband noise (see below) that induced a permanent hearing loss. Two weeks after the noise exposure, a final ABR was performed, which was followed immediately by the same electrophysiological recording experiment as performed in control rats.

2.3. Noise exposure

While under ketamine (80 mg/kg; i.p.) and xylazine (5 mg/kg; i.p.) anesthesia, rats were bilaterally exposed for 2 h to a calibrated broadband noise (0.8–20 kHz) at 120 dB SPL. This noise exposure protocol was similar to one used by Popelar et al. (2008) in rats to induce persistent changes in auditory processing at the level of the ABR as well as the auditory cortex. The broadband noise was generated with TDT software and hardware (RPvdsEx; RZ6 module), and delivered by a super tweeter (T90A; Fostex, Tokyo, Japan) which was placed 10 cm in front of the rat. A homeothermic heating pad was used to maintain body temperature at ~37 °C.

2.4. Surgical procedure

Immediately following the final hearing assessment, each rat was maintained under ketamine/xylazine anesthesia, the foam earplug was removed from the left ear, and the animal was fixed in