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Synaptic morphology and the influence of auditory experience

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ABSTRACT

The auditory experience is crucial for the normal development and maturation of brain structure and the maintenance of the auditory pathways. The specific aims of this review are (i) to provide a brief background of the synaptic morphology of the endbulb of Held in hearing and deaf animals; (ii) to argue the importance of this large synaptic ending in linking neural activity along ascending pathways to environmental acoustic events; (iii) to describe how the re-introduction of electrical activity changes this synapse; and (iv) to examine how changes at the endbulb synapse initiate trans-synaptic changes in ascending auditory projections to the superior olivary complex, the inferior complex, and the auditory cortex.

1. Introduction

Auditory experience has long been known to play a critical role in the developing mammalian auditory system. Neural activity is important for normal construction and maintenance of auditory structure and function (Parks et al., 2004; Shepherd et al., 2006; Walmsley et al., 2006; Ryugo and Limb, 2009; Sanes and Bao, 2009). It influences the refinement of the genetic blueprint for circuitry including axonal distribution, pruning, and synapse formation (Leake and Hradek, 1988; Baker et al., 2010). The absence of auditory stimulation introduces a series of pathological and atrophic changes that include more widespread distributions of axonal projections (Leake and Hradek, 1988), abnormal projections (Moore and Kitzes, 1985; Nordeen et al., 1983a,b), delayed maturation (Sanes, 1993; Kandler, 2004), and language impairments (Robbins, 2006). The effects of re-introduction of auditory activity through electrical stimulation on synaptic morphology and function have been studied using models of congenital deafness that include both hereditary deafness and chemical deafening, surgical ablation of the organ of Corti, and acoustic trauma. Collectively, these data emphasize the malleability of auditory synapses in response to variations in the acoustic environment.

In the present report, we review the evidence addressing the pathological consequences of sensory deprivation and the restorative influences brought about by the introduction of neural activity through cochlear implantation. The main focus concerns morphological plasticity observed at the level of the auditory nerve in the cochlear nucleus (CN). Not surprisingly, changes at these synapses have consequences further on up the system at the superior olivary complex (Schwartz and Higa, 1982; Russell and Moore, 1995; Kapfer et al., 2002; Sanes and Bao, 2009; Tirko et al., 2009), inferior colliculus (Snyder et al., 1995, 2000), and auditory cortex (Heid et al., 1998; Klinke et al., 1999, 2001; Kral et al., 2000, 2001). We will discuss several observations that have advanced our knowledge of synaptic plasticity and expanded our understanding of the effect that functional manipulations have on the auditory system.

Synapses are definable not only by presynaptic characteristics at the release site such as synaptic vesicle size and shape, transmitter chemicals, neuromodulators, and transporter molecules but also by the postsynaptic composition of transmitter receptor subunits, shape and curvature of the postsynaptic density (PSD), ion channels, and associated second messenger and retrograde signaling systems. Moreover, there must also be consideration of size and distribution of the terminal, target compartment (e.g., cell body, dendritic shaft, spine), and location of the cell bodies that give rise to the projection. Proper transmission of acoustic signals from neuron to neuron depends in large part on the precise spatial arrangement of these factors at the release site. The corollary to this notion is that abnormalities of synaptic structure will impair signal

Abbreviations: AVCN, Anteroventral cochlear nucleus; CN, Cochlear nucleus; IC, Inferior colliculus; ILD, Interaural level difference; ITD, Interaural time difference; LSO, Lateral superior olive; MSO, Medial superior olive; MNTB, Medial nucleus of the trapezoid body; SBC, Spherical bushy cell.

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transmission, thereby corrupting the neural representation of the acoustic stimulus.

Our ability to hear and understand sound commences with the receptor sensory organ of the ear, the cochlea. For the processing of sound, neural activity in the central nervous system must be tightly coupled to acoustic events. The hair cell receptors within the cochlea transduce sound energy into neural signals in auditory nerve fibers that are conveyed to the CN (Kiang et al., 1965). The CN receives all incoming auditory information and gives rise to the ascending auditory pathways. Different sounds are revealed by distinctive characteristics in their time-varying features. Thus, timing of neural activity within the central auditory pathways must not only be time-locked to the external sound stimuli but also to the evoked patterns of activity transmitted along the ascending pathways. Synchrony along the various parallel pathways is essential, and aberrations in these pathways will corrupt processing and disturb how sound is perceived.

Auditory nerve fibers are the major source of excitation to cells of the ventral CN (Koerber et al., 1966). In the anteroventral cochlear nucleus (AVCN), myelinated auditory nerve fibers give rise to large, axosomatic synaptic endings known as endbulbs of Held (Held, 1893; Ramón y Cajal, 1909; Lorente de Nó, 1981). Endbulbs have a calyx-like appearance where the end of the fiber is marked by the emergence of several thick, gnarled branches that divide repeatedly to form an elaborate arborization of *en passant* and terminal swellings to embrace the postsynaptic spherical bushy cell (SBC, Ryugo and Fekete, 1982). These endbulbs are among the largest synaptic endings in the brain (Lenn and Reese, 1966), and one-to-three endbulbs selectively contact a single SBC (Brawer and Morest, 1975; Cant and Morest, 1979; Ryugo and Sento, 1991; Ryugo and Fekete, 1982; Nicol and Walmsley, 2002). They contain up to 2000 release sites (Ryugo et al., 1996) and transmit activity with high fidelity to the postsynaptic SBC (Pfeiffer, 1966; Babalian et al., 2003). The size and evolutionary conservation of endbulbs among vertebrates emphasize its importance in enabling spike activity to be yoked in time to acoustic events (Fig. 1).

The endbulb synapse has been implicated in the pathway that processes the precise timing features of sound that is crucial for binaural hearing (Yin and Chan, 1990; Fitzpatrick et al., 1997). SBCs send projections from the AVCN to the superior olivary complex (Cant and Casseday, 1986). These projections terminate onto ipsilateral neurons of the lateral superior olive and bilaterally upon bipolar neurons of the medial superior olive (MSO). In the MSO, inputs from the right CN terminate on the dendrites extending to the right, whereas inputs from the left CN terminate on the dendrites extending to the left. The MSO is the first nucleus to process synaptic input from both ears (Fig. 2).

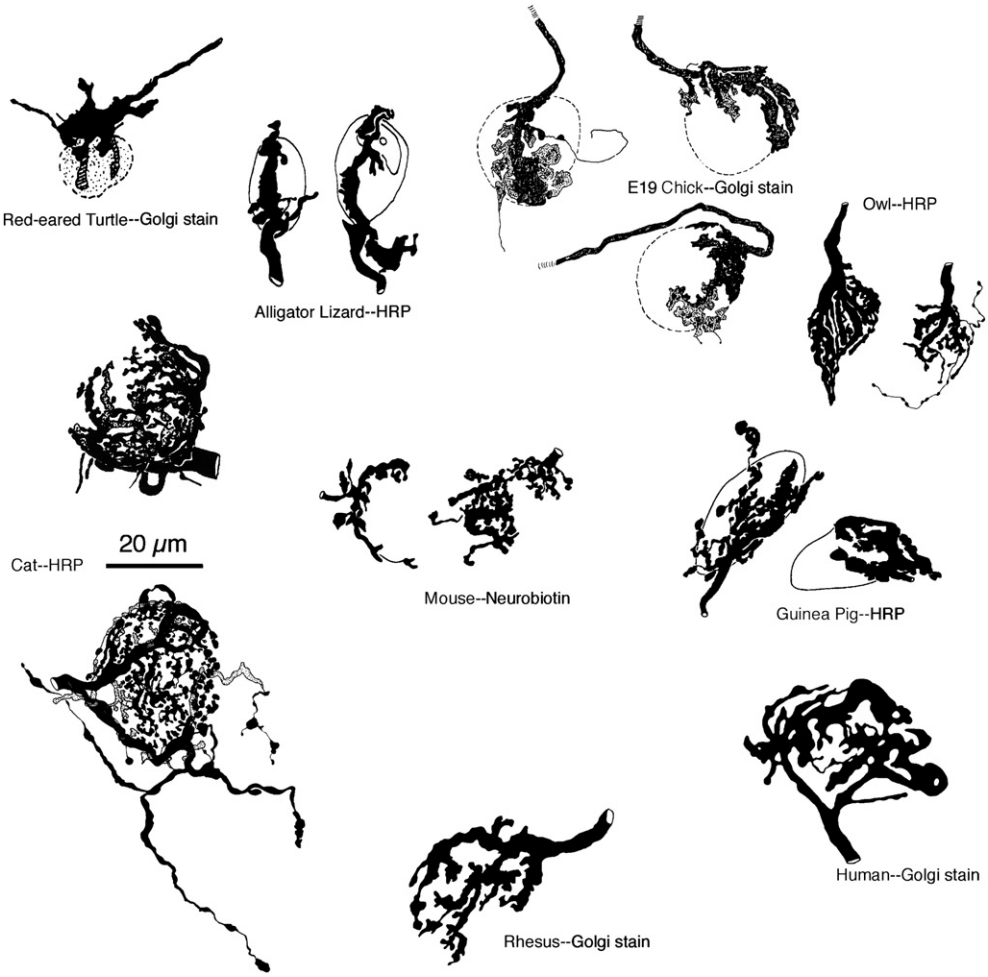

Fig. 1. Examples of endbulbs of Held from various terrestrial vertebrates. This important axosomatic terminal is found in turtles (Browner and Marbey, 1988), alligator lizards (Szpir et al., 1990), chicken (Jhaveri and Morest, 1982), barn owl (Carr and Boudreau, 1991), mouse (Limb and Ryugo, 2000), guinea pig (Tsuji and Liberman, 1997), cat (Ryugo et al., 1996, 1998), rhesus monkey (Ryugo, unpublished observations), and human (Adams, 1986). The large size and evolutionary conservation of this synaptic terminal indicates it importance in hearing. From Ryugo and Parks, 2003.