Chapter 6

Anatomy of Vocal Communication and Hearing in Rodents

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Abstract

Many animals produce sounds to communicate different types of information. More often than not, such sounds are vocal in nature and elicit a predictable behavioral response from the listener. While much of the literature on vocal communication derives from classic neuroethological studies in a number of vertebrates, rodents are fast becoming the group of choice to study vocalizations for a variety of reasons, not least of which is the advantage they offer for genetic manipulation. Central to the study of vocal communication is the need to understand how the nervous system mediates vocal production and how the auditory system accesses the information within a communication signal that leads to an appropriate behavioral response. A key goal is to determine the essential features of communication signals, what information they transmit, how they are categorized and, in combination with information derived from other sensory modalities, how they are interpreted and linked to a context-appropriate motor response. There is a substantial body of literature on the anatomy and physiology of the neural pathways that mediate vocalizations in rodents, but exciting new research lines are investigating the role of learning in vocal communication and how the rodent nervous system processes complex vocal communication signals.

Keywords Auditory processing · Auditory system · Rodent · Vocal control · Vocal learning

6.1 Introduction

Sounds in nature are a rich source of information and animals can make sense of what they hear, for example, to detect and escape from an approaching predator or detect and capture moving prey (Bradbury et al. 1998). Animals also actively produce sounds—frequently vocal sounds—to communicate different types of information (Suthers et al. 2016).

Communication signals often elicit a predictable response by the receiver, so the study of vocal communication cannot be divorced from the role it plays in natural behavior. It thus comes as no surprise that a large proportion of those working on vocal communication systems identify themselves as neuroethologists. Tinbergen (1963) identified four fundamental problems that ethologists seek to solve: those related to causation, survival, evolution, and ontogeny. In the context of vocal communication these four problems can be reframed as the following questions:

(1) What are the specific mechanisms that mediate the production of vocal communication signals?

(2) What roles do these signals play in survival and reproduction?

(3) What are the ancestral features that characterize vocal communications and how have they evolved in different lineages?

(4) How are these vocal signals acquired and/or modified during development?

Throughout the neuroethological literature, studies of vocal communication can help address any of these four questions, and this framework is used in this chapter.

Vocal signals are used to communicate a wide range of information, such as alerting others to the presence of a predator, communicating distress, resolving conflict, initiating courtship, mating, and defending a territory (Bradbury et al. 1998). Vocalizations are initiated in a variety of contexts, and their role is to produce a

predictable response from the listener (Griffiths and Warren 2004; Bennur et al. 2013). Acoustic signals must convey the right kind of information, and the listener, in turn, must be able to detect, discriminate, and categorize the information contained in the signal in order to produce an appropriate response. Most vertebrates have vocal repertoires in the audible range, and many vertebrates also produce vocal signals with frequencies in the ultrasound (over 20 kHz). In general, hearing sensitivities are such that they match the spectral range of the animal's vocal signals (Wilczynski and Ryan 2010).

This chapter describes what is known about how vocal signals are produced, detected, and categorized by rodents. Sections 6.2 and 6.3 describe what is known about how communications are produced, and the neural pathways that form part of the vocal production and auditory systems. How the nervous system is able to process information contained in vocal communication signals is considered in Sect. 6.4 and how these principles apply to specific examples of rodent communication is covered in Sect. 6.5. The role of learning in the shaping of communication signals and the evidence for learning in rodents is discussed in Sect. 6.6 and, finally, Sect. 6.7 considers how vocal signals are integrated into an appropriate behavioral response.

6.2 Vocal Production Mechanisms

In any discussion of vocalizations, it is helpful first to make a distinction between *phonation* and *vocalization*. Although the verb *phonate* is defined (by the Concise Oxford Dictionary) as "to utter a vocal sound," more is frequently implied by *vocalization* than just the production of a vocal sound. A cough is a vocal sound, but usually would not be called a vocalization. The basic requirements of vocal sound production (i.e., phonation) in terrestrial mammals and amphibia are a larynx and an

externally directed air stream. When the latter passes through the former with sufficient speed and/or resistance, audible sounds are produced, even in excised larynges. In life, when terrestrial mammals vocalize, modulation of sounds takes place to a greater or lesser degree through the combined action of expiration (usually), partial or full closure of the laryngeal glottis (by adduction of the vocal folds in mammals), and the use of a supralaryngeal component of the vocal tract to ensure a filtering and articulation of sounds produced by the vocal organ (Simonyan and Horwitz 2011). All these actions entail the coordinated neural control of a great many muscles (Jürgens 2009), and lack of this coordination or control—as evidenced in humans, for instance—is reflected in a wide range of vocal impairments (or impediments) from stuttering to the total inability to vocalize, such as can result from cerebral vascular accidents (CVA or stroke) or brain lesions. The ability to phonate (make sounds) in these cases, however, is usually retained, unless the lesion includes the midbrain periaqueductal gray (see Sect. 6.2.1).

In addition, it is evident that vocal production can also be impaired due to a variety of defects. These may be of a genetic (e.g., *FoxP2*; Fisher and Scharff 2009), signaling pathway (Hedgehog; Tabler et al. 2017) or molecular (cadherin-6; Fischer and Hammerschmidt 2011; Nakagawa et al. 2012) nature, or to problems affecting the larynx itself. Laryngeal issues range from nodules on the vocal folds to laryngeal carcinoma. There are also a variety of developmental ciliathapies that have recently been highlighted in a thorough examination of the developmental biology of the larynx (Tabler et al. 2017) in which mice were used as model experimental subjects.

Comparative aspects of the mammalian larynx are considered in Harrison (1995), who notes that rodents (including rats, mice, gerbils (Family: Muridae),, and hamsters (Family Cricetinae)) possess a larynx that does not differ in any significant way from

that of other mammals (Fig. 6.1), even though, unlike most other mammals, they produce both a variety of ultrasonic sounds in different behavioral and social contexts and sounds (cries) audible to the human ear. This apparent lack of laryngeal specialization in rodents has puzzled researchers for many years (Roberts 1975; Riede 2013). A recent analysis in mice has shown how ultrasounds can be produced by an air jet passing through an inter-arytenoid glottis, which then impinges on the planar inner wall of the upper thyroid (and perhaps the epiglottis). Feedback may be generated in this way, but exactly how is not yet clear (Mahrt et al. 2016). This analysis in no way denies the contributions of the laryngeal nerves, anatomy, and neural control involved in the respiratory-vocal mechanisms that mediate ultrasonic vocalizations or audible cries (Herbst 2016).

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6.2.1 Neural Control

Forty muscles, their nerves, and the brain nuclei involved in mammalian vocalization are listed by Jürgens (2009). The cricothyroid muscle, which is involved in changes in pitch, is innervated by the external branch of the superior laryngeal nerve, while all other laryngeal muscles are innervated by the recurrent branch of the inferior laryngeal nerve. In humans, at least, this simple textbook description does not do justice to the variability of innervation of laryngeal muscles by the laryngeal nerves or the degree to which the muscles are innervated from both sides. The motoneurons projecting to both nerves lie in nucleus ambiguus (the nucleus of the vagal cranial nerve X), which extends as a narrow column deep in the reticular formation of the medulla.

This fundamental brainstem circuitry is headed by a midbrain center, which in mammals comprises parts of the periaqueductal gray (PAG) (Jürgens 2002). The PAG

neurons project their axons downstream to various nuclei involved in respiratory-vocal control, the principal one being nucleus retroambiguus (NRA) in the caudal medulla. The NRA is the only nucleus to have direct access to all the cranial and spinal motoneurons involved in this control (Holstege 1989; Holstege et al. 1997). Electrical or chemical stimulation of appropriate parts of PAG evoke realistic-like vocalizations (Phillips and Peek 1975; Zhang et al. 1994), and lesions of PAG result in mutism in animals, including humans (Brown 1965; Esposito et al. 1999).

This last observation is central to the idea that PAG and its limbic associated (anterior cingulate) afferent cortex (Newman et al. 1989; Dujardin and Jürgens 2005) control unlearned, innate, or emotional vocalizations (e.g., cries and laughter in humans), whereas the precentral motor (laryngeal) cortex is required for the learning and production of learned vocalizations, specifically, speech in humans (Jürgens 2009; Simonyan and Horwitz 2011; Simonyan 2014). Songbirds, likewise, possess a telencephalic nucleus (robustus arcopallialis, RA) that is essential for the learning and production of learned vocalizations ("song", Nottebohm et al. 1976) but the homologous relationship of this nucleus to any part of the cortex is unclear. Nevertheless, laryngeal motor cortex in humans and RA in songbirds both project directly upon vocal motoneurons in nucleus ambiguous in humans (Kuypers 1958; Iwatsubo et al. 1990) and nucleus tracheosyringealis in songbirds (Nottebohm et al. 1976). Those projections are not found in nonhuman primates or in birds that do not produce song, none of which learn their vocalizations (Wild et al. 1997; Simonyan and Jürgens 2003). It occasioned some surprise, therefore, when the laryngeal motor cortex was shown in mice to have a direct, albeit very sparse, direct projections upon laryngeal motoneurons (Arriaga et al. 2012), supporting the idea that ultrasonic vocalizations (USVs) are learned by mice, or have a learned component (Arriaga and

Jarvis 2013). It is controversial, however, as to whether auditory feedback is necessary for the learning of USVs in mice (Hammerschmidt et al. 2012; Arriaga and Jarvis 2013), but mice lacking a cerebral cortex appear to develop normal USVs (Hammerschmidt et al. 2015). In addition, innate emotional vocalizations in certain strains of very young *FoxP2* mutant mice are not affected by the experimental knockdown (Gaub et al. 2010), suggesting that the midbrain vocal control pathway remains intact in these mice.

6.3 Organization of the Auditory System

What is known about the organization of the auditory system in vertebrates has come from a variety of disciplines and a large number of species. The description of the organization of the auditory system below follows that of Malmierca (2003) for the rat.

6.3.1 The Middle Ear

The presence of three ossicles in the middle ear is one of the distinguishing characteristics of mammals, although substantial variation and evolutionary novelties are seen in the organization of mammalian ears (Fritzsch et al. 2013; Mason 2013). For example, in many rodents the ear is semi-isolated from the skull, having a bony shell that connects the ear to the skull by small bridges and cartilages (Fleischer 1978). As a rule of thumb, animals whose ears are smaller and stiffer and have smaller tympanic membrane and footplate areas are better at hearing high frequencies, whereas those that have larger ears that are less stiff and have larger tympanic and foot plate areas are better at hearing lower frequencies (Rosowski 1994).

The size of the middle ear generally scales to body size, although there are some exceptions. The *microtype ear* is of particular interest (Fleischer 1978). Found only in species with small body size, these ears tend to be smaller than what would be expected for their body size, the malleus tends to be bigger than expected, and the area of the stapedial footplate tends to be smaller as well. Mason suggested that these are specializations for high frequency hearing (Rosowski 1994; Mason 2013). Not all small mammals, however, have a microtype ear. For example, voles, hamsters, gerbils, and dormice have freely mobile ossicles (where the malleus complex is anchored to the tympanic membrane through a ligament) or transitional ossicles, and no microtype ears are found in the squirrel-related clade (Fleischer 1978; Mason 2013). In the mouse-related clade, specializations are found that probably evolved from the microtype ear (Lavocat and Parent 1985; Mason 2013).

Guinea pigs (*Cavia sp.*), chinchillas (*Chinchilla sp.*), and their relatives (Ctenohystrica) have an unusual middle ear related to, but somewhat distinct from, the typical freely mobile ear (Mason 2013). The malleus has a distinctive morphology with the anterior process being small or missing altogether, such as in the guinea pig ear. An unusual stapedious muscle is found in guinea pig and chinchilla, although it has been lost in many members of Ctenohystrica. In species that lack the stapedius muscle, the malleus and incus are fused (Rosowski 1994; Mason 2013).

Subterranean mammals show middle ear specializations, including the loss of middle ear muscles, and adaptations in the arrangement of the ear ossicles that lead to less overall middle ear stiffness, which may improve low-frequency hearing. Burda and colleagues (1992) described a flattening of the articulation at the incudal-mallear joint, an enlarged incus, varied stapes morphologies, and a reduction in middle ear muscles associated with subterranean life. The reduction in middle ear muscles is said

to be an adaptation for low frequency hearing, as increased stiffness due to contraction of the stapedius muscle reduces low frequency transmission. It should be noted, however, that small mammals that show low-frequency hearing, such as sciurids and Mongolian gerbils, do not have reduced middle ear muscles.

Fossorial species that have limited high frequency hearing also show some middle ear adaptations, including an enlargement of the floorplate of the stapes; the size of the stapes and the mass of the malleus and incus are not different from those of nonfossorial species (Lavocat and Parent 1985; Mason 2001). Describing the mammalian middle ear simply as a three-ossicle ear does not do justice to the amount of variation present.

6.3.2 The Inner Ear

All mammals have an elongate basilar membrane with the sensory hair cells (inner hair cells) that are involved in transducing the vibrations in the fluids of the inner ear (caused by sounds) into a neural signal that is transmitted to the brain via the auditory nerve (AN), and outer hair cells (OHC) which receive efferent projections from the barinstem (Fig. 6.2). The size and degree of coiling of the cochlea, the bony structure that houses the basilar membrane, varies among mammals, and the organization of hair cells along the basilar membrane exhibit profound differences when compared to other vertebrates (Fritzsch et al. 2013; Manley 2017).

The coiled cochlea of therian mammals formed after the appearance of the three-ossicle middle ear between 220 and 150 Ma, before marsupials and placentals split into two separate lineages (Manley 2017). One characteristic of the inner ear of therian mammals is that bone integrates into the organ of Corti, encapsulates the acoustic ganglion, and forms longitudinal ridges on the side of the basilar membrane

that may provide the basilar membrane with greater stiffness to support higher frequency hearing.

In a study of the inner ears of rodent species, West (1985) found a correlation between the number of spiral coils and the octave range of hearing. While the number of turns was not correlated to the length of the basilar membrane, the basilar membrane length appeared to be related to the upper and lower limits of the hearing range. Heffner and colleagues (2001) showed that rodents have higher variability in the upper limit of their hearing range than other mammals, and animals with smaller heads tended to have higher frequency-hearing limits. High-frequency hearing may be important for sound localization in animals with small heads, with the exception of subterranean mammals, in which sound localization is not expected to play an important role.. Subterranean rodents have a higher hair cell number in the inner ear than rats, and there are indications that the regions that map best frequency may be over-represented (Lange et al. 2007).

A distinguishing feature of modern mammals is their sensitivity to ultrasound frequencies, although a number of small rodents (e.g., chipmunks, *Tamias striatuts*; hamsters) show some of the lowest frequency hearing (below 100 Hz) (Manley 2017). Presentation of ultrasounds up to 50 kHz can elicit reflexes (twitching of the ears or vibrissa) and can be used successfully in conditioning experiments (Dent, Screven, and Kobrina, Chap. 4). Sensitivity to ultrasound also has been shown using the cochlear microphonic in laboratory rats, Mongolian gerbils (*Meriones unguiculatus*), and kangaroo rats (*Dupodomis merriami*). Although it is clear that some rodents are able to hear and process ultrasounds, no obvious specialization for ultrasound hearing has been found in rodent ears (Sales and Pye 1974).

6.3.3 The Spiral Ganglion

The sensory hair cells along the cochlea respond to different frequency components that are contained in an auditory stimulus (highest frequencies at the base; lowest frequencies at the apex) . This information is then carried as spike trains of the AN to the central auditory system. The cell bodies of the neurons that form the AN lie in the spiral ganglion, which is housed in the modiolus of the bony cochlea.

The peripheral endings of the majority of spiral ganglion cells (Type I) synapse on IHCs and a smaller population of peripheral fibers (Type II) synapses on the OHCs. The central processes of spiral ganglion neurons enter the brainstem and immediately bifurcate to innervate different regions of the cochlear nucleus complex (CN) (Ramón y Cajal 1904; Lorente de No 1933). This early bifurcation is thought to support the separation of parallel channels that process different features of the auditory stimulus. The tonotopic arrangement that begins at the basilar membrane in the cochlea is maintained in the AN, and in the organization of the auditory processing nuclei in the central nervous system to the cortex. .

6.3.4 The Cochlear Nuclear Complex

In mammals, afferents of the AN project to the CN, which can be divided into three regions: dorsal cochlear nucleus (DCN), posterior and anterior ventral cochlear nuclei (PVCN and AVCN, respectively). The descending branch of the AN makes synapses with cells in the PVCN, and axons continue beyond that to innervate the dorsal cochlear nucleus (DCN). The ascending branch of the AN synapses on neurons of the anterior ventral cochlear nucleus (AVCN) (Fig. 6.3A, black coloring). Type I afferents from the AN make large calyceal synapses on cells of the AVCN; the calyceal synapses are good at maintaining the temporal features of the auditory

stimulus. In the PVCN the AN synapses form boutons on the dendrites of octopus cells. The basic patterns and the parallel pathways of the auditory system emerge in the CN (Winer and Schreiner 2005).

The DCN is laminated in rodents, as it is in most mammals, and consists of three outer layers and a central core, the latter being poorly developed in rats (Malmierca 2003). Willard and Ryugo (1983) describe the mouse DCN as consisting of two superficial layers that surround a core below which is a fourth basal layer that contains the fibers that will join the dorsal acoustic stria. The dendrites and cell bodies of the pyramidal (fusiform) cells, which are the main projection cells of the DCN, are found in the outer layers. The DCN is interesting in that it receives inputs not just from the auditory nerve and higher auditory areas, but also from non-auditory regions of the brain, and it is possible that more complex transformations of the auditory input may take place there (Montgomery and Bodznick 1994; Wigderson et al. 2016), including the cancellation of self-generated sounds (Singla et al. 2017).

In rats and some other rodents, a group of cells forms the interstitial nucleus of the vestibulocochlear nerve or auditory nerve nucleus, located lateral to VCN (between the a Schwann glia cell border and the zone of bifurcation of the auditory nerve). These cells, which receive collaterals from primary afferents and project mainly to the contralateral pontine nucleus, may be involved in the acoustic startle reflex (Harrison and Warr 1962). The axons of these cells have a variety of targets but do not appear to project to other nuclei of the auditory system (López et al. 1999; Nodal and López 2003).

Since acoustic stimuli can be deconstructed relatively easily into simpler acoustic parameters, such as frequency and amplitude modulation (FM, AM), and duration, it comes as no surprise that a large body of literature describes the properties of auditory

neurons in the context of stimulation with simple tones or reduced representations of time-varying artificial stimuli. Each auditory nerve fiber carries information over a narrow frequency range and may also carry some AM information, which is transferred to neurons in the CN (Heil and Peterson 2015). Some neurons in the CN encode AM and amplify the depth of the AM envelope with high fidelity (Frisina 2001; Joris et al. 2004), but it is perhaps in the DCN where more complex transformations of spectral and temporal aspects of the auditory input occur (Winer and Schreiner 2005).

The branching of the auditory nerve to synapse on cells in different parts of the CN suggests that this is where the mapping of different features of the stimulus begins to emerge and diverge. Neurons in the ventral cochlear nucleus extract and enhance timing and frequency inputs from the auditory nerve and their projections establish two broad parallel pathways. Neurons in the AVCN project to the superior olivary complex (SOC) where interaural time and intensity differences are used for sound localization (the sound localization pathway). Some neurons in the PVCN bypass the SOC and project to the nuclei of the lateral lemniscus (NLL) and the central nucleus of the inferior colliculus (CIC), conveying spectrotemporal representations (the sound identification pathway) (Eggermont 2001). Both the sound localization and sound identification pathways converge at the level of the inferior colliculus (IC).

6.3.5 The Superior Olivary Complex

The series of nuclei in the SOC are found in the ventral tegmentum; their numbers and sizes vary between species (Fig.6. 2A, blue tones) (Malmierca 2003). The lateral superior olive (LSO), medial superior olive (MSO), and the medial nucleus of the trapezoid body (MNTB) can be consistently identified in mammals. In rats, the

ventral nucleus of the trapezoid body (VNTB) is conspicuous, as is a superior paraolivary nucleus (SPON) that projects to the ipsilateral IC (Malmierca 2003). Most of the inputs to these nuclei originate in the AVCN, and some neurons of the SOC project topographically and bilaterally back to the CN or to the cochlea, where they modulate dynamic aspects of the basilar membrane. Bilateral inputs to neurons in the SOC form the basis of the interaural comparisons between intensity and temporal information that are used for sound localization (Winer and Schreiner 2005).

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6.3.6 The Lateral Lemniscus and Nuclei of the Lateral Lemniscus

The lateral lemniscus is a large tract that ascends through the ventrolateral brainstem to terminate in the IC. Embedded within the lateral lemniscus are several groups of cells collectively known as the nuclei of the lateral lemniscus (NLL) (Fig. 63A, green tones). The NLL vary in size in different species: they are described as modest in rats, well developed in cats, and hypertrophied in some echolocating bats (Winer and Schreiner 2005). Many axons of the lateral lemniscus make collaterals that synapse on NLL neurons, while other axons continue to the IC without branching. The lateral lemniscus carries axons from the contralateral VCN and DCN and axons from the SOC that terminate in the IC. The axons of the octopus cells of the PVCN terminate in the ventral nucleus of the lateral lemniscus (VNLL). The majority of axons from NLL neurons join the lateral lemniscus and terminate in the ipsilateral CIC; some neurons from the dorsal NLL (DNLL) cross the midline to synapse in the contralateral IC. The functional division of the NLL into a ventral mainly monaural component and a dorsal binaural component reflects parallel processing along the auditory pathway (Malmierca 2003). Although not mentioned by Malmierca, an intermediate division of the NLL that projects bilaterally to the IC has been described in mice (Willard and

Ryugo 1983). Excitatory and inhibitory inputs converge in DNLL where the cells respond to most signals that contain energy within their excitatory response region. A strong inhibitory projection originating in DNLL targets neurons in the IC (Pollak 2013).

6.3.7 The Inferior Colliculus

The auditory midbrain (the IC in mammals) is considered the main point of convergence of auditory input in the brainstem. The IC receives tonotopically organized inputs from the ascending axons of the lateral lemniscus as well as axons entering the IC via the commissure of Probst, which connects the ICs on the right and left side of the brain. The IC also projects back upon the lower auditory nuclei and receives descending inputs from cortical areas. Aside from its auditory inputs, the IC receives projections from other regions of the brain, thereby allowing multisensory integration (Fig. 63A, B, orange tones).

The largest region of the IC is formed by the CIC, which is surrounded by a smaller lateral nucleus and a dorsal cortex (Malmierca 2003). Each can be further subdivided into smaller regions based on cellular architecture and connectivity. In the mouse, Willard and Ryugo (1983) describe four IC regions: a central nucleus, a dorsomedial nucleus, an external cortex (which is parceled into two layers with different inputs), and a dorsal cortex. Different regions of the IC receive different combinations of inputs (Fig. 63A, B). The CIC is primarily auditory and retains the tonotopic organization of the ascending fibers; the lateral nucleus is multisensory and the dorsal cortex receives inputs from cerebral cortex. In addition to their tonotopic organization, neurons in the IC also appear to be organized on the basis of other

internal representations (e.g., onset latency, thresholds, receptive fields), probably resulting from differences in ascending inputs (Cant and Benson, 2006).

The lateral nucleus of the IC receives ascending inputs from the dorsal column nuclei and the trigeminal system, which carry somatosensory information from the body, and descending cortical inputs. This region of IC receives little, if any, input from the lateral lemniscus, and auditory information is brought in from commissural projections with no apparent tonotopic mapping.

The dorsal cortex of the IC contains broadly tuned neurons that respond more robustly to vocal stimuli than to noise (Aitkin et al. 1994). Although cells appear to be organized in a laminated structure, these do not seem to be related to tonotopy. The dorsal cortex also receives commissural axons from contralateral IC and descending axons from cortical areas. Cortical inactivation through cooling of the auditory cortex (AC) of female rats has effects on neuronal responses in IC, particularly the dorsal and external cortices (Popelář et al. 2016). Ascending axons from the IC bilaterally innervate the medial geniculate body (MGB) in the thalamus (Winer and Schreiner 2005). In addition, efferents from the dorsal cortex of the IC project to midbrain tegmental areas that are implicated in the production of vocalizations.

The IC integrates inhibitory and excitatory inputs and the neurons are tuned to temporal features of sound (e.g., sound duration, frequency modulation) (Eggermont 2001). About 30–50% of neurons in the IC show combination sensitivity that can be facilitatory or inhibitory (Woolley and Portfors 2013). The response patterns of neurons in the IC to tones and white noise are not too different from the responses found at lower levels of the auditory pathway, but since these change when inhibition is blocked locally, it is likely that the IC response patterns are at least partly generated locally rather than inherited from the afferent fibers (Pollak 2013).

Responses in IC neurons could be shaped by a balance of the magnitude of the incoming excitatory and inhibitory inputs or, alternatively, by the timing of the two inputs. The timing hypothesis is particularly attractive since it can explain neuronal responses to FM (Kuo and Wu 2012); however, the timing hypothesis assumes a linear transformation of inputs, and many IC neurons do not appear to linearly transform their inputs (Pollak 2013). The auditory system also tracks the duration of stimuli quite reliably, and neurons sensitive to the duration of the stimulus have been found in the IC of frogs, bats, chinchilla, rats, mice, and guinea pigs (Xia et al. 2000; Sayegh et al. 2011). In mice, Xia and colleagues (2000) described duration sensitive IC neurons that respond within the range of natural mouse vocalizations (3–300 ms). The duration-sensitive neurons could be grouped into four categories: duration selective, short-duration selective, bandpass, and all pass.

From this level on, the auditory system is often described as being organized in *core* (lemniscal) tonotopic regions and *belt* (nonlemniscal) regions where there is less tonotopic organization and often a higher degree of influence from nonauditory inputs. Lemniscal and nonlemniscal inputs from the IC project to different regions of the auditory thalamus.

6.3.8 The Medial Geniculate Body

The auditory thalamus of mammals (medial geniculate body, MGB) is generally divided into ventral, dorsal, and medial (magnocellular) subdivisions (Fig. 6.3, purple tones). The ventral MGB receives lemniscal inputs from the CIC, whereas non-lemniscal projections terminate in the dorsal and medial subdivisions of the MGB (He 2003; Lee 2013). Like the IC, the MGB receives cortical descending inputs, however

the inputs to MGB are more robust than those terminating in the IC (Anderson et al. 2007; Anderson and Linden 2011).

As in the CIC, the ventral MGB is tonotopically organized. Most axons originating from the IC terminate in this subdivision, and the response properties of neurons in this region resemble the properties seen in CIC (Malmierca 2003; Hackett 2011). The ventral MGB of Mongolian gerbil has been further parcelled into a pars lateralis, a pars ovoidea, and a rostral pole (Saldeitis et al. 2014). Neurons from the ventral MGB project to primary auditory areas in cerebral cortex. Ventral MGB neurons receive descending inputs from primary AC (A1) and, to a lesser extent, from association cortices that show tonotopic organization (Winer 1992).

The dorsal subdivision of the MGB has a more complex organization. It, too, receives inputs from the CIC but also from the peripheral portions of IC, from reticular thalamic nucleus, and from ventral MGB and other thalamic regions. In the Mongolian gerbil, the dorsal MGB can be subdivided further into a deep dorsal nucleus and a dorsal MGB proper (Saldeitis et al. 2014). Dorsal MGB projects mainly to association auditory regions of cortex and has been implicated in maintaining auditory attention (Kraus et al. 1994).

The medial portion of MGB receives afferents from the lateral nucleus of the IC, axonal terminations from vestibular nuclei, spinal cord nuclei, the midbrain superior colliculus, and also from the SOC and lateral lemniscus. Neurons in medial MGB project to all auditory cortices but also to nonauditory cortices (e.g., somatosensory and prefrontal cortex), putamen, and amygdala. All cortical auditory areas and some nonauditory areas project back to this medial division, suggesting that the medial MGB might play a role as a multisensory arousal system. One interesting feature is that the different portions of the MGB do not appear to connect with each other,

suggesting that the different regions represent true separate pathways with different processing tasks (Winer 1992; Hu 2003; Malmierca 2003).

Each thalamic nucleus receives a unique combination of inputs from different portions of the IC and provides a distinct set of inputs to different areas of cortex (Anderson and Linden 2011; Hackett 2011). A direct projection from lower auditory brainstem that bypasses the IC provides the MGB with short-latency inputs that may prepare the thalamus for the auditory information that will arrive from IC (Pannese et al. 2015). Descending inputs from cortex, in turn, modulate the responses in MGB (He 2003). A proposed role for thalamus stems from the observation that thalamic neurons have two modes of firing: bursting and tonic. Burst firing is commonly seen in anaesthetized animals. In awake animals, thalamic neurons primarily show tonic firing patterns but switch to bursting in association with a salient stimulus. It is then suggested that the switch from tonic to bursting may act as a wake-up call alerting the cortex to the presence of a biologically relevant stimulus (Sherman 2001; He 2003). Thus, the auditory thalamus might modify the responsiveness of AC in the context of attention. Inputs from the amygdala put the auditory thalamus in a position to evaluate the emotional valence of auditory stimuli (Anderson and Linden 2011).

The posterior intralaminar nucleus (PIL) and the peripeduncular nucleus (PP) of the posterior parathalamic nuclei receive inputs from IC and, in turn, project to AC. Malmierca (2003) thus considers them part of the rat thalamocortical pathway..

6.3.9 Auditory Regions of the Cerebral Cortex

The auditory cortex receives inputs from a variety of regions in the forebrain, including the contralateral AC and other auditory-related areas, and subcortical inputs originating from the auditory thalamus and other sensory thalamic nuclei (Hackett

2011). Using anatomical criteria, regions of the cortex receiving input from the auditory thalamus are defined as auditory (Hackett 2011). As is the case in IC and MGB, the AC can be parceled into a primary region that is tonotopically organized and primarily concerned with specific auditory processing (core), and other regions involved with more complex, cross-modality processing (belt).

The AC has been parcelled into different regions in different species. As many as fourteen cortical fields have been identified in the cat, and twelve cortical fields were identified in the moustached bat (He 2003; Shamma and Fritz 2009). In rats, the AC consists of a primary AC (Te1, area 41) and nonprimary auditory fields: a caudally positioned Te2 and a rostroventral Te3 (Fig. 63, red tones) (Winer 1992). In mice, Willard and Ryugo (1983) divide the AC into three areas: primary or koniocortex (area 41), area 22 (dorsal to area 41), and area 36 (ventral to area 41). Stiebler and colleagues (1997) divided the mouse AC into five fields: two that are tonotopically organized (primary auditory field or AI and anterior auditory field AAF), an ultrasound field (UF) that responded to frequencies above 40 kHz, a secondary auditory field (AII), and a dorsoposterior field (DP). Tsukano and colleagues (2017) considered a different organization in the mouse: AI, a dorsomedial field (DM), A2 and AFF, all tonotopically organized; and two nontonotopic fields, dorsoanterior field (DA) and dorsoposterior field (DP). Ultrasound responses are found not in a separate field but within A1, AAF, A2 and DM. In the Mongolian gerbil, Budinger and colleagues (2000) identify eight fields: two koniocortical fields (AI and AAF), with a dorsal subfield of AI, two smaller tonotopic fields (DP and a ventroposterior field), a dorsal field, and ventrally the anteroventral, ventral, and a ventromedial fields.

Outputs from AC target a number of cortical and subcortical structures, including not only a large majority of the auditory nuclei of the ascending auditory pathway

(Schofield and Coomes 2006; Hackett 2011) but also the basal ganglia and other premotor and brainstem nuclei, the amygdala, and others (Fig. 63B, red tones) (Winer 2006). Descending inputs to the CN are usually described as targeting the DCN. In guinea pigs, A1 and the dorsocaudal auditory field (but not secondary cortex) project to all subdivisions of the ipsilateral CN in addition to some contralateral projections that originate in low frequency regions (Jacomme et al. 2003).

Responses to features of acoustic stimuli such as FM and AM are seen in all cortical areas (Harris et al. 2011; Honma et al. 2013). In guinea pigs, responses in A1 are nonhomogenous: the dorsal belt of AC responds more strongly to broadband noise than to pure tones, whereas the ventral belt responds better to pure tones (Suta et al. 2008). Wang and colleagues (2016) examined the responses to stimulus duration in the A1 of mice and found that about half of the neurons were sensitive to duration, a proportion similar to that seen in the IC. However, after blocking the neurotransmitter GABA (gamma-aminobutyric acid), 60% of those neurons lost their duration sensitivity, underscoring how similar representations of acoustic features may arise at different levels of the auditory system.

The AC shows a collection of maps and selective filters, and cortical neurons appear to respond to higher order features of sounds (Nelken 2008). The responses observed in AC are influenced by anaesthesia. Responses to sustained stimuli and nonsynchronized responses to long repetitive stimuli are almost absent under anesthesia (Wang 2007). Temporal responses to sinusoidal AM stimuli in Mongolian gerbil AC are altered under anaesthesia, although the effects of anaesthesia in IC are not as pronounced (Ter-Mikaelian et al. 2007). These state-dependent responses in the cortex suggest that cortical neurons engage with acoustic stimuli such that they are actively transformed in a context-dependent way (Wang 2007; Harris et al. 2011).

Although cortical neurons are good at tracking fast temporal fluctuations of auditory stimuli, there is a general decrease in the temporal following rates from periphery to central areas (Escabí and Read 2003; Gaucher et al. 2013b). Spike trains appear to carry less information in A1 and MGB than in IC, although there is increasing redundancy of information moving from IC to MGB to A1 (Huetz et al. 2011). It seems now that both a rate and a temporal code may operate along the entire auditory axis. Temporal codes, rather than rate codes, may underlie discrimination of vocalizations in cortex, in which the computing unit is probably a neuronal population (Eggermont 2001; Ter-Mikaelian et al. 2013).

Traditionally, ascending projections of the auditory system are referred to as either lemniscal or nonlemniscal. The lemniscal pathway carries tonotopic projections from core regions of the auditory nuclei and runs in parallel with projections from the nonlemniscal pathway, which carries information under the influence of nonauditory centers. Recordings in mice (Anderson and Linden 2011) suggest that it is more appropriate to categorize the ascending inputs to cortex into three rather than two pathways: a tonotopic, a nontonotopic or diffuse, and a polysensory pathway. In this view, the tonotopic pathway would be made up of projections of the central IC to ventral MGB, which then projects to laminae III/IV of A1. The nontonotopic or diffuse pathway would be made up of IC inputs from the external and dorsal cortex of IC to the dorsal MGB, which then projects to layers I, I, III, IV and VI of secondary AC. The polysensory pathway would include the medial MGB that receives projections from all IC regions plus ventral NLL, DCN, and nonauditory areas and projects to all cortices (layers I, III, IV, and VI) (Eggermont 2001; Anderson and Linden 2011).

6.4 Processing of Vocal Signals

Vocal signals are rhythmic sequences of units with characteristic temporal and spectral structures, and they can be described based on agreed classification criteria that recognize the variation in the structure and the sequence of different units (Espmark et al. 2000). Information is contained in the signal's inherent properties (e.g., repetition, ordering, overlapping, and timing of elements) (Kershenbaum et al. 2016). Vocal output may also carry elements that are not used as part of the information conferred by the signal, as when ultrasound frequencies are present as a by-product of the vocal production but may be outside the hearing range of the listener. Different parts of the sequence may also carry different meanings (Okanoya and Screven, Chap. 2). The initial segment of a sequence, for example, may only operate to get the listener's attention, with the segment that follows carrying the information needed to release a behavioral response. There is no a priori reason, then, to expect a 1:1 matching between the vocal signal (influenced by production mechanisms) and the perceptual construct (influenced by sensory and perceptual mechanisms; Dent, Screven, and Kobrina, Chap. 4). Those parts of the vocalization that do carry biologically relevant information must, however, have enough distinctiveness so that they can be grouped in a perceptual construct that the animal can use to adequately respond, especially when additional cues (such as vision or olfaction) are not available to supplement the categorization (Marler 1957).

How the nervous system accesses the information contained within a communication signal to produce a response is central to the study of vocal communication. The process begins with the transformation of the input from a time-varying acoustic waveform to a perceptual abstract representation or *auditory object* (Bizley and Cohen 2013). Species-specific vocalizations, like other natural sounds,

are quite stereotypical (to the extent that they can be described with a certain degree of accuracy) but with embedded variation that depends on the type of call and the individual caller. The nervous system thus needs to account for this inherent variability to produce an efficient neural representation (Eggermont 2001; Theunissen and Elie 2014).

Researchers, then, need to understand how acoustic structures are transformed into neural responses, how neuronal response patterns are used to identify and categorize a signal and, ultimately, how this information is linked to the motor decision and control regions that mediate the response. The challenge is to establish what constitutes the neural representation of an auditory categorical percept, keeping in mind that there is not necessarily a 1:1 map with a behavioral response, and acknowledging the influence of experience, attention, and hormonal states (King et al. 2015; Hurley and Kalcounis-Ruppell, Chap. 8). The more that is known about the relationship between stimulus and behavior, the easier it is to identify the underlying neural code (Gentner and Margoliash 2003; Sanes and Woolley 2011).

Artificial stimuli, such as those used to establish the best frequency of a neuron, do not vary much in the time domain, and the response of the neurons can often be described in terms of the overall number of spikes produced. Variations in spike probabilities related to the onset and offset of the stimulus have also been used to describe cell types, especially in the CN and IC. The neural responses in the auditory system are often shaped by interactions of excitatory and inhibitory inputs to create specific neuronal responses that can be influenced by development and experience (Pollak 2013; Theunissen and Elie 2014). Many auditory neurons respond preferentially to a subset of categories of vocal stimuli (selectivity) or to specific acoustic features (specificity) (Gentner and Margoliash 2003).

Where responses are neatly synchronized to the temporal properties of the stimulus (isomorphic) it is possible that information is being relayed rather than processed. Feature extraction of the stimulus is more likely to occur in nonisomorphic representations.. Auditory neurons may carry stimulus information in their mean firing rate (rate code) and/or in the fine grain temporal pattern of the spike train (temporal code) (Huetz et al. 2011; Woolley and Portfors 2013). A temporal code is often thought to be in play when the stimulus can be discriminated based on the temporal pattern of spikes produced (but not on the basis of total spike count alone) or when the pattern in which the spikes are produced varies in accordance with the rate of change of the stimulus (Huetz et al. 2011). When neuronal responses to natural stimuli are very reliable and reproducible across presentation trials, yet with spike patterns that are different for different stimuli, then it is likely that a temporal code is being used (Huetz et al. 2011; Gaucher et al. 2013b). For nonvarying artificial stimuli, a rate code approach may be sufficient to describe the neuronal responses, but a temporal code seems to more appropriately describe the neural representations of vocal signals and natural stimuli that show a high degree of spectrotemporal variation (Gaucher et al. 2013b).

A second consideration when examining neural responses to natural stimuli is to determine whether the representation of a combination of features can be achieved by a single neuron (feature detectors) or whether it requires a coordinated set of neurons (Huetz et al. 2011; Schneidman 2016). The *feature detector hypothesis* posits that a neuron (or a small set of neurons) can respond to particular features or combinations of features within the acoustic stimulus. The existence of feature detectors requires that stimuli be processed hierarchically in parallel pathways that converge on feature detector neurons that respond to specific combinations of features (Gentner and

Margoliash 2003). Alternatively, *the population hypothesis* states that perception of a signal emerges through distributed neuronal assemblies in which each neuron provides some coarse representation of a particular stimulus feature which, when put together, creates the representation of the stimulus as a whole (Gentner and Margoliash 2003; Schneidman 2016). Since the construction of an auditory object requires combining multiple sets of information, its representation is likely to be distributed and spanning multiple cortical networks (Eggermont 2001; He 2003).

While natural stimuli can be described in terms of their individual features, the ability to categorize natural sounds depends on more than just the sum of the parts (Geissler and Ehret 2004). Neuronal responses obtained by presenting isolated features of vocal signals contrast with those obtained when the entire vocalization is used as stimulus. Neurons may respond strongly to natural and behaviorally significant sounds, but not to their simpler components (Woolley and Portfors 2013). In most neurons of the MGB of the guinea pig, for instance, a neuron's response to communication signals could not be predicted based on its frequency-tuning curve (Tanaka and Taniguchi 1991). Similar results are seen in the IC of mammals and the auditory midbrain of birds (Woolley and Portfors 2013). Thus, responses to natural stimuli involve nonlinear transformations that produce a representation of the higher order statistics of natural sounds (Theunissen and Elie 2014).

The search for a neural code ultimately seeks to identify the set of rules that relate neural activity to a stimulus or a behavior (Eggermont 2001). The code may take different forms at different levels of processing and for different types of stimuli. Whatever the pattern of the neural responses may be, it can be considered to be part of a neural code in as much as it occurs under natural conditions and is elicited by natural stimuli. As Eggermont (2001) pointed out, knowing that the information

necessary to represent a stimulus property is present in the firing of a neuron is different from knowing whether the nervous system uses part of all of the information.

6.5 Vocal Communication in Rodents

Rodents produce calls that have energy in the audible and/or ultrasound range (Okanoya and Screven, Chap. 2). Special attention has been focused on the production of ultrasonic vocalizations that include the infant calls that elicit parental responses, or calls between adults associated with mating and agonistic behaviors. The auditory system shows robust and preferential response to conspecific vocalizations over other natural sounds (including heterospecific vocalizations; Dent , Screven, and Kobrinaet al., Chap. 4). The main question that needs to be answered is whether there is something special about the neural substrates through which vocal communication signals are processed or whether preferential responses to biologically significant sounds merely emerge through repeated exposure (Poremba et al. 2013).

Selectivity for communication sounds first emerges in the IC (Pollak 2013). In DNLL, responses to vocalizations are nonspecific, but in IC neurons are reported to selectively respond to some natural vocalizations but not others (Pollak 2013). Blocking GABA and glycine inhibition results in an expansion of the tuning curves of IC neurons and reduces the selectivity to vocalizations (Woolley and Portfors 2013). In the auditory midbrain of birds, neurons are also tuned to specific spectrotemporal modulations of the conspecific song (Woolley 2012). Responses to vocalizations in rodents are seen in the IC (Suta et al. 2003; Portfors et al. 2009), and selectivity and specificity can arise through rate codes or temporal codes. The neural responses to natural vocalizations in mice and guinea pigs are described below.

6.5.1 Adult Mouse Vocalizations Males of laboratory mice strains produce at least two types of USVs when they encounter a female or her urine, each related to a different phase of copulation (Portfors 2007; Nyby 2010). Male mice USVs seem to be regulated by androgens and pheromones, such as those found in the female urine, and they are probably processed redundantly by the vomeronasal and olfactory systems (Nyby 2010). Females responding to male songs appear to maintain close contact with the vocalizing males, and they will approach a speaker playing USV sounds (Portfors 2007; Nyby 2010).

Neurons in IC are selective to conspecific vocalizations (Portfors et al. 2011; Pollak 2013). In female mice, Garcia-Lazaro and colleagues (2015) reported that while only 9% of neurons in the CN respond to vocalizations, responses are seen in 59% of neurons in the IC. Robust responses to USVs in the IC are shaped by inhibition and are sensitive to perturbations of the acoustic features of the USVs (Portfors and Felix 2005; Egnor and Seagraves 2016). Responses in IC are modulated by dopamine and may also be modulated by social interactions through the influence of serotoninergic inputs (Gittelman et al. 2013; Egnor and Seagraves 2016). The IC of female mice shows heterogeneous responses, increased encoding efficiency, and a distinct neural representation for different vocalizations (Holmstrom et al. 2010). In general, hearing sensitivities are such that they match the spectral range of the vocal signals (Wilczynski and Ryan 2010; Dent, Screven, and Kobrina, Chap. 4); however, ultrasound frequencies are not highly represented in the IC tonotopic map despite their behavioral relevance (Portfors et al. 2009). Instead, IC neurons respond to conspecific vocalizations with energies outside the neuron's tuning curve, perhaps by exploiting cochlear distortions created by combinations of high frequencies in the USV (Holmstrom et al. 2010; Woolley and Portfors 2013). A population code is

proposed to lead to the representation of each vocalization (Portfors et al. 2009). In A1, neuronal responses to USVs seem to be correlated with the neuron's frequency tuning curve. Neurons responded more strongly to natural rather than time-reversed versions of USVs, and responses were also less robust when the USVs had been temporally distorted (Carruthers et al. 2013).

6.5.2 Guinea Pig Vocalizations

Guinea pigs produce at least eleven types of vocalizations composed of multiple acoustical attributes (Berryman 1976). Neurons within individual nuclei in the auditory pathway may be responsible for extracting particular features or combination of features (Suta et al. 2008).

Responses in the IC of guinea pigs are less selective than in other rodents with a lower proportion of neurons showing call selectivity (Suta et al. 2003; Syka 2010). Neuronal responses are higher for vocalizations than for tones, noise, or time-reversed presentations of the vocalization but show little preference for one call over another (Suta et al. 2003; Pollak 2013). Vocalizations are encoded spatially across the tonotopic map, matching the spectral content of the vocalization. A small number of neurons appeared to be sufficient to encode a representation of the vocalizations, although increasing the number of neurons involved increased discrimination (Lyzwa et al. 2015).

The responses in the thalamic MGB show less selectivity than in IC (Syka 2010). Neurons in the MGB in guinea pigs respond both to tones and to species-specific vocalizations, although these appear to be nonselective (Tanaka and Taniguchi 1991; Philibert et al. 2005). The representation of spectral features appears to be preserved in calls with wider frequency spectra but to be less precise for lower frequency calls

(chutter and purr, for example). In ventral and medial MGB, Suta and colleagues (2008) showed that neurons that phase lock to the fundamental frequency of the call also showed responses to the call that were strongly dependent on its spectral composition In contrast, Tanaka and Taniguchi (1991) recording from MGB concluded that the majority of neurons showed discharge patterns to vocalizations that could not be predicted by the neuron's frequency tuning curves.

Neurons in MGB and A1 in awake and anaesthetized animals showed similar firing rates for vocalizations with only a few producing spike trains that carried a significant amount of information (Gaucher et al. 2013a). A significant amount of information was contained in the discharge patterns of neurons in MGB and AC in awake animals, as compared to anaesthetized animals (Huetz et al. 2009). The reliability of spike timing was similar for both the natural and time-reversed version of the vocalization and was higher in nonanaesthetized animals, although the responses were not mirror images of each other, suggesting they were sensitive to a specific sequence of signal presentation (Huetz et al. 2009).

The information in the temporal spike patterns also increases between MGB and AC. Severe loss of spectral information did not seem to prevent AI neurons from correctly classifying individual calls, but the representation of natural calls became degraded following temporal disturbances of the vocal stimulus (Ter-Mikaelian et al. 2013). Wang and colleagues (1995) suggested that the coding in cortex is different for sounds that have a behavioral relevance and sounds that do not. Ultimately, the representation of acoustic vocal communication signals must be integrated with other regions of the brain where the combination of context and internal state can elicit an appropriate behavior.

6.6 Learning in the Context of Vocal Production Manipulating the behavioral significance of a particular acoustic feature may lead to a corresponding representation of that feature in the brain. This has been shown in rat cortex using conditioned stimuli for the representation of tones, sound intensity, and temporal information (de Villers-Sidani et al. 2007). For example, rat pups exposed to different sequences of tone pips differentially represent those frequencies in cortex based on the pups' developmental experience (Köver et al. 2013). Thus, early experience may help to shape the representation of auditory categories in cortex (Han et al. 2007).

Contextual learning, whereby a signal becomes associated with a new context as a result of experience (Janik and Slater 1997, 2000), is common in mammals, including rodents such as rats and guinea pigs, and may underlie the association of conspecific vocalizations with a biological meaning. It appears that the 22 kHz group of rat calls may not be innately recognized as an alarm call but acquires that meaning as a consequence of associative learning (Wöhr et al. 2010). The USVs produced by mouse pups carry no behavioral relevance for nonmaternal females, so it has been suggested that the relevance emerges as the result of experience raising pups, which leads to the recognition of the pup call (Shepard et al. 2015). Thus, learning can influence the central mapping and meaning of acoustic structures (Hurley and Kalcounis-Ruppell, Chap. 8).

The possibility of vocal learning in the courtship USVs of mice was recently examined (Arriaga et al. 2012). It is suggested that there is a pathway of vocal control that is shared by all vertebrates that mediates the production of innate vocalizations. This *innate pathway* involves the PAG that acts on vocal motoneurons via the lower brainstem respiratory/vocal nuclei (or equivalent nuclei in nonmammalian species) (see Sect. 6. 2.1). Learning acquisition involves a cortical pathway (present in humans

and absent in nonhuman primates) that has direct descending projections from cortical regions into primary laryngeal motoneurons (Fitch et al. 2010). An equivalent cortico-bulbar pathway is present in songbirds that also show learning acquisition (Doupe and Kuhl 1999).

Arriaga and colleagues (2012) showed activation of immediate early gene *erg1* in singing mice in a cortical region near the anterior commissure that included some parts of motor cortices and anterodorsal striatum, but those increases in expression were not seen in mice that were hearing but not singing. After injecting a trans-synaptic label into the laryngeal muscles, retrogradely labeled neurons were observed in the same region of the motor cortex thereby establishing a connection between these cortical structures and laryngeal motoneurons. Chemical lesions in this area did not prevent the mice from singing; their songs had a similar syllable composition, although some changes in the spectral composition were seen within days. Mice that were deafened also produced courtship USVs with similar syllable composition and some deteriorated spectral composition, but the deterioration was seen only after a period of eight months. These results are in contrast with those of others. For instance, the vocalizations of congenitally deaf transgenic mice or mice that were deafened before the onset of hearing appear to be no different from the vocalizations produced by hearing- animals (Hammerschmidt et al. 2012; Heckman et al. 2016). When separated from their mothers, mice pups with a *FoxP2* knockout (a gene that has been implicated in vocal learning, see Sect. 6.2.1) vocalize less in the sonic range and utter fewer ultrasound whistles than do the heterozygous and wild-type counterparts (Scharff and Haesler 2005), although it should be noted that *FoxP2* knockout pups also exhibit a number of general brain abnormalities. Furthermore, mice lacking a cerebral cortex appear to develop normal USVs (Hammerschmidt et al. 2015).

Arriaga and colleagues (2012) acknowledge that the projection from cortex to the medulla in mice is not robust and that further studies are needed to establish the possibility of learning acquisition in mice.

6.7 Behavioral Responses to Vocal Communication Signals

Vocal signals in nature do not happen in isolation, especially short range signals are usually accompanied by stimulation of other sensory modalities (e.g., olfaction, vision) that contribute to the elicitation of a behavioral response. Grasshopper mice (*Onychomys leucogaster*) produce their adult type IV vocalization accompanied with clear postural displays: standing on their hind legs, preferentially from an elevated position, suggesting that both acoustic and visual information play a part in the signal (Hafner and Hafner 1979). Guinea pigs that were presented with wideband noise paired with a light stimulus showed that the visual input had a suppressive effect on the auditory responses in AC (Kubota et al. 2017). The auditory system has substantial connections with nonauditory centres in the brain, especially through the nonlemniscal pathways, which may provide the contextual information to incorporate attention and affective qualities in stimulus processing (Pannese et al. 2015).

Holstege and Subramanian (2016) proposed that vocal behavior in humans was controlled by an ”emotional motor pathway” that connects the amygdala, hypothalamus and other areas with the PAG, brainstem and spinal cord, and a voluntary pathway originating in motor cortex. Nonlemniscal regions of the thalamus send axons to a number of limbic structures (e.g., the amygdala, association cortex, and striatum) (Hu 2003). The amygdala is implicated in the processing of emotion and affective value of stimuli, and it shows early activation when socially relevant stimuli, such as conspecific calls, are presented. Playback of artificial 20 kHz sine

waves to rats increases the expression of the immediate early gene *cFos* in PAG, amygdala, hypothalamus, and thalamus (Wöhr and Schwarting 2010). Lesions of the amygdala reduce both male mouse courtship behavior and female directed USVs (Matsumoto et al. 2012). Olfactory stimuli are relayed to a number of brain regions, including amygdala and lateral entorhinal cortex (Hashikawa et al. 2016). The amygdala may play a role in mediating approach or evasive behaviors toward odors, and neurons there may be under the regulation of sex hormones (Hashikawa et al. 2016). The hypothalamus, a target for amygdalar inputs and somatosensory inputs from genital areas, also may be critical for the expression of innate social behaviors, such as sexual behavior (Hashikawa et al. 2016). The hypothalamus also influences the striatum in relation to motivation and reward, mediated by dopaminergic cells in the ventral tegmental area. The striatum is thought to participate in reward-related decisions and action selection (Lee 2015). The dorsal raphe nucleus, a brain region that is activated by arousal, acoustic stimuli, and social interactions, provides serotoninergic inputs to all auditory nuclei, particularly the IC, where levels of serotonin increase during social interactions in mice (Pollak 2013; Pannese et al. 2015). Therefore, understanding how the auditory system interacts with nonauditory regions to elicit appropriate responses to vocal signals is important.

A central role in production and perception of vocal behavior is attributed to the PAG, which is intermediary between hypothalamus, brainstem, and motoneurons in the spinal cord (Pannese et al. 2015; Hashikawa et al. 2016). Lesions of PAG accelerate male mounting behavior, and trigger aggressive behaviors in rats. It is suggested PAG has a behavior-gating function, helping to select and initiate behaviors that are associated with a social dimension. Thus socially relevant vocal communication signals involve the processing of features along the auditory pathway

plus integration with other brain centers that mediate the appropriate behavioral response. The study of vocal communication signals is not an auditory/motor problem, but a systems level problem.

6.8 Conclusions

According to Theunissen and Elie (2014), studies of vocal communication have followed two main approaches that now may be merging. On the one hand, auditory physiologists have sought to explain auditory processing by studying neuronal responses to isolated features of natural sounds. A neuroethological approach has, on the other hand, sought to take a more integrated approach that considers the natural context in which the social signals are used. A key goal in the analysis of vocal communication signals is to determine the essential features of these signals, what information they transmit, how they are categorized and, equally important, how they act in combination with information derived from other sensory modalities, are interpreted and are acted upon by the receiver.

As Pollak and colleaguges (2003) say, it is important to understand not just "how acoustic information is progressively transformed" but also "the functional consequences of those transformations." Auditory neurons clearly respond to vocal communication signals and, especially in the IC and higher levels, show nonlinearities that emphasize that responses to vocal communication signals cannot be explained by the isolated features of the call. Further, it is important to consider the social role that vocal communication signals play, along with other environmental and social variables that contribute to the processing of vocal signals, even (or especially) when they may not be easily reproduced in the laboratory (Beecher 1996). Mice, in particular, increasingly have become a species of choice to study hearing function and

disease, primarily from a genetic perspective (Ohlemiller et al. 2016; Ohlemiller, Chap. 7), but other rodent models, for which the communication signals and responses they elicit in natural settings can be readily described, may significantly contribute to our understanding of vocal communication (Hauser 1999; Bennur et al. 2013).

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Compliance with Ethics Statement

M. Fabiana Kubke declares that she has no conflicts of interest.

J. Martin Wild declares that he has no conflicts of interest.

References

Aitkin, L., Tran, L., & Syka, J. (1994). The responses of neurons in subdivisions of the inferior colliculus of cats to tonal, noise and vocal stimuli. *Experimental Brain Research*, 98(1), 53–64.

Anderson, L. A., & Linden, J. F. (2011). Physiological differences between histologically defined subdivisions in the mouse auditory thalamus. *Hearing Research*, 274(1-2), 48–60.

Anderson, L. A., Wallace, M. N., & Palmer, A. R. (2007). Identification of subdivisions in the medial geniculate body of the guinea pig. *Hearing Research*, 228(1-2), 156–167.

Arriaga, G., & Jarvis, E. D. (2013). Mouse vocal communication system: Are ultrasounds learned or innate? *Brain and Language*, 124(1), 96–116.

Arriaga, G., Zhou, E. P., & Jarvis, E. D. (2012). Of mice, birds, and men: The mouse ultrasonic song system has some features similar to humans and song-learning birds. *PLoS One*, 7(10), e46610.

Beecher, M. D. (1996). Birdsong learning in the laboratory and field. In D. E. Kroodsma & E. H. Miller (Eds.), *Ecology and evolution of acoustic communication in birds* (pp. 61–78). Ithaca, New York: Comstock Publishing.

Bennur, S., Tsunada, J., Cohen, Y. E., & Liu, R. C. (2013). Understanding the neurophysiological basis of auditory abilities for social communication: A perspective on the value of ethological paradigms. *Hearing Research*, 305, 3–9.

Berryman, J. C. (1976). Guinea-pig vocalizations: Their structure, causation and function. *Zeitschrift für Tierpsychologie*, 41(1), 80–106.

Bizley, J. K., & Cohen, Y. E. (2013). The what, where and how of auditory-object perception. *Nature Reviews*, *Neuroscience*, 14(10), 693–707.

Bradbury, J. W., Vehrencamp, S., & Bradbury, J. W. (1998). *Principles of animal communication* (1st edition). Sunderland, MA: Sinauer Associates.

Brown, J. L. (1965). Loss of vocalization caused by lesions in the nucleus mesencephalicus lateralis of the redwinged blackbird. *American Zoologist*, 5, 693.

Budinger, E., Heil, P., & Scheich, H. (2000). Functional organization of auditory cortex in the Mongolian gerbil (*Meriones unguiculatus*). III. Anatomical subdivisions and corticocortical connections. *European Journal of Neuroscience*, 12(7), 2425–2451.

Burda, H., Bruns, V., & Hickman, G. C. (1992). The ear in subterranean Insectivora and Rodentia in comparison with ground-dwelling representatives. I. Sound conducting system of the middle ear. *Journal of Morphology*, 214(1), 49–61.

Cant Nell B., Benson Christina G. (2006) Organization of the inferior colliculus of the gerbil (*Meriones unguiculatus*): Differences in distribution of projections from the cochlear nuclei and the superior olivary complex. *Journal of Comparative Neurology*, 495(5):511–28.

Carruthers, I. M., Natan, R. G., & Geffen, M. N. (2013). Encoding of ultrasonic vocalizations in the auditory cortex. *Journal of Neurophysiology*, 109(7), 1912–1927.

Doupe, A. J., & Kuhl, P. K. (1999). Birdsong and human speech: Common themes and mechanisms. *Annual Review of Neuroscience*, 22(1), 567–631.

Dujardin, E., & Jürgens, U. (2005). Afferents of vocalization-controlling periaqueductal regions in the squirrel monkey. *Brain Research*, 1034(1-2), 114–131.

Eggermont, J. (2001). Between sound and perception: Reviewing the search for a neural code. *Hearing Research*, 157, 1–42.

Egnor, S. R., & Seagraves, K. M. (2016). The contribution of ultrasonic vocalizations to mouse courtship. *Current Opinion in Neurobiology*, 38, 1–5.

Escabí, M. A., & Read, H. L. (2003). Representation of spectrotemporal sound information in the ascending auditory pathway. *Biological Cybernetics*, 89, 350–362.

Espmark, Y., Amundsen, T., & Rosenqvist, G. (2000). *Animal signals: Signalling and signal design in animal communication*. Trondheim (Norway*),* Tapir Academic Press.

Esposito, A., Demeurisse, G., Alberti, B., & Fabbro, F. (1999). Complete mutism after midbrain periaqueductal gray lesion. *Neuroreport*, 10(4), 681–685.

Fischer, J., & Hammerschmidt, K. (2011). Ultrasonic vocalizations in mouse models for speech and socio-cognitive disorders: Insights into the evolution of vocal communication. *Genes*, *Brain*, *and Behavior*, 10(1), 17–27.

Fisher, S. E., & Scharff, C. (2009). FOXP2 as a molecular window into speech and language. *Trends in Genetics*, 25(4), 166–177.

Fitch, W. T., Huber, L., & Bugnyar, T. (2010). social cognition and the evolution of language: Constructing cognitive phylogenies. *Neuron*, 65(6), 795–814.

Fleischer, G. (1978). *Evolutionary principles of the mammalian middle ear*. Berlin: Springer-Verlag.

Frisina, R. D. (2001). Subcortical neural coding mechanisms for auditory temporal processing. *Hearing Research*, 158(1-2), 1–27.

Fritzsch, B., Pan, N., Jahan, I., Duncan, J. S., et al. (2013). Evolution and development of the tetrapod auditory system: An organ of Corti-centric perspective. *Evolution & Development*, 15(1), 63–79.

Garcia-Lazaro, J. A., Shepard, K. N., Miranda, J. A., Liu, R. C., & Lesica, N. A. (2015). An overrepresentation of high frequencies in the mouse inferior colliculus supports the processing of ultrasonic vocalizations.*PLoS ONE* , 10(8), e0133251.

Gaub, S., Groszer, M., Fisher, S. E., & Ehret, G. (2010). The structure of innate vocalizations in *Foxp*2-deficient mouse pups. *Genes*, *Brain and Behavior*, 9(4), 390–401.

Gaucher, Q., Huetz, C., Gourévitch, B., & Edeline, J.-M. (2013a). Cortical inhibition reduces information redundancy at presentation of communication sounds in

the primary auditory cortex. *The Journal of Neuroscience*, 33(26), 10713–10728.

Gaucher, Q., Huetz, C., Gourévitch, B., Laudanski, J., et al. (2013b). How do auditory cortex neurons represent communication sounds? *Hearing Research*, 305, 102–112.

Geissler, D. B., & Ehret, G. (2004). Auditory perception vs. recognition: Representation of complex communication sounds in the mouse auditory cortical fields. *European Journal of Neuroscience*, 19(4), 1027–1040.

Gentner, T. Q., & Margoliash, D. (2003). The neuroethology of vocal communication: perception and cognition. In A. M. Simmons, R. R. Fay & A. N. Popper (Eds.), *Acoustic communication* (Vol. 16, pp. 324–386). New York: Springer-Verlag.

Gittelman, J. X., Perkel, D. J., & Portfors, C. V. (2013). Dopamine modulates auditory responses in the inferior colliculus in a heterogeneous manner. *Journal of the Association for Research in Otolaryngology*, 14(5), 719–729.

Griffiths, T. D., & Warren, J. D. (2004). What is an auditory object? *Nature Reviews, Neuroscience*, 5(11), 887–892.

Hackett, T. A. (2011). Information flow in the auditory cortical network. *Hearing Research*, 271(1-2), 133–146.

Hafner, M. S., & Hafner, D. J. (1979). Vocalizations of grasshopper mice (Genus *Onychomys*). *Journal of Mammalogy*, 60(1), 85–94.

Hammerschmidt, K., Whelan, G., Eichele, G., & Fischer, J. (2015). Mice lacking the cerebral cortex develop normal song: Insights into the foundations of vocal learning. *Scientific Reports*, 5, 8808.

Hammerschmidt, K., Reisinger, E., Westekemper, K., Ehrenreich, L., et al. (2012). Mice do not require auditory input for the normal development of their ultrasonic vocalizations. *BMC Neuroscience*, 13(1), 40.

Han, Y. K., Köver, H., Insanally, M. N., Semerdjian, J. H., & Bao, S. (2007). Early experience impairs perceptual discrimination. *Nature Neuroscience*, 10(9), 1191–1197.

Harris, K. D., Bartho, P., Chadderton, P., Curto, C., et al. (2011). How do neurons work together? Lessons from auditory cortex. *Hearing Research*, 271(1-2), 37–53.

Harrison, D. F. N. (1995). *The anatomy and physiology of the mammalian larynx*. Cambridge, UK: Cambridge University Press.

Harrison, J. M., & Warr, W. B. (1962). A study of the cochlear nuclei and ascending auditory pathways of the medulla. *The Journal of Comparative Neurology*, 119(3), 341–379.

Hashikawa, K., Hashikawa, Y., Falkner, A., & Lin, D. (2016). The neural circuits of mating and fighting in male mice. *Current Opinion in Neurobiology*, 38, 27–37.

Hauser, M. D. (1999). *The design of animal communication*. Cambridge, MA: MIT Press.

He, J. (2003). Corticofugal modulation of the auditory thalamus. *Experimental Brain Research*, 153(4), 579–590.

Heckman, J., McGuinness, B., Celikel, T., & Englitz, B. (2016). Determinants of the mouse ultrasonic vocal structure and repertoire. *Neuroscience & Biobehavioral Reviews*, 65, 313–325.

Heffner, R. S., Koay, G., & Heffner, H. E. (2001). Audiograms of five species of rodents: Implications for the evolution of hearing and the perception of pitch. *Hearing Research*, 157(1–2), 138–152.

Heil, P., & Peterson, A. J. (2015). Basic response properties of auditory nerve fibers: A review. *Cell and Tissue Research*, 361(1), 129–158.

Herbst, C. T. (2016). Biophysics of vocal production in mammals. In R. A. Suthers, W. T. Fitch, R. R. Fay, & A. N. Popper (Eds.), *Vertebrate sound production and acoustic communication* (pp. 159–189). New York: Springer International Publishing.

Holmstrom, L. A., Eeuwes, L. B. M., Roberts, P. D., & Portfors, C. V. (2010). Efficient encoding of vocalizations in the auditory midbrain. *The Journal of Neuroscience*, 30(3), 802–819.

Holstege, G. (1989). Anatomical study of the final common pathway for vocalization in the cat. *The Journal of Comparative Neurology*, 284(2), 242–252.

Holstege, G., & Subramanian, H. H. (2016). Two different motor systems are needed to generate human speech. *The Journal of Comparative Neurology*, 524(8), 1558–1577.

Holstege, G., Kerstens, L., Moes, M. C., & VanderHorst, V. G. J. M. (1997). Evidence for a periaqueductal gray–nucleus retroambiguus–spinal cord pathway in the rat. *Neuroscience*, 80(2), 587–598.

Honma, Y., Tsukano, H., Horie, M., Ohshima, S., et al. (2013). Auditory cortical areas ativated by slow frequency-modulated sounds in mice.*PLoS ONE*, 8(7), e68113.

Hu, B. (2003). Functional organization of lemniscal and nonlemniscal auditory thalamus. *Experimental Brain Research*, 153(4), 543–549.

Huetz, C., Philibert, B., & Edeline, J.-M. (2009). A spike-timing code for discriminating conspecific vocalizations in the thalamocortical system of anesthetized and awake guinea pigs. *The Journal of Neuroscience*, 29(2), 334–350.

Huetz, C., Gourévitch, B., & Edeline, J.-M. (2011). Neural codes in the thalamocortical auditory system: From artificial stimuli to communication sounds. *Hearing Research*, 271(1-2), 147–158.

Iwatsubo, T., Kuzuhara, S., Kanemitsu, A., Shimada, H., & Toyokura, Y. (1990). Corticofugal projections to the motor nuclei of the brainstem and spinal cord in humans. *Neurology*, 40(2), 309.

Jacomme, A. V., Nodal, F. R., Bajo, V. M., Manunta, Y., et al. (2003). The projection from auditory cortex to cochlear nucleus in guinea pigs: An in vivo anatomical and in vitro electrophysiological study. *Experimental Brain Research*, 153(4), 467–476.

Janik, V. M., & Slater, P. J. B. (1997). Vocal learning in mammals. In P. J.B. Slater, J. S. Rosenblatt, C. T. Snowdon, & M. Milinski (Eds.), *Advances in the study of behavior*. Volume 26 (pp. 59–99). New York: Academic Press.

Janik, V. M., & Slater, P. J. B. (2000). The different roles of social learning in vocal communication. *Animal Behaviour*, 60(1), 1–11.

Joris, P. X., Schreiner, C. E., & Rees, A. (2004). Neural processing of amplitude-modulated sounds. *Physiological Reviews*, 84(2), 541–577.

Jürgens, U. (2002). Neural pathways underlying vocal control. *Neuroscience & Biobehavioral Reviews*, 26(2), 235–258.

Jürgens, U. (2009). The neural control of vocalization in mammals: A review. *Journal of Voice*, 23(1), 1–10.

Kershenbaum, A., Blumstein, D. T., Roch, M. A., Akçay, Ç., et al. (2016). Acoustic sequences in non-human animals: A tutorial review and prospectus. *Biological Reviews of the Cambridge Philosophical Society*, 91(1), 13–52.

King, J., Insanally, M., Jin, M., Martins, A. R. O., et al. (2015). Rodent auditory perception: Critical band limitations and plasticity. *Neuroscience*, 296, 55–65.

Köver, H., Gill, K., Tseng, Y.-T. L., & Bao, S. (2013). Perceptual and neuronal boundary learned from higher-order stimulus probabilities. *The Journal of Neuroscience*, 33(8), 3699–3705.

Kraus, N., McGee, T., Littman, T., Nicol, T., & King, C. (1994). Nonprimary auditory thalamic representation of acoustic change. *Journal of Neurophysiology*, 72(3), 1270–1277.

Kubota, M., Sugimoto, S., Hosokawa, Y., Ojima, H., & Horikawa, J. (2017). Auditory-visual integration in fields of the auditory cortex. *Hearing Research*, 346, 25–33.

Kuo, Richard I., & Wu, Guangying K. (2012). The generation of direction selectivity in the auditory system. *Neuron*, 73(5), 1016–1027.

Kuypers, H. G. J. M. (1958). Some projections from the peri-central cortex to the pons and lower brain stem in monkey and chimpanzee. *The Journal of Comparative Neurology*, 110(2), 221–255.

Lange, S., Burda, H., Wegner, R. E., Dammann, P., et al. (2007). Living in a "stethoscope": Burrow acoustics promote auditory specializations in subterranean rodents. *Die Naturwissenschaften*, 94(2), 134–138.

Lavocat, R., & Parent, J.-P. (1985). Phylogenetic analysis of middle ear features in fossil and living rodents. *Evolutionary Relationships among Rodents* (pp. 333–354). NATO Advanced Science Institutes Series A: Life Sciences. Volume 92.

Boston: Springer. Lee, C. C. (2013). Thalamic and cortical pathways supporting auditory processing. *Brain and Language*, 126(1), 22–28.

Lee, C. C. (2015). Exploring functions for the non-lemniscal auditory thalamus. *Frontiers in Neural Circuits*, 9, 69.

López, D. E., Saldaña, E., Nodal, F. R., Merchán, M. A., & Warr, W. B. (1999). Projections of cochlear root neurons, sentinels of the rat auditory pathway. *The Journal of Comparative Neurology*, 415(2), 160–174.

Lorente de No, R. (1933). Anatomy of the eighth nerve. III. General plan of stucture of the primary cochlear nuclei. *Laryngoscope*, 43, 327–350.

Lyzwa, D., Herrmann, J. M., & Wörgötter, F. (2015). Natural vocalizations in the mammalian inferior colliculus are broadly encoded by a small number of independent multi-units. *Frontiers in Neural Circuits*, 9, 91.

Mahrt, E., Agarwal, A., Perkel, D., Portfors, C., & Elemans, C. P. H. (2016). Mice produce ultrasonic vocalizations by intra-laryngeal planar impinging jets. *Current Biology*, 26(19), R880–R881.

Malmierca, M. S. (2003). The structure and physiology of the rat auditory system: An overview. *International Review of Neurobiology*, 56, 147–211.

Manley, G. A. (2017). Comparative auditory neuroscience: Understanding the evolution and function of ears. *Journal of the Association for Research in Otolaryngology*, 18(1), 1–24.

Marler, P. (1957). Specific distinctiveness in the communication signals of birds. *Behaviour*, 11(1), 13–38.

Mason, M. J. (2001). Middle ear structures in fossorial mammals: A comparison with non-fossorial species. *Journal of Zoology*, 255(4), 467–486.

Mason, M. J. (2013). Of mice, moles and guinea pigs: Functional morphology of the middle ear in living mammals. *Hearing Research*, 301, 4–18.

Matsumoto, Y. K., Okanoya, K., & Seki, Y. (2012). Effects of amygdala lesions on male mouse ultrasonic vocalizations and copulatory behaviour. *Neuroreport*, 23(11), 676–680.

Montgomery, J. C., & Bodznick, D. (1994). An adaptive filter that cancels self-induced noise in the electrosensory and lateral line mechanosensory systems of fish. *Neuroscience Letters*, 174(2), 145–148.

Nakagawa, R., Matsunaga, E., & Okanoya, K. (2012). Defects in ultrasonic vocalization of Cadherin-6 knockout mice. *PLoS ONE*, 7(11), e49233.

Nelken, I. (2008). Processing of complex sounds in the auditory system. *Current Opinion in Neurobiology*, 18(4), 413–417.

Newman, D. B., Hilleary, S. K., & Ginsberg, C. Y. (1989). Nuclear terminations of corticoreticular fiber systems in rats. *Brain, Behavior and Evolution*, 34(4), 253–264.

Nodal, F. R., & López, D. E. (2003). Direct input from cochlear root neurons to pontine reticulospinal neurons in albino rat. *The Journal of Comparative Neurology*, 460(1), 80–93.

Nottebohm, F., Stokes, T. M., & Leonard, C. M. (1976). Central control of song in the canary, Serinus canarius. *The Journal of Comparative Neurology*, 165(4), 457–486.

Nyby, J. G. (2010). Adult house mouse (*Mus musculus)* ultrasonic calls: Hormonal and pheromonal regulation. In S. M. Brudzynski (Ed.), *Handbook of behavioral neuroscience* . Volume 19 (pp. 303–310). New York: Elsevier.

Ohlemiller, K. K., Jones, S. M., & Johnson, K. R. (2016). Application of mouse models to research in hearing and balance. *Journal of the Association for Research in Otolaryngology*, 17(6), 493–523.

Pannese, A., Grandjean, D., & Frühholz, S. (2015). Subcortical processing in auditory communication. *Hearing Research*, 328, 67–77.

Philibert, B., Laudanski, J., & Edeline, J. M. (2005). Auditory thalamus responses to guinea-pig vocalizations: A comparison between rat and guinea-pig. *Hearing Research*, 209(1–2), 97–103.

Phillips, R. E., & Peek, F. W. (1975). Brain organization and neuromuscular control of vocalization in birds. In P. Wright, P. Caryl, & D. Vowles (Eds.), *Hormones and behavior in vertebrates* (pp. 243–274). Amsterdam: Elsevier.

Pollak, G. D. (2013). The dominant role of inhibition in creating response selectivities for communication calls in the brainstem auditory system. *Hearing Research*, 305, 86–101.

Pollak, G. D., Burger, R. M., & Klug, A. (2003). Dissecting the circuitry of the auditory system. *Trends in Neurosciences*, 26(1), 33–39.

Popelář, J., Šuta, D., Lindovský, J., Bureš, Z., et al. (2016). Cooling of the auditory cortex modifies neuronal activity in the inferior colliculus in rats. *Hearing Research*, 332, 7–16.

Poremba, A., Bigelow, J., & Rossi, B. (2013). Processing of communication sounds: Contributions of learning, memory, and experience. *Hearing Research*, 305, 31–44.

Portfors, C. V. (2007). Types and functions of ultrasonic vocalizations in laboratory rats and mice. *Journal of the American Association for Laboratory Animal Science*, 46(1), 28–34.

Portfors, C. V., & Felix, R. A. (2005). Spectral integration in the inferior colliculus of the CBA/CaJ mouse. *Neuroscience*, 136(4), 1159–1170.

Portfors, C. V., Roberts, P. D., & Jonson, K. (2009). Over-representation of species-specific vocalizations in the awake mouse inferior colliculus. *Neuroscience*, 162(2), 486–500.

Portfors, C. V., Mayko, Z. M., Jonson, K., Cha, G. F., & Roberts, P. D. (2011). Spatial organization of receptive fields in the auditory midbrain of awake mouse. *Neuroscience*, 193, 429–439.

Ramón y Cajal, S. (1904). *Textura del sistema nervioso del hombre y de los vertebrados* (Edicion Facsimil 1992,, Volume II). Alicante, Spain: Graficas Vidal Leuka.

Riede, T. (2013). Stereotypic laryngeal and respiratory motor patterns generate different call types in rat ultrasound vocalization. *Journal of Experimental Zoology, Part A, Ecological Genetics and Physiology*, 319(4), 213–224.

Roberts, L. H. (1975). The functional anatomy of the rodent larynx in relation to audible and ultrasonic cry production. *Zoological Journal of the Linnean Society*, 56(3), 255–264.

Rosowski, J. J. (1994). Outer and Middle Ears. In R. R. Fay & A. N. Popper (Eds.), *Comparative hearing: Mammals* (pp. 172–247). New York: Springer-Verlag.

Saldeitis, K., Happel, M. F. K., Ohl, F. W., Scheich, H., & Budinger, E. (2014). Anatomy of the auditory thalamocortical system in the mongolian gerbil: Nuclear origins and cortical field-, layer-, and frequency-specificities. *The Journal of Comparative Neurology*, 522(10), 2397–2430.

Sales, G., & Pye, D. (1974). *Ultrasonic communication by animals*. New York: Springer-Verlag.

Sanes, Dan H., & Woolley, Sarah M. N. (2011). A behavioral framework to guide research on central auditory development and plasticity. *Neuron*, 72(6), 912–929.

Sayegh, R., Aubie, B., & Faure, P. A. (2011). Duration tuning in the auditory midbrain of echolocating and non-echolocating vertebrates. *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology*, 197(5), 571–583.

Scharff, C., & Haesler, S. (2005). An evolutionary perspective on FoxP2: Strictly for the birds? *Current Opinion in Neurobiology*, 15(6), 694–703.

Schneidman, E. (2016). Towards the design principles of neural population codes. *Current Opinion in Neurobiology*, 37, 133–140.

Schofield, B. R., & Coomes, D. L. (2006). Pathways from auditory cortex to the cochlear nucleus in guinea pigs. *Hearing Research*, 216, 81–89.

Shamma, S. A., & Fritz, J. B. (2009). Auditory cortex: Models. In L. R. Squire (Ed.), *Encyclopedia of Neuroscience* (pp. 709–714). Oxford, UK: Academic Press.

Shepard, K. N., Lin, F. G., Zhao, C. L., Chong, K. K., & Liu, R. C. (2015). Behavioral relevance helps untangle natural vocal categories in a specific subset of core auditory cortical pyramidal neurons. *The Journal of Neuroscience*, 35(6), 2636–2645.

Sherman, S. M. (2001). Tonic and burst firing: Dual modes of thalamocortical relay. *Trends in Neurosciences*, 24(2), 122–126.

Simonyan, K. (2014). The laryngeal motor cortex: Its organization and connectivity. *Current Opinion in Neurobiology*, 28, 15–21.

Simonyan, K., & Jürgens, U. (2003). Efferent subcortical projections of the laryngeal motorcortex in the rhesus monkey. *Brain Research*, 974(1-2), 43–59.

Simonyan, K., & Horwitz, B. (2011). Laryngeal motor cortex and control of speech in humans. *The Neuroscientist*, 17(2), 197–208.

Singla, S., Dempsey, C., Warren, R., Enikolopov, A. G., & Sawtell, N. B. (2017). A cerebellum-like circuit in the auditory system cancels responses to self-generated sounds. *Nature Neuroscience*, 20(7), 943–950.

Stiebler, I., Neulist, R., Fichtel, I., & Ehret, G. (1997). The auditory cortex of the house mouse: Left-right differences, tonotopic organization and quantitative analysis of frequency representation. *Journal of Comparative Physiology A: Sensory, Neural, and Behavioral Physiology*, 181(6), 559–571.

Suta, D., Kvasnák, E., Popelár, J., & Syka, J. (2003). Representation of species-specific vocalizations in the inferior colliculus of the guinea pig. *Journal of Neurophysiology*, 90(6), 3794–3808.

Suta, D., Popelár, J., & Syka, J. (2008). Coding of communication calls in the subcortical and cortical structures of the auditory system. *Physiological research/Academia Scientiarum Bohemoslovaca*, 57 Suppl 3, 149–159.

Suthers, R. A., Fitch, W. T., Fay, R. R., & Popper, A. N. (Eds.). (2016). *Vertebrate sound production and acoustic communication* (Vol. 53). New York, N.Y.: Springer International Publishing.

Syka, J. (2010). Subcortical responses to species-specific vocalizations. In S. M. Brudzynski (Ed.), *Handbook of behavioral neuroscience*. Volume 19. (pp. 99–112): Elsevier.

Tabler, J. M., Rigney, M. M., Berman, G. J., Gopalakrishnan, S., et al. (2017). Cilia-mediated hedgehog signaling controls form and function in the mammalian larynx. *eLife*, 6.

Tanaka, H., & Taniguchi, I. (1991). Responses of medial geniculate neurons to species-specific vocalized sounds in the guinea pig. *Japanese Journal of Physiology*, 41(6), 817–829.

Ter-Mikaelian, M., Sanes, D. H., & Semple, M. N. (2007). Transformation of temporal properties between auditory midbrain and cortex in the awake Mongolian gerbil. *The Journal of Neuroscience*, 27(23), 6091–6102.

Ter-Mikaelian, M., Semple, M. N., & Sanes, D. H. (2013). Effects of spectral and temporal disruption on cortical encoding of gerbil vocalizations. *Journal of Neurophysiology*, 110(5), 1190–1204.

Theunissen, F. E., & Elie, J. E. (2014). Neural processing of natural sounds. *Nature Reviews, Neuroscience*, 15(6), 355–366.

Tinbergen, N. (1963). On aims and methods of Ethology. *Zeitschrift für Tierpsychologie*, 20(4), 410–433.

Tsukano, H., Horie, M., Ohga, S., Takahashi, K., et al. (2017). Reconsidering tonotopic maps in the auditory cortex and lemniscal suditory thalamus in mice. *Frontiers in Neural Circuits*, 11, 1–8.

de Villers-Sidani, E., Chang, E. F., Bao, S., & Merzenich, M. M. (2007). Critical period window for spectral tuning defined in the primary auditory cortex (A1) in the rat. *The Journal of Neuroscience*, 27(1), 180–189.

Wang, X. (2007). Neural coding strategies in auditory cortex. *Hearing Research*, 229(1-2), 81–93.

Wang, X., Merzenich, M. M., Beitel, R., & Schreiner, C. E. (1995). Representation of a species-specific vocalization in the primary auditory cortex of the common marmoset: Temporal and spectral characteristics. *Journal of Neurophysiology*, 74(6), 2685–2706.

Wang, X., Qi, Q., Huang, C., Chomiak, T., & Luo, F. (2016). Duration sensitivity of neurons in the primary auditory cortex of albino mouse. *Hearing Research*, 332, 160–169.

West, C. D. (1985). The relationship of the spiral turns of the cochlea and the length of the basilar membrane to the range of audible frequencies in ground dwelling mammals. *The Journal of the Acoustical Society of America*, 77(3), 1091–1101.

Wigderson, E., Nelken, I., & Yarom, Y. (2016). Early multisensory integration of self and source motion in the auditory system. *Proceedings of the National Academy of Sciences of the Unites States of America*, 113(29), 8308–8313.

Wilczynski, W., & Ryan, M. J. (2010). The behavioral neuroscience of anuran social signal processing. *Current Opinion in Neurobiology*, 20(6), 754–763.

Wild, J. M., Li, D., & Eagleton, C. (1997). Projections of the dorsomedial nucleus of the intercollicular complex (DM) in relation to respiratory-vocal nuclei in the brainstem of pigeon (*Columba livia*) and zebra finch (*Taeniopygia guttata*). *The Journal of Comparative Neurology*, 377, 392–413.

Willard, F. H., & Ryugo, D. K. (1983). Anatomy of the central auditory system. In J. F. Willott (Ed.), *The Auditory Psychobiology of the Mouse* (pp. 201–304). Springfield, MA: Charles C. Thomas.

Winer, J. A. (1992). The functional architecture of the medial geniculate body and the primary auditory cortex. In D. B. Webster, A. N. Popper, & R. R. Fay (Eds.), *The mammalian auditory pathway: Neuroanatomy* (pp. 222–409): Springer New York.

Winer, J. A. (2006). Decoding the auditory corticofugal systems. *Hearing Research*, 212(1-2), 1–8.

Winer, J. A., & Schreiner, C. E. (2005). The central auditory system: A functional analysis. In J. A. Winer & C. E. Schreiner (Eds.), *The inferior colliculus* (pp. 1–68). New York: Springer Science + Media Publishing.

Wöhr, M., & Schwarting, R. K. W. (2010). Activation of limbic system structures by replay of ultrasonic vocalization in rats. In S. M. Brudzynski (Ed.), *Handbook of Behavioral Neuroscience*. Volume 19 (pp. 113–124): Elsevier.

Wöhr, M., Oddi, D., & D'Amato, F. R. (2010). Effect of altricial pup ultrasonic vocalization on maternal behavior. In S. M. Brudzynski (Ed.), *Handbook of Behavioral Neuroscience*. Volume 19 (pp. 159–166). New York: Elsevier.

Woolley, S. M. N. (2012). Early experience shapes vocal neural coding and perception in songbirds. *Developmental Psychobiology*, 54, 612–631.

Woolley, S. M. N., & Portfors, C. V. (2013). Conserved mechanisms of vocalization coding in mammalian and songbird auditory midbrain. *Hearing Research*, 305, 45–56.

Xia, Y. F., Qi, Z. H., & Shen, J. X. (2000). Neural representation of sound duration in the inferior colliculus of the mouse. *Acta Oto-Laryngologica*, 120(5), 638–643.

Zhang, S. P., Davis, P. J., Bandler, R., & Carrive, P. (1994). Brain stem integration of vocalization: Role of the midbrain periaqueductal gray. *Journal of Neurophysiology*, 72(3), 1337–1356.

Table 6.1 Abbreviations

AAF	anterior auditory field
AC	auditory cortex in text; arytenoid cartilage in fig. 6.1
A1	primary auditory cortex
A2	secondary auditory cortex
AI	primary auditory field
AII	secondary auditory field
AM	amplitude modulation
AN	auditory nerve
AVCN	anterior ventral cochlear nucleus
CIC	central nucleus of the inferior colliculus
CN	cochlear nucleus complex
DCN	dorsal cochlear nucleus
DNLL	dorsal nucleus of the lateral lemniscus
DM	dorsomedial field
DP	dorsoposterior field
FM	frequency modulation
IC	inferior colliculus
IHC	inner hair cells
LSO	lateral superior olive
MGB	medial geniculate body
MNTB	medial nucleus of the trapezoid body
MSO	medial superior olive
NLL	nuclei of the lateral lemniscus
NRA	nucleus retroambiguus

OHC	outer hair cell
PAG	periaqueductal gray
PIL	posterior intralaminar nucleus
PP	peripendicular nucleus
PVCN	posterior ventral cochlear nucleus
RA	robustus archopallialis
SOC	superior olivary complex
SPON	superior paraolivary nucleus
UF	ultrasound field
USV	ultrasound vocalization
VCN	ventral cochlear nuclei
VNLL	ventral nucleus of the lateral lemniscus
VNTB	ventral nucleus of the trapezoid body

Figure legends

Fig. 6.1 Anatomy of the mouse larynx. (**A**) Diagram representing ventral view of mouse laryngeal anatomy. *Dashed lines* indicate sectional plane represented in panels **C–F**. (**B**) Ventral view of an excised adult larynx stained with alcian blue, marking cartilage. (**C–E**) H&E staining of horizontal sections of E18.5 mouse larynx. Sectional plane is indicated in **A**. Diagrams indicate anatomy observed in sections. (**F**) H&E staining of sagittal section of E18.5 mouse larynx. Diagram indicates anatomy represented in section. *Scale bar* indicates 500 μm. *V* and *D* indicate dorso-ventral axes. *Abbreviations*: AC, arytenoid cartilage; CC, cricoid cartilage; CT, cricothyroid muscle; E, esophagus; G, glottis; L, larynx; LCA, lateral cricoarytenoid muscle; PCA, posterior cricoarytenoid muscle; T, tongue; TAM, thyroarytenoid muscle; TC, thryoid cartilage; TgCT, thyroglottal connective tissue; Tr, trachea; VL, vocal ligament; VM, vocalis muscle; VF, vocal fold. [Image and legend from Tabler et al. (2017); © 2017, Tabler et al., distributed under the terms of the Creative Commons Attribution License. DOI: http://dx.doi.org/10.7554/eLife.19153.004]

Fig. 6.2. Schematic organization of the inner ear of mouse (A) and organ of Corti of mouse (A), gerbil (B), rat (C) and mole rat (E: basal end, F: apical end). *Abbreviations*: DC: Deiters cells; HC: Hensen's cells; IHC: inner hair cells; ISC: inner sulcus cells; OC: organ of Corti; OHC: outer hair cells, OtC: otic capsule; Rm: Reissner's membrane; SG: spiral ganglion; SL: spiral ligament; SM: scala media; ST: scala timpani; StV: stria vascularis; SV: scala vestibuli; TC: tunnel of Corti; Tm: tectorial membrane; ZA: arcuate zone of basilar membrane; ZP: pectinate zone of basilar membrane. [(c) 2018 Kubke and Vlajkovic, distributed under the terms of the

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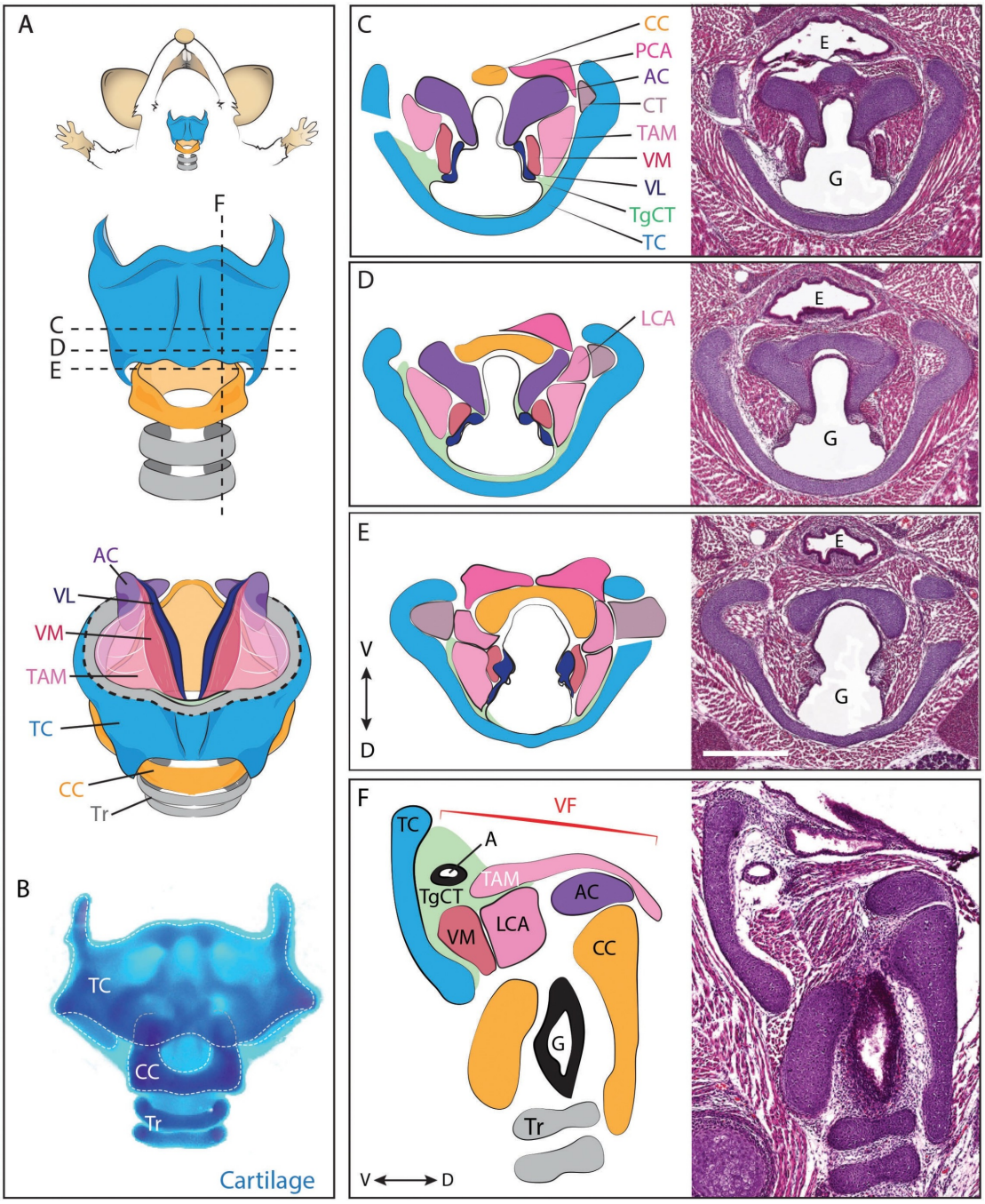
Fig. 6.3 Schematic of the auditory pathway showing ascending (**A**) and descending (**B**) projections. Projections from the ear and cochlear nucleus complex are shown in *black*; superior olivary complex in *blue*; nuclei of the lateral lemniscus in *green tones*; inferior colliculus in *orange tones*, auditory thalamus in *purple tones* and auditory cortex in *red tones*. *Dotted lines* represent known inhibitory projections.
Abbreviations: CIC: central nucleus of the inferior colliculus; DCIC: dorsal cortex of the inferior colliculus; DCN: dorsal cochlear nucleus; DNLL: dorsal nucleus of the lateral lemniscus; ECIC: external cortex of the inferior colliculus; INVN: interstitial nucleus of the vestibulocochlear nerve; LNTB: lateral nucleus of the trapezoid body ; LSO: lateral superior olive; MGD: dorsal subdivision of the medial geniculate body; MGM: medial subdivision of the medial geniculate body; MGV: ventral subdivision of the medial geniculate body; MNTB: medial nucleus of the trapezoid body; MSO: medial superior olive; PIL: posterior intralaminar nucleus; PP: peripendicular nucleus; PRN: pontine reticular nucleus; Rt: reticular thalamic nucleus; SPON: superior paraolivary nucleus;Te1: primary auditory cortex ; Te2: caudal auditory field; Te3: rostroventral auditory field; VCN: ventral cochlear nucleus; VNLL: ventral nucleus of the lateral lemniscus; VNTB: ventral nucleus of the trapezoid body.

FIGURE 1


A
F
C
D
E
AC
VL
VM
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TC
CC
Tr
B
TC
CC
Tr
Cartilage
C
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PCA
AC
CT
TAM
VM
VL
TgCT
TC
E
G
D
LCA
E
G
E
V
D
E
G
F
VF
TC
A
TAM
TgCT
AC
VM
LCA
CC
G
Tr
V
D

FIGURE 2

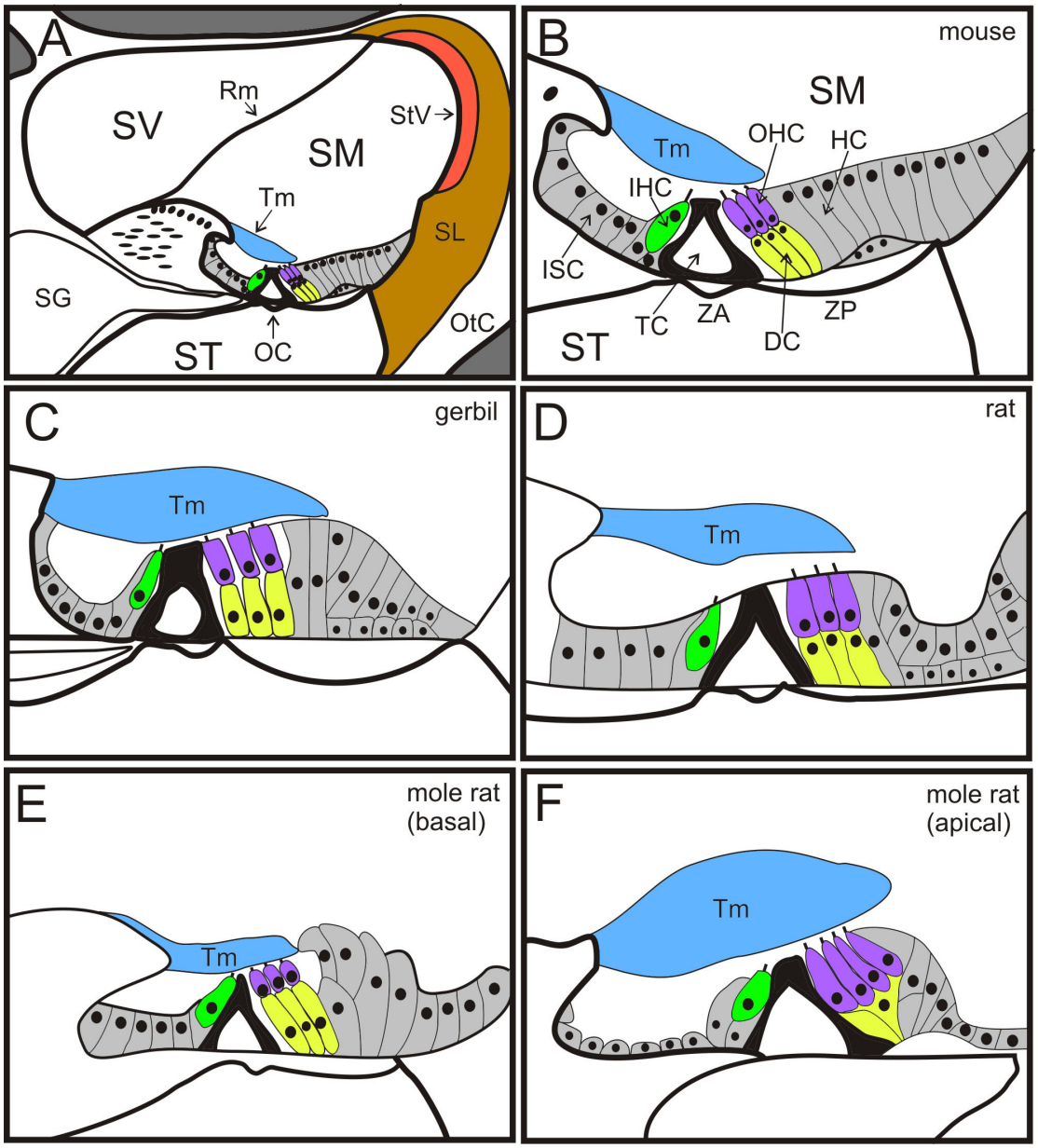

A
SV
Rm
StV
SM
Tm
SL
SG
OtC
ST
OC
B
mouse
SM
Tm
OHC
HC
IHC
ISC
TC
ZA
DC
ZP
ST
C
gerbil
Tm
D
rat
Tm
E
mole rat
(basal)
Tm
F
mole rat
(apical)
Tm

FIGURE 3a

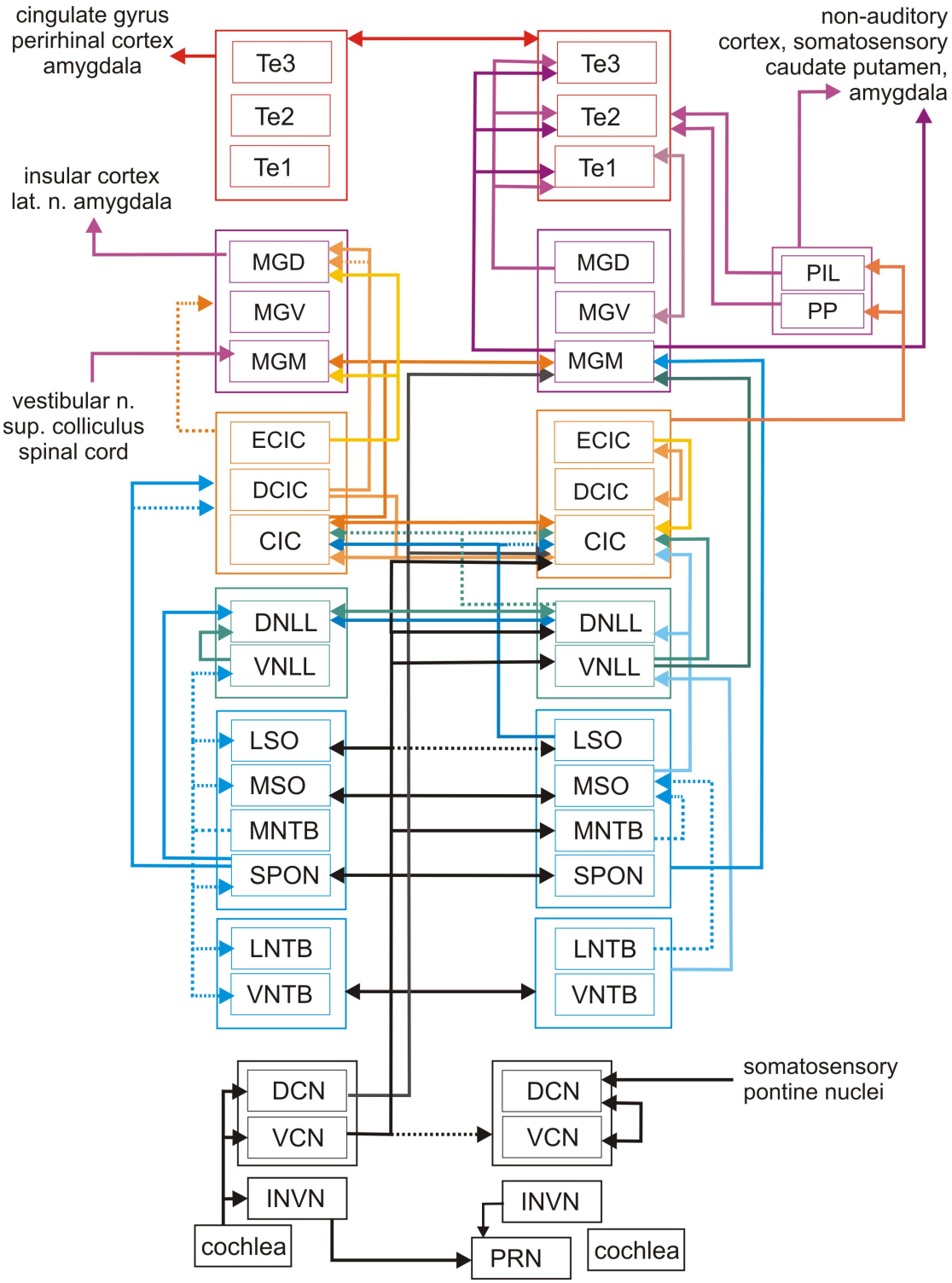
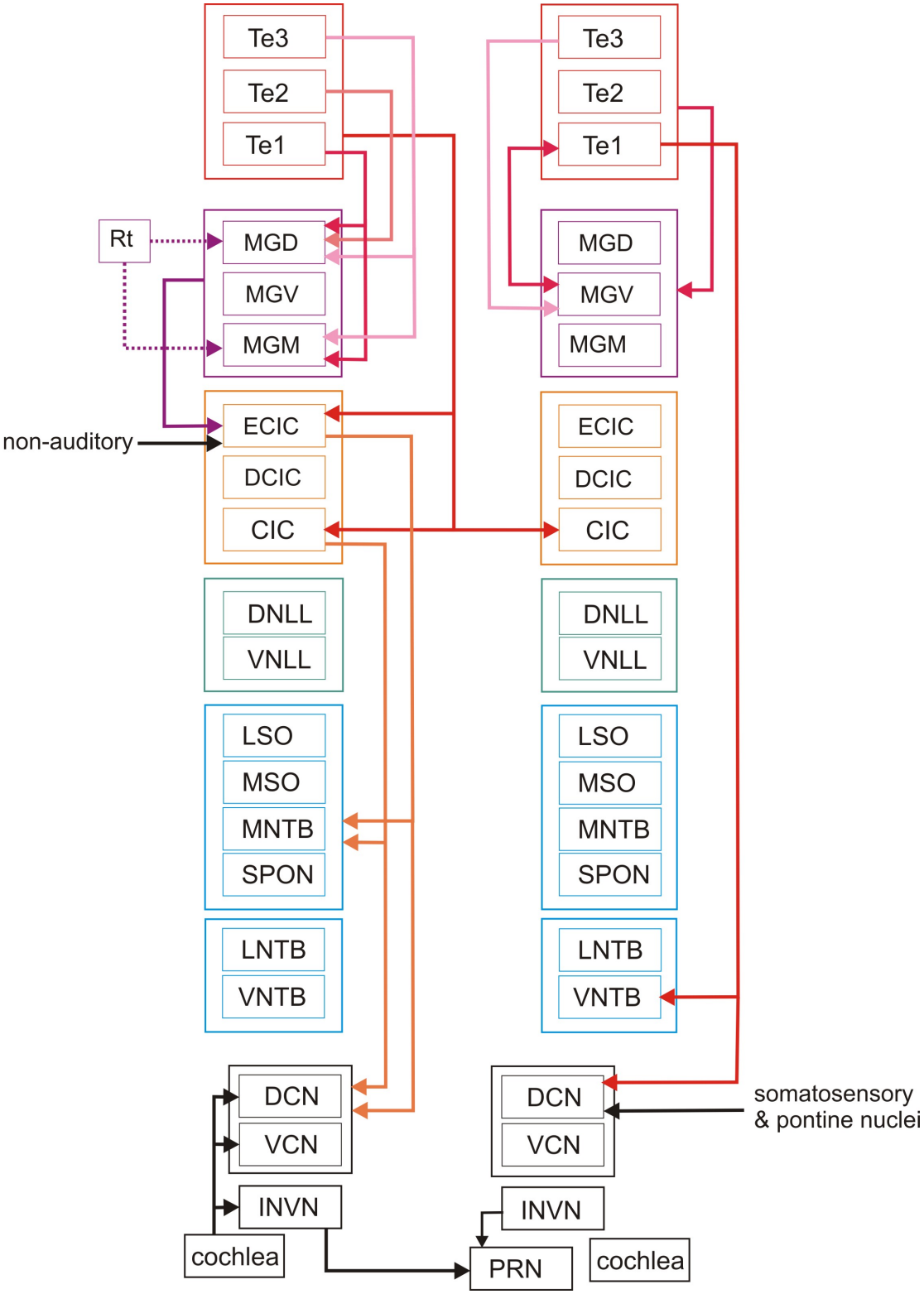

cingulate gyrus
perirhinal cortex
amygdala
insular cortex
lat. n. amygdala
vestibular n.
sup. colliculus
spinal cord
non-auditory
cortex, somatosensory
caudate putamen,
amygdala
Te3
Te2
Te1
MGD
MGV
MGM
PIL
PP
ECIC
DCIC
CIC
DNLL
VNLL
LSO
MSO
MNTB
SPON
LNTB
VNTB
DCN
VCN
INVN
cochlea
PRN
somatosensory
pontine nuclei

FIGURE 3B


Te3
Te2
Te1
Te3
Te2
Te1
Rt
MGD
MGV
MGM
MGD
MGV
MGM
non-auditory
ECIC
DCIC
CIC
ECIC
DCIC
CIC
DNLL
VNLL
DNLL
VNLL
LSO
MSO
MNTB
SPON
LSO
MSO
MNTB
SPON
LNTB
VNTB
LNTB
VNTB
DCN
VCN
DCN
VCN
somatosensory
& pontine nuclei
INVN
INVN
cochlea
PRN
cochlea