

Auditory Cortical Processing in Primates and Rodents

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Abstract

Auditory cortex is the first stage in cortical processing of auditory stimuli and is essential for the perception of sounds. Research of this area has increased in two closely related groups, rodents and non-human primates. However, no comparisons between these two popular animal models have been made to evaluate similarities and differences that could contribute to understanding how mammalian auditory cortex is involved in processing sounds. The most striking commonality among the two groups is evidence of serial and parallel processing. This review seeks to compare the physiology, anatomy, and histology of basic structures of monkey and rodent auditory cortex in order to understand the common roles of this region in these two groups.

Keywords

Auditory
Cortex
Thalamus
Primates
Rodents
Tonotopy
Anatomy

Hearing is an important component of experiencing the world we live in and interacting with our environment. At any given moment, an individual is exposed to many different sounds occurring simultaneously in time and from various locations and sources. It is the purpose of the central auditory system to interpret these sounds and filter out sounds that are irrelevant for the situation.

There are many structures in the brain that process auditory information, but auditory cortex is the first stage in cortical auditory processing and is necessary for perception of sounds¹. Additionally, there are many areas of cerebral cortex involved in hearing, but other areas of cortex depend on auditory cortex for auditory input. Therefore, auditory cortex is an ideal place to research how sounds are coded by neural circuits, assigned meaning, and relayed to other areas so the individual can perceive sounds, associate them with emotions and memories, and make decisions about behavior. There are three major ways in which to define auditory cortical areas: (1) physiology, (2) anatomy or connectivity, and (3) histology.

In terms of physiology, different parameters can be used to describe how neurons in different fields behave in response to different stimuli being presented to the ear. These measurements often include response latency, spike rates, and properties of tuning curves. The most common tool used to differentiate subdivisions is by defining a reversal in tonotopy^a, which indicates the border of two adjacent areas.

a. **Tonotopy** is the topographic arrangement of frequency representation that is conserved along the lemniscal pathway of the central auditory system from the cochlea to auditory cortex.

In terms of anatomy and connectivity, areas can be defined based on their connectional patterns with thalamus and other parts of cortex. These pathways are most commonly examined using anatomical tracers. In terms of histology, tissue staining techniques can highlight differences in the architecture among various auditory areas. By combining these three techniques, each area of auditory cortex has a unique profile consisting of physiological, connectional, and architectural properties.

Non-human primate research has surged in the past ten years to focus on the neural mechanisms of processing and generation of species-specific vocalizations that may be similar to speech processing and generation in humans. Over the past two decades, rodents have become common models for researching the neural mechanisms of diseases and cortical plasticity. Rodents are the closest relatives of non-human primates, but little has been done to compare the two bodies of literature of these two popular models in auditory research. This review, therefore, seeks to compare the basic structures of monkey and rodent auditory cortex in order to understand the common roles of cortex in these two groups.

Core, belt, and parabelt of monkey auditory cortex

Non-human primates have become essential models for investigating neural components of speech by studying neural coding of species-specific vocalizations. The current primate model of auditory cortex was first suggested by Hackett et al² using histological techniques to define different regions that could be further subdivided into dif-

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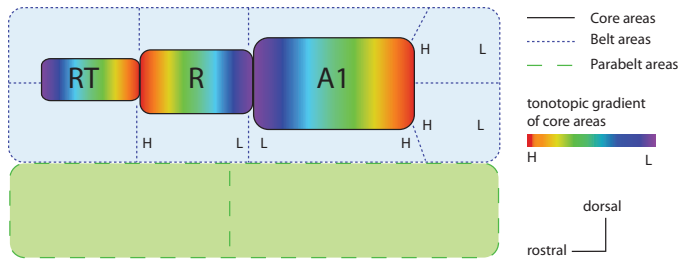


Figure 1. Schematic of primate auditory cortex. Core areas are shaded by tonotopic gradients. Subdivisions of belt and parabelt are indicated by dashed lines. Tonotopic gradients of belt areas are indicated by H (high) and L (low) frequency representation.

ferent areas based on physiological features and connection patterns. This model (Figure 1) describes three levels of processing, where each level occurs in a region that is further divided into separate areas. The first stage occurs in the “core” and consists of one primary and two primary-like areas; the second level is in the “belt” region of eight areas narrowly surrounding the core; the third region is the “parabelt,” which has been divided into two general areas.

Physiological properties of primate auditory cortex. Early electrophysiological recordings of monkey auditory cortex utilized tuning curves to determine the best frequency of a neuron or a group of neurons in order to create a tonotopic map used to define fields within auditory cortex. Merzenich and Brugge³ described several distinct areas, including primary auditory area (A1), an area rostral to A1 that they termed RL, and an area caudomedial to A1 called CM. These areas were further investigated in macaques by Morel et al⁴, who proposed that A1 and RL, which they renamed R, were part of the core, while CM was part of the belt. A third core area was proposed by Morel and Kaas⁵ in owl monkeys that was rostral to R called the rostrotemporal area (RT). The general consensus today is that these three areas – A1, R, and RT – make up the core region (Figure 1). Other tonotopic areas had been described as well, but they were later categorized as belt areas that receive tonotopic information from adjacent core areas.

In addition to being tonotopically organized and responding well to pure tones, the three core areas have been differentiated based on neuronal responses. Of the three areas, neurons in A1 have the shortest response latency⁶⁻¹⁰ and the highest spike rates when stimuli were presented at the preferred sound level^{7,9}. Neurons in area R have significantly longer minimum latencies, compared to A1⁶⁻¹⁰ and have narrow intensity and frequency tuning compared to

A1⁸. A smaller portion of neurons in RT respond well to pure tones, though the field overall was tonotopic. Neurons in RT also possessed a lower threshold for sound level, narrower bandwidth, and long minimum and peak response latencies. RT neurons were also found to have longer response duration compared to A1 but not to R, which may indicate that response duration increases among fields going caudal to rostral⁹.

Belt areas have been shown to have different physiology than core areas. Neurons in the belt region are active when pure tones are presented to the ear, but tuning curves are broad^{6,7,11}. Belt neurons also tend to have lower firing rates to both tones and noise¹¹ compared to responses in core neurons. Furthermore, neurons in the belt prefer increasingly complex stimuli¹¹⁻¹³ such as FM sweeps¹⁴ or band-pass noise^{6,10,15}.

Overall, neurons in the core region have short response latencies, respond best to pure tones than to complex stimuli, and possess narrow tuning curves. Neurons in belt areas, however, have long latencies, possess broader tuning, and do not respond well to pure tones but rather seem to prefer complex stimuli. In this sense, it appears as though stimulus preference gets more complex from core to belt to parabelt, thus a general flow of information is set up in a hierarchical order from core to belt to parabelt. Parallel processing is also occurring among subdivisions within regions. One important study that illustrates this involved recording from two core areas A1 and R as well as a belt area CM while presenting either pure tones or broad-band noise clicks to the contralateral ear. After establishing tonotopic maps and that each area responded to both clicks and tones, the authors removed A1. After ablation of A1, the researchers recorded again from R and CM, which would be devoid of inputs from A1, and found that neurons in CM no longer responded well to pure tones, but maintained responses to clicks. Neurons in R, however, maintained responses to both pure tones and clicks. This study provides strong evidence of both serial and parallel processing in the auditory cortex. Parallel processing was evidenced by the fact that in the absence of A1, neurons in R maintained responses to both pure tones and clicks. The fact that CM lost its responses to pure tones is evidence that it receives tonal information from A1, showing not only that CM was a secondary level of processing but also that information flowed from a core area to a belt area⁶.

Anatomy and histology of primate auditory cortex. Using anatomical tracers, connections between the auditory thalamus and different parts of auditory cortex have been described

and employed to define cortical regions. In general, the core region receives preferential input from the ventral division of the medial geniculate body (MGv), while belt and parabelt regions receive preferential input from the dorsal division (MGd). All regions receive inputs from the medial or magnocellular division (MGm)¹⁶. Thalamocortical connections provide evidence of parallel processing because divisions within the thalamus project to multiple areas within a level of processing in cortex. Connections within auditory cortex have also been described. The belt region receives input from core; the parabelt region receives input from the belt; but parabelt does not receive input from core areas. This provides additional evidence of serial processing within auditory cortex, where information is passed from core to belt to parabelt, but not from core to parabelt¹⁷⁻¹⁸.

The histological commonalities for sensory areas have been described in macaques and marmosets. The core region is heavily myelinated and has a thick, densely packed cell layer IV. Core areas also express dense staining of cytochrome oxidase (CO) which labels the metabolic enzymes in the cells, the vesicular glutamate transporter-2 (VGLuT2), and the calcium-binding protein Parvalbumin. This is likely because the core region is highly metabolic and active since it is the first stage of cortical processing. Within the core, the extents of these properties are less apparent going from rostral to caudal areas. However, these properties are still more common in the core than belt regions^{2,18}. The cytoarchitecture between the core, belt, and parabelt regions also differs. Aside from the prominent layer IV, the core region possesses tightly packed columns of cells. The lateral belt contains similar columns spaced apart; layer IV is narrower; and prominent pyramidal cells can be seen in layer V. The parabelt layer III seems to be broader, and the columns appear to be more striking in appearance than in the belt region¹⁸. By combining these histological techniques and looking at the specific histological signatures of the various types of tissues, the three regions were further divided into three core areas, eight belt areas, and two parabelt areas. This differentiation among regions and areas provides additional evidence of parallel processing in the implied functional differences that come with histological differences.

Primary and secondary regions of rodent auditory cortex

Rodents have been used in auditory research as ideal models for plasticity and deafness or hearing disorders. Unlike primate auditory cortex, there is no general model for rodents. The bulk of basic research in the descriptions of auditory cortical fields has been well-described in guinea pigs, rats, mice, and gerbils, where there may be at least five

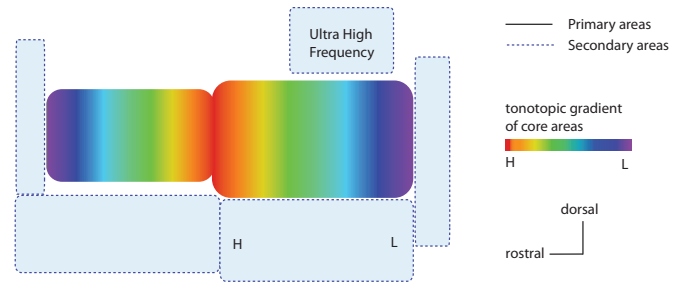


Figure 2. Schematic of a hypothetical rodent auditory cortex. Primary areas are shaded depicting tonotopic gradients. Example belt areas are indicated by dashed lines. Tonotopic gradients of belt areas are indicated by H (high) and L (low) frequency representations.

(mice¹⁹ and rats²⁰) and up to as many as seven (gerbils²¹) or eight (guinea pigs²²) areas based on physiological distinctions and tonotopic reversals. This portion of the review will focus on the common properties described in the primary and secondary areas in these species. Figure 2 shows a general schematic of a hypothetical “typical” rodent.

Physiological properties of rodent auditory cortex. Of the rodents studied, at least two prominent adjacent tonotopic fields are found. These two primary fields show mirrored tonotopy and possess neurons with short response latencies and narrow tuning curves¹⁹⁻²⁴. In addition to these two areas, another tonotopic primary area containing neurons with broad tuning curves and long latencies has been found in guinea pigs²²⁻²³, gerbils²¹, and rats²⁰. These are characteristics similar to core areas in non-human primates. Also similar to primates, multiple core-like areas have been described, indicating parallel processing.

Common secondary areas have also been shown in these rodent models. One non-tonotopic area has been implicated as having neurons with short response latencies and broad tuning²¹⁻²². Another secondary area is described as tonotopic, but these neurons prefer more complex stimuli to pure tones^{19,21-22}. Similarly, neurons in another area also have broad tuning and prefer complex stimuli, but tuning curves are consistently multi-peaked^{19-20,22}. In rats²⁰ and gerbils²¹ an additional secondary area has been demonstrated to contain neurons with variable responses. These areas are distinctly different but, in general, are characteristic of secondary areas.

In addition to characteristic primary and secondary areas, rodents may also have specialized fields. For example,

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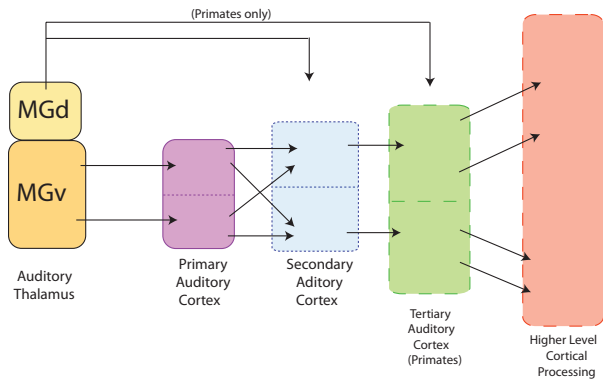


Figure 3. Schematic of serial and parallel processing in auditory cortex. Subdivisions of auditory cortex are indicated by dashed lines.

mice have a specialized ultrasonic field that possesses neurons that are active only when frequencies above 45kHz are present¹⁹. Similarly, rats²⁰ and gerbils²¹ have an area with no clear tonotopy, but neurons in these regions prefer high frequencies.

Anatomy and histology of rodent auditory cortex. Among the physiologically defined primary areas, the densest projections come from the ventral division of the medial geniculate body (MGv) with sparse connections from the medial division (MGm)^{20,25-26}. Some of the areas also receive sparse input from the dorsal division (MGd), but these are much less by comparison. Other primary areas receive preferential input from MGm rather than from MGv²⁵. Physiologically defined secondary areas receive preferential input from MGd²⁶. The specialized ultrasonic field in mice also has dense innervation from MGd, suggesting it may be a secondary level of processing²⁷. The general trend of thalamic input to different levels of cortical processing is similar to primates, but the projection patterns are not necessarily as straightforward. For example, in gerbils, connections with the thalamus have shown that all cortical areas are connected with MGv, MGd, and MGm, but relative strengths of these connections differ among the areas. Primary areas are predominately innervated by MGv, but some are also predominately innervated by MGm. Similarly, secondary areas receive densest projections from MGd and MGv²⁸.

The topography of these projections has been examined, and it is evident that different parts of the divisions of the medial geniculate project to different areas of cortex, indicating parallel inputs. This is further evidence of parallel processing in auditory cortex whereby areas receive similar projections from the divisions of the thalamus in parallel.

For example, in rats, the rostral portion of the MGv projects to the primary area A1; conversely, the caudal portion of the MGv projects to the ventral auditory field²⁰.

Unlike in non-human primates, the corticocortical connectivity patterns in rodent auditory cortex do not indicate a clear hierarchical processing. Rather, tracer injections into different fields of auditory cortex show that areas are highly interconnected ipsilaterally and contralaterally. For connections between tonotopically organized fields, connections are generally between tonotopically matched frequency representations²⁹.

The histological evidence for auditory cortical areas in rodents has been described in guinea pigs and gerbils. Consistent with other primary sensory areas, the cytoarchitecture of the two most prominent primary areas of rodent auditory cortex are granular in nature²¹. Staining patterns of cytochrome oxidase (CO) and myelin have been described for auditory cortical areas in guinea pigs. The primary areas contain the densest staining for CO and myelin. All other cortical areas showed low levels of CO staining. Similarly, primary areas show higher levels of myelination than secondary areas²².

Concluding Remarks

In looking at the organization of auditory cortex in non-human primates and rodents, it is apparent that the two groups share a common feature of hierarchical processing from primary-like areas to secondary areas and parallel processing within these levels (Figure 3). Primates appear to have three distinct levels of serial processing while rodents only possess two. This may be attributed to demands of more complex communication such as species-specific vocalizations. It is worth noting, however, that the majority of conclusions on primate auditory cortex have come from studies of macaques and marmosets, which are highly evolved and possess specializations that may not generalize to all primates. In addition, the thalamocortical projections that define these areas in the primate model do not appear to be as strong of a marker for defining similar areas in rodents. Therefore, examining the cortical organization and thalamocortical connections of other non-human primates would further refine the model to describe all primates and what underlying principals occur in mammalian auditory cortex. In particular, looking to an animal model from the more primitive branch of primates would provide insight into the basics of primate auditory cortex across primates. Prosimian galagos (*Otolemur garnettii*) are a good candidate for this question. Understanding differences and similarities between galagos and the current model would allow

for more precise comparisons of primates to other species such as rodents. If the organization of galago auditory cortex is similar to that of the primate model, this would imply that the model could serve as a true template for all primate species because it would hold true for two drastically different primate groups. If the two are different, it would increase our knowledge of the role auditory cortex plays in processing sounds for different demands and environmental pressures and provide insight into the evolution of primate auditory cortex.

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