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Primer

The auditory cortex

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Recognizing other people, animals or objects by the sound they make is something that most of us take for granted. In fact, this ability relies on a series of rich and complex processes that begin when sounds are transduced into electrical signals by the exquisitely sensitive hair cell receptors that lie inside the cochlea of the inner ear. These messages are then encoded as volleys of action potentials by the axons of the vestibulo-cochlear nerve and transmitted via a complex chain of nuclei in the brainstem, midbrain and thalamus towards the auditory cortex (Figure 1A), where the interpretation and recognition of sounds is thought to take place. Compared to other sensory systems, in which information reaches the cortex more directly, auditory signals are heavily pre-processed by the time they arrive at the cortex, and, in many animal species, this subcortical processing can mediate quite complex auditory tasks.

Because much of the neural processing necessary for our perception of the acoustic environment seems to occur subcortically, we are left to wonder what is left for the auditory cortex to do. Valuable insights into this can be obtained by observing the consequences of cortical damage. While the extent of the impairments vary widely among different mammalian species, it is clear that in primates, including humans, auditory cortex lesions can result in a severe hearing loss, at least temporarily, and an inability to recognize complex sounds or to pinpoint sound source locations. Auditory cortex thus plays a crucial role in hearing, but how it does this is still very poorly understood.

Common principles of cortical organization

In many ways, the functional organization of the auditory cortex resembles that of the cortices devoted to other sensory modalities, like the visual or the somatosensory cortex. In each case, one or more primary fields can be identified, representing the first stage of cortical processing, together with a number of surrounding areas that may differ according to their cellular fine structure, anatomical connections and physiological response properties (Figure 1B,C). The primary fields receive much of the ascending input via the thalamus and in turn project to 'higher-level' areas, which also receive some direct input from the thalamus.

A common feature of the primary cortical areas in different sensory systems is that they contain topographic representations or maps of the appropriate receptor surface. Thus, neighbouring neurons in the primary visual cortex (V1) receive inputs from adjacent parts of the retina in the eye, which results in the presence of a map of the visual world across the surface of the cortex. Similarly, each region of the skin is represented in a different part of the primary somatosensory cortex (S1), producing a cortical map of the body surface. The same principle applies in the auditory system, except that hair cells located at different points along the length of the cochlea are tuned to different sound frequencies rather than to different locations in space. The topographically organized projection from the thalamus to the primary auditory cortex (A1) therefore gives rise to a 'tonotopic' map of sound frequency.

In addition to these topographic representations, researchers have often suspected that other functional or organizational principles might be shared across different sensory modalities. When viewed under the microscope, for example, A1 is virtually indistinguishable from S1, as it exhibits an almost identical six-layered structure. V1 is more easily distinguished from

other cortical areas, because of the presence of a white stripe of myelinated axons — the stria of Gennari — in layer IV, which serves as a high-bandwidth input layer suited for handling the very large visual data rates that many mammals encounter as they move quickly through their cluttered environments. While useful for histologists or imagers wishing to determine the location of V1 in the brain, this anatomical detail does not alter the possibility that cortex is cortex, whether auditory, visual or somatosensory.

This notion received a spectacular boost through a series of ingenious experiments carried out on ferrets in the laboratory of Mriganka Sur at MIT in the late 1990s. By removing its normal auditory inputs, Sur and colleagues found that retinal projections could be re-routed to the auditory thalamus, which therefore gave rise to visual responses in A1. Remarkably, the A1 neurons in these 'rewired' ferrets exhibited many of the response properties — such as selectivity for the orientation and direction of movement of visual stimuli — that had previously been established as characteristic of V1. Moreover, behavioural studies suggested that the animals interpreted the visual activation of A1 as visual stimuli.

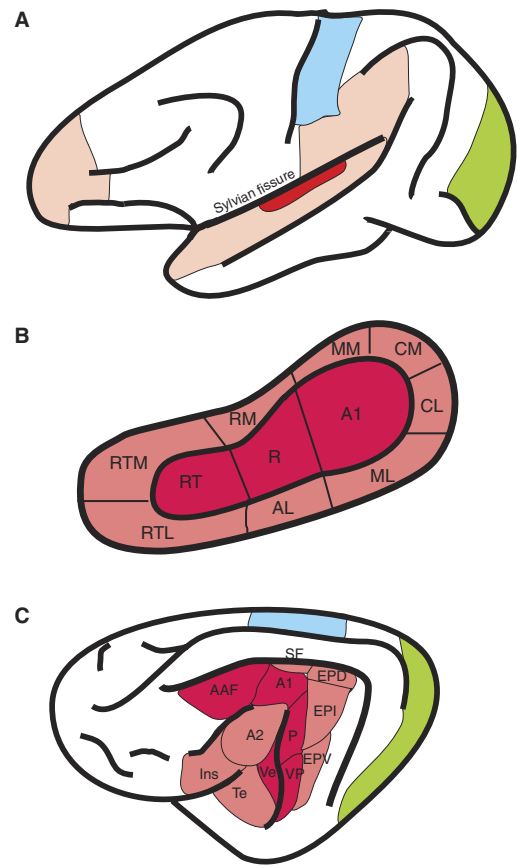
Does auditory cortex work like visual cortex?

So, if rewired A1 appears to be able to 'see' the visual world in much the same way as V1 does, then perhaps normal A1 might 'hear' the world using neural processing strategies that are similar to those used in vision. Attractive though this notion is, there are clear differences in the way in which information is processed in these two cortical areas. For instance, many of the features detected by V1 neurons, including line orientation and binocular disparity, are emergent properties of the cortex, arising as a result of convergence among the incoming thalamic axons and processing within the circuitry of the cortex itself.

By contrast, although sensitivity to certain sound attributes is

Figure 1. Sensory cortices.

(A) Side view of the cerebral cortex of the rhesus monkey. The visual cortex is shown in green and the somatosensory cortex in blue. The auditory cortex is shown in red, but note that, in many primates, much of the auditory cortex lies buried inside the Sylvian fissure which separates the temporal and parietal lobes of the cortex. The light pink shading shows areas in the frontal and temporal cortex which, although not classically considered auditory cortex, nevertheless contribute to the processing of acoustic information. The layout of the human brain is very similar. (B) Subdivisions of the auditory cortex of the rhesus monkey. This is thought to contain three 'core' or primary-like areas, A1, R and RT, which receive independent thalamic inputs mainly from the ventral part of the medial geniculate complex. The core fields project to a number of surrounding 'belt' areas (shown in pink), representing a higher level of auditory processing, which are, in turn, connected with 'parabelt' areas (not shown). Neurons in the belt and parabelt also receive inputs from other divisions of the medial geniculate complex and are connected to the temporal, parietal and frontal lobes of the cortex. The core areas and some of the belt areas contain tonotopic maps of sound frequency, and reversals in frequency gradient are often used to determine the boundaries of these fields. (C) Side view of the cerebral cortex of the cat. As in the monkey, the cat auditory cortex is subdivided into numerous fields, including both 'primary-like', tonotopically organized (red) and higher-level areas (pink). With the exception of the primary field A1, these are referred to by different names as auditory neuroscientists have not yet been able to establish with certainty which cat areas are homologous to the various subdivisions of monkey auditory cortex.



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certainly transformed in the cortex, the most well studied response properties of A1 neurons, such as their tonotopic organization and responses to stimulation of the two ears, are already found at subcortical levels. Consequently, one of the problems encountered by auditory researchers is a poor appreciation for the stimuli that are 'optimal' for the study of A1, in the sense that moving, oriented bars appear to be optimal for V1. A wide range of stimuli have therefore been used to probe the responses of A1 neurons, from tones and clicks to species-specific vocalizations, but these studies have failed to advance our understanding

of auditory processing in the way that Hubel and Wiesel's use of moving bars of light revolutionized the study of V1 in the 1950s.

One approach that has met with success in recent years is to measure the spectrotemporal properties of A1 neurons using techniques that go beyond a simple characterization of their frequency tuning curves. The results of one of these studies led to the suggestion that A1 neurons are able to detect stimulus 'edges' in either frequency or time and might therefore be analogous to orientation or directionally selective neurons in V1. Although the interpretation of this study is

open to debate, it does suggest that A1 neurons can act as linear filters of the acoustic stimulus.

This is important because in V1 neurons are classified as 'simple' or 'complex' according to whether they respond in a linear fashion or not. Linear neurons can be identified by their responses to sinusoidal grating stimuli — alternating bands of light which gradually fade from bright to dark and back to bright. As these stripes move across their receptive fields, V1 neurons respond to the ebb and flow of increasing and decreasing brightness. These neurons fall into two fairly well separable classes: linear simple cells, which echo these sinusoidal modulations of their input with an equivalent sinusoidal modulation of their output firing patterns, and non-linear complex cells, which, as the name implies, respond in more 'complex' ways.

In recent years, auditory neurophysiologists have attempted an equivalent approach in A1, constructing 'spectral ripple' stimuli in which sinusoidally modulated noise spectra systematically shift across the frequency-tuned neural filters of the cochlea. In apparent analogy to the simple cells of V1, one can observe A1 neurons that respond to the ripples with a sinusoidal modulation of their firing rates, suggesting that they most likely carry out an approximately linear summation of inputs across the excitatory and inhibitory frequency bands that constitute their receptive fields. When the same criteria adopted for V1 neurons are applied to auditory cortex, however, it turns out that most A1 neurons fall right on the simple/complex boundary, implying that they do not readily fit with the operational scheme thought to underlie visual processing.

Attempts to predict responses of A1 neurons with simple linear filter models have accordingly met with decidedly mixed success. While linear A1 receptive field models are surprisingly successful at predicting responses to brief, binaurally presented noise bursts — as

they might be experienced in a sound localization task — the same type of models are much less successful in predicting responses to complex sounds that develop and unfold over time, like speech or animal vocalizations. How such models might be improved remains an active research topic, as it would clearly be of great interest to know the transformations of the incoming sound that auditory cortex neurons compute, but progress is slow and it is uncertain whether further analogies with vision can bring about fresh breakthroughs.

A number of studies have now shown that the response properties of A1 neurons can change over different time scales, indicating that they are sensitive to the context in which stimuli are presented. This plasticity allows the filter properties of the neurons to be rapidly retuned according to the stimuli that have occurred previously and the task that is being performed. These findings have important consequences for the way in which combinations of different sounds are represented in the cortex and argue against the presence within A1 of an invariant representation of the physical features of sound sources.

Organization of response properties within auditory cortex

Although many details of the response properties of individual auditory cortex neurons remain poorly understood, valuable insights into the way in which information is analysed can be obtained by investigating how the sensitivity of neurons to particular stimulus attributes varies across the surface of the cortex. Within the retinotopic framework of V1, for example, neurons are organized into finer-scale, intertwined maps according to their preferences for stimulus orientation and spatial frequency, as well as eye of input. Because A1 contains a one-dimensional gradient of sound frequency, attention has focused on how neuronal sensitivity to other stimulus parameters is represented within the region

of the cortex corresponding to the iso-frequency contours that extend approximately orthogonal to the tonotopic axis. Within these regions of constant best frequency, non-random — and sometimes interrelated — distributions have been described for diverse properties, including response threshold, dynamic range and shape of response-level functions, sharpness of frequency tuning, sensitivity to frequency modulation, and the type of binaural interaction exhibited by the neurons.

These findings have been interpreted as evidence for a modular organization akin to that found in V1. In particular, alternating binaural interaction bands — defined according to how the neurons respond to stimulation of each ear — have been described across the isofrequency axis. Largely because of the possible analogy with ocular dominance bands in V1, this finding — perhaps unfortunately — has been reproduced in a number of textbooks. Although binaural neurons clearly play an important role in directional hearing, just as binocular neurons do in visual depth perception, more recent studies have characterized the interactions between the ears in more detail and shown that they are organized into smaller clusters, rather than continuous bands of neurons with similar properties.

Functional specialization beyond the primary areas

Another area where studies of auditory cortex have been influenced by earlier work on the visual system concerns what happens in the auditory areas that lie outside A1. It is now well established that functionally specialized processing streams emerge from distinct compartments within V1. After varying degrees of crosstalk, these streams project either ventrally to the inferotemporal cortex or dorsally to the posterior parietal cortex, where they appear to mediate object recognition and visuomotor control, respectively.

The possibility that dual processing streams are also found within auditory cortex has received support over the last few years from anatomical, electrophysiological and imaging studies. The first clear-cut evidence that non-primary cortical fields play different roles in processing acoustical signals came from investigations of the way in which biosonar signals, which are used for locating objects in space during flight, are represented in the cortex of echolocating bats. We now know that functional differences between cortical areas also exist in other species — particularly primates — but the precise nature of those differences remains a matter of debate.

Inspired by the division of labour in the visual pathways of the cerebral cortex, it has been proposed that separate cortical pathways exist for sound identification and localization. Although this remains a controversial idea, recent data from both human and non-human primates suggest that a region lying anterior and lateral to A1 is specifically involved in the perception of pitch, an aspect of hearing which plays a vital role in communication and in our ability to hear a musical melody. In humans, nearby areas are activated when subjects listen to phonetic cues or intelligible speech, further hinting that this general region of the cortex could be part of a sound identification pathway.

By contrast, the analysis of spatial information appears to rely on more posterior regions of the auditory cortex, particularly the caudomedial (CM) and caudolateral (CL) belt areas in the monkey (Figure 1B) and the posterior auditory field (P) in the cat (Figure 1C). Nevertheless, there is no evidence for a single 'space-processing centre' and the areas activated during different auditory tasks overlap to a large degree. Thus, although these findings are broadly consistent with a 'what' versus 'where' dissociation of brain activity, it is possible that this segregation of function relates more to differences in how information is processed than to clear

categorical distinctions in what is processed there.

Descending pathways from the cortex

No description of what the auditory cortex does would be complete without considering the descending pathways that project back to subcortical nuclei. As in other sensory systems, the auditory thalamus receives a massive descending projection, with four times more inputs arising from the cortex than from the ascending pathways. Cortical neurons also innervate the midbrain as well as various targets in the brainstem, nuclei that do not have direct access to the cortex, indicating that their influence on subcortical processing is likely to be very pervasive.

Only recently have scientists started to investigate what the various corticofugal pathways do. For instance, focal inactivation or electrical stimulation of small portions of the auditory cortex has been shown to alter the frequency tuning and other response properties of subcortical neurons. These findings have led to the suggestion that corticofugal axons may be involved in selectively filtering information in the midbrain and thalamus, which may enable us to pay particular attention to certain aspects of our auditory environment while ignoring others. This, in turn, would lead to an enhanced representation of stimuli that are frequently encountered or of particular significance, and could trigger longer-term, use-dependent plasticity.

Concluding remarks

Research on the auditory cortex is at an exciting stage. Although its vital contribution to various aspects of auditory perception has long been recognized, we still have only a preliminary understanding of the nature of the processing that underlies those functions. Future progress will rely on the choice of appropriate stimuli for probing the sensitivity of cortical neurons — including their role

in segregating sequences of sounds corresponding to different sources — and the establishment of closer ties between physiological and behavioural approaches.

A better understanding of the transformations that take place from the thalamus to the cortex and between different cortical fields will shed light on the extent to which the processing of biologically important information is parsed into parallel functional streams. At the same time, elucidating the functions and mechanisms of action of the many descending corticofugal projections will provide insights into both the dynamic coding of information throughout the auditory pathway and the role of the cortex itself. Finally, a complete description of how the auditory cortex works also has to take into account how inputs from other sensory modalities — now known to be widespread in the temporal lobe — as well as cognitive factors, such as attention and memory, influence the activity of its neurons.

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