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Cortical processing of complex sound: a way forward?

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The organization of the cortical auditory system remains controversial. In particular, the extent to which there is regional specialization in the cortical processing of complex sound is unclear. Here, we ask whether we are currently asking the right questions of auditory cortex, or using the appropriate techniques to do so. A key factor that will promote such understanding in the future will be increasing dialogue between workers using electrophysiological recording methods to assess the response properties of single neurons and those using imaging techniques to map regional organization. In the future, further insights will be obtained by efforts to test hypotheses developed on the basis of one approach by the use of the other. Imaging can tell the neurophysiologists where to look, and work on single neurons can constrain network models based on imaging. There is a crucial need for better understanding of the anatomy of the auditory cortex in different species and for comparative studies that will underpin both approaches.

We consider here the problem of how the network of different auditory areas in the cerebral cortex of mammals might process systematically the bewildering array of sounds in the acoustic world. There is general agreement across species that multiple cortical areas are involved in the processing of complex sound. In animals, these areas have been defined by neurophysiological responses, in particular by frequency gradient reversals in neighbouring tonotopically organized areas. However, such techniques are not adequate to define all 'auditory' areas (e.g. frontal area ventral premotor cortex and some belt areas of the macaque). Moreover, recent electrophysiological studies, some using awake (rather than anaesthetized) animals, have revealed highly complex, variable and plastic electrophysiological responses at the single neuron and neuronal population levels [1–3]. Accurate definition of cortical areas and inter-areal connections therefore requires additional approaches, including both anatomical methods (cytoarchitectonic, histochemical [4–6] and tract-tracing studies [7,8]) and functional imaging (positron emission tomography, functional magnetic resonance imaging, electroencephalography, magnetoencephalography, 2-deoxyglucose autoradiography [9] and optical imaging [10–12]). In general, these techniques can be applied to humans as well as to other species, although optical imaging and anatomical tracing studies are more much more limited in humans.

A key question is 'what do the different auditory cortical areas do?' Two extreme positions constrain the limits of this debate: the first is that all of the areas do something similar, with each processing many different sound features in parallel; the second is that different areas each have specialized functions that can be precisely characterized. The debate is made more difficult by the need both to reconcile results from different techniques assessing different levels of neuronal organization, and to identify whether corresponding auditory areas can be identified across different species. If this can be achieved, neuroscience studies in animals and imaging experiments in humans will become more mutually informative.

Recent evidence

The best-studied auditory field is primary auditory cortex, A1, which has been identified in many mammals (bats, rodents, carnivores, monkeys, primates and humans). The role of A1 in hearing is not fully established. Inactivation of A1 can impair certain low-level auditory processing tasks, but these deficits often disappear over time [13]. Imaging studies show that auditory stimuli strongly activate A1 in humans, but most stimulus manipulations do not cause differential responses that would appear on statistical parameter maps. In both anaesthetized and awake animals, A1 units exhibit narrow frequency tuning and are tonotopically organized. However, these neuronal responses are, in many respects, less specific than those of lower auditory centres: tuning curves are wider, temporal response properties much more sluggish, and responses are much more labile. This could reflect population-level encoding of the properties of sound stimuli.

It is often assumed, at least implicitly, that A1 contains a representation of sounds in terms of their physical properties, somewhat similar to the representation of visual scenes in primary visual cortex in terms of line

orientation, motion direction, spatial frequency, binocular disparity and so on. However, recent evidence in the cat, ferret and marmoset suggests a more complex stimulus representation that is sensitive to temporal [2,3] and spectral [1,14] context over timescales of seconds and minutes. Comparisons between responses of neurons in A1 and in subcortical stations suggest that A1 might serve as a general-purpose hub of the auditory pathway, forming a basis for the representation of the features of auditory objects. Higher auditory centers could then further process and abstract high-level properties used in object identification.

Auditory processing beyond the primary auditory cortex

In terms of the relationship between A1 and other cortical areas, Rauschecker and colleagues [15] originally proposed that distinct pathways for processing different aspects of acoustic stimuli exist in the macaque: according to this scheme, there is an anteriorly directed pathway for processing 'what' and a posteriorly directed pathway for processing 'where', analogous to the functional streams previously proposed in visual cortex.

Although the presence of dual processing streams within auditory cortex is supported by anatomical, physiological and imaging data, several single- or multi-unit recording studies in animals have failed to find clear differences in the spatial – or object – coding properties of neurons among different cortical fields. This might, in part, reflect limitations in the stimuli or analytical methods used or in the cortical areas that have been sampled. Work in the cat carried out by Middlebrooks and colleagues [16], for example, has revealed few differences in spatial selectivity between neurons recorded in the primary and secondary fields and in the anterior ectosylvian sulcus. However, a recent study by the same group suggests that the posterior auditory field in this species might be more specialized for spatial analysis [17], and this is further supported by emerging evidence from studies in which the behavioural consequences of reversibly inactivating different cortical areas have been examined [18].

Recent evidence regarding acoustic processing in the posterior superior temporal lobe of primates does not lead to a straightforward conclusion, either. In the macaque, recordings from medial and lateral belt areas in the posterior superior temporal lobe [19,20] have shown greater spatial selectivity than in anterior cortical fields. However, some posterior belt neurons show selective responses to call sounds [19] (although less commonly than in anterior areas), so there is no absolute demarcation of spatial from call-specific processing. Functional imaging in humans indicates that different spectrotemporal features are processed in the posterior temporal lobe, although responses specific to spatial sound properties have been demonstrated only in recent work using realistic broadband stimuli. Experiments carried out by the groups of Zatorre [21] and Griffiths [22,23] can be broadly interpreted as showing that regional selectivity for particular acoustic attributes exists in the posterior part of the human temporal lobe. However, this regional selectivity might be based on spectrotemporal features [21,24], specific correlates of spatial location [22] or correlates of

sound-source segregation [23]. Additionally, Wise and Scott have emphasized the possible relevance in humans of connections between posterior temporal lobe and speech production areas [25,26], which might represent a human pathway for vocal mimicry.

The evidence regarding acoustic processing in the anterior superior temporal lobe of primates is likewise open to interpretation. Although microelectrode [15,19] and lesion [27] studies suggest that this region selectively processes conspecific call sounds in the macaque, it is not known precisely 'what' (stimulus properties, recognition of acoustic objects or call-sound meaning) is represented. In humans, Scott and colleagues have demonstrated an anteriorly directed stream for the processing of intelligible speech [28], although more linguistic (or lexical) aspects of speech processing could involve the ventral temporal lobe [29,30].

The way in which the primate mechanisms might relate to the analysis of sound by non-primates is hard to ascertain in view of the difficulty in establishing anatomical homology across species. There are grounds for optimism, however, based on emerging evidence suggesting that it might be possible to establish meaningful functional homologies between primates and non-primate species [17,18,31].

A way forward?

Recent work on primates, including humans, is difficult to interpret in terms of distinct cortical mechanisms based on categorical distinctions between stimulus constructs (e.g. 'what' versus 'where') from mechanisms based on types of processing (e.g. 'temporal processing' versus 'spectral processing') [19,21,24]. *A priori*, this might reflect:

(i) Absence of any categorical distinction or a partial distinction. Several lines of evidence suggest that functional differences between cortical areas do exist, so perhaps graded distinctions prevail.

(ii) Ill-posed questions. Experimental tests of hypotheses directed at a level at which cortical areas do not operate will not be illuminating. The questions imagers ask of auditory cortex might be too complex, if the cortex is primarily concerned with generic processing strategies or the transmission of preprocessed information to higher centres. Conversely, the questions electrophysiologists usually ask might be too simple, as suggested by experiments on foreground–background processing [32,33]. The processing of single stimuli in most laboratory environments is unlike the analysis of multiple objects in the real acoustic world.

One approach that could reduce the uncertainty surrounding the nature of auditory cortical processing is to look for 'generic' processing mechanisms. Such an approach might inform our understanding of (certain) mechanisms common to different species. Examples would include:

(i) Using techniques, including measurements of the spectrotemporal receptive fields [34] of individual neurons, to investigate the extent to which acoustic information is processed using linear or non-linear coding strategies. For example, although certain properties of the acoustic environment might be efficiently encoded by linear mechanisms [35,36], non-linear mechanisms are likely to be involved in

processing speech (and possibly conspecific call sounds [37]) or tasks related to auditory scene analysis, such as segregation and grouping of acoustic components in time and frequency [14,38].

(ii) Exploration of the processing of 'generic' stimuli. For example, it would seem reasonable to suggest that all mammalian species might process stimulus properties such as periodicity (related to pitch), binaural disparities (related to spatial perception), and 'gestalt' features such as common amplitude modulation, continuity [39] and so on. In fact, it has been argued [33] that statistical regularities in the structure of natural sound should be reflected in generic auditory mechanisms, largely independent of the species. Examples of this kind could release auditory research from its dependence on species-specific vocalizations, with their high species specificity, as the prime examples of behaviourally relevant complex sound processing.

This approach could be applied to appropriate mammalian models. Demonstration of 'generic' cortical mechanisms in a non-primate species would suggest processing strategies that might apply to primates and non-primates alike. A growing number of studies of auditory cortical processing are being carried out using primates but there are very good reasons why certain non-primate species should continue to be used, including the wealth of data already available (cats) and suitability for behavioural or developmental studies (ferrets) or for neuroethological studies (bats). Difficulties in relating anatomy across different species are often emphasized, but the identification of generic processing mechanisms in non-primary auditory areas might suggest cross-species functional homologies, even if the exact anatomical homology cannot be established. It seems likely that common neural substrates will be revealed by focussing on tasks, such as figure–ground segregation, that are likely to require the cortex irrespective of the species in question.

An approach based on generic processing mechanisms alone is not sufficient. Specifically, although all species need to process the acoustic environment, they will all derive different information from it, and produce different responses to it. For example, it is possible that the processing of intelligible speech in humans might be based on an information-processing mechanism that could be used in other species for different purposes. Such issues are potentially of broad relevance to problems such as the functional basis for hemispheric asymmetry in different mammalian species.

Better understanding of species homologies will improve our understanding of generic mechanisms that might cross species boundaries. Interpretation of human functional imaging data using models derived from non-human primates is now becoming almost routine, without full justification in terms of cytoarchitechtonics, cortical connections and electrophysiological properties. Moreover, arguments about cortical processing based on comparisons between primates and other species will never be resolved without some means of comparing the anatomy.

One possible basis for consensus is the growing appreciation that the auditory cortex does not work in isolation. Generative models [40] of the function of auditory cortices

might be based on interactions between auditory and other areas concerned with action and cognition. Again, a better understanding of anatomy will be essential. For example, there have been careful and informative studies of frontal connectivity patterns in the macaque [41], but macaque and human frontal cortices are very different. Nevertheless, evidence for modulation of auditory cortical function by 'top-down' influences is emerging from both animal electrophysiology [42] and human functional imaging studies [43].

Some preliminary conclusions

The evidence from several species, and primates in particular, strongly suggests that there are differences between the types of processing occurring in different auditory cortical areas, but there are no firm grounds for confidence that we are currently asking the right questions of the cortex. The hypothesis that common areas for certain types of processing exist across species is a reasonable and testable one, especially for aspects of the perception of the acoustic environment (e.g. auditory localization and object segregation) that are performed by all species. Caution is needed, however, because some generic processing tasks could vary widely in the extent to which they engage cortex in different species.

The existence of generic information-processing mechanisms should be tested in different species (while recognizing that the use made of the derived auditory information might vary between them). Identifying interspecies differences in the extraction and use of auditory information represents an important challenge that will potentially shed light on both generic and species-specific mechanisms of auditory processing.

Recommendations

Continued dialogue between psychoacousticians, cognitive psychologists, auditory anatomists, neurophysiologists and imagers is essential. No one technique or model will explain how the cortex works, and workers (and funding agencies) should be aware of and acknowledge this. Several specific factors might facilitate further progress:

(i) Although there are valid, technical reasons why recording studies in animals are often carried out under anaesthesia, there is no doubt that the move towards recording from awake animals, and preferably those engaged in behavioural tasks, should be encouraged.

(ii) Imaging studies of auditory cortical functions in humans, including those with neurological and other disorders, could be carried out as tests of hypotheses derived from studies of animal neurophysiology, behaviour and anatomy. Human functional imaging experiments in turn have the potential to generate testable hypotheses for single-unit electrophysiological recording in animals, which remains the only systematic method available for investigating how complex sounds are processed and encoded at the neuronal level. The synergy between these techniques will be facilitated if researchers using both techniques make an effort to formulate clear testable hypotheses that arise from their work, especially those that might be tested using complementary experimental techniques. The simultaneous acquisition of imaging and

electrophysiological data in animals (pioneered in visual cortex by Logothetis [44]) would greatly facilitate the interpretation of human functional imaging studies.

(iii) Further anatomical work and establishment of cross-species homologies will inform both neurophysiological and imaging studies and facilitate the development of hypotheses that can be tested across species. It is crucial that anatomists are made aware of this issue, to stimulate efforts to establish cross-species homologies.

(iv) Quantitative techniques for analyzing the responses of cortical neurons, including their information content, should be developed as a means of assessing generic auditory cortical mechanisms common to different species [34,45,46].

(v) Improvements in the delivery and manipulation of precisely controlled complex sounds will benefit both neurophysiologists and imagers. For example, recent electrophysiological and imaging studies have benefited greatly from the application of virtual acoustic space stimuli [36,47,48], which facilitates faster and more detailed sampling of auditory space than is generally possible with traditional free-field stimulation techniques, and also facilitates investigations of cortical development and plasticity. This should also help to avoid criticisms of studies that have attempted to infer stimulus specificity based on the presentation of a limited range of stimulus parameters. The same is true for processing of call-specific or speech-specific responses, where development of appropriate complex stimuli will allow better controls and a clearer specification of the nature of such specificity and the level at which it arises [1,37].

Aside from these specific factors, in our view the single most important determinant of progress will be the extent to which auditory researchers engage each other and other neuroscientists. Recent meetings in Cambridgeshire and Magdeburg have encouraged this, and we hope that the views put forward in this article will promote further dialogue and collaboration within the neuroscience community.

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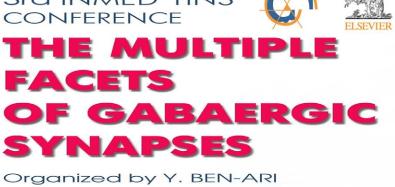
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