Interdisciplinary auditory neuroscience

The Organization of Hearing, Speech and Music in the Human Auditory System, Wellcome Trust Frontier Meeting 22–23 March 1999, Cambridge, UK.

The focus of this meeting, held at Hinxton Hall, near Cambridge, was the processing of complex sounds in the auditory system from cochlea to cortex. The more general purpose was to review recent advances in interdisciplinary auditory neuroscience and promote it as a field in its own right.

The auditory pathway

The principal components of the auditory pathway from the cochlea to primary auditory cortex are shown in Fig. 1. In the brain, they all lie in a frontal plane that proceeds vertically from the auditory canal to the upper surface of the central portion of the temporal lobe. The figure preserves the relative anatomical positions of the components and their sizes and shows that the auditory pathway differs considerably from the visual pathway. There are three processing centres between the end organ and the thalamus, and they perform significant transformations on the neural pattern as it proceeds up the pathway[1]. In the visual system, after light is transduced by the retina, the neural impulses proceed to visual cortex at the back of the brain with virtually no intervening processing. The anatomical differences would appear to reflect an important physiological difference that featured prominently at the meeting; the temporal precision of the auditory system is about two-and-a-half orders of magnitude greater than that of the visual system. Auditory nerve fibers fire in phase with the stimulus wave up to about 5000 Hz, and the modules that process this sub-millisecond information need to be close to the source to minimize temporal distortions.

The first half of the meeting was concerned with the processing performed by the brainstem with emphasis on temporal precision; the second half was concerned with thalamic and cortical processing and recent improvements in physiological and imaging techniques.

The brainstem

Our knowledge of brainstem function is based largely on anatomical and physiological studies of small mammals, and this area has a reputation for being formidably complex. At this meeting, however, the anatomist Carole Hackney (Keele, UK) and physiologists Ian Winter (Cambridge, UK) and Alan Palmer (Nottingham, UK) focused on the structure and function of the human brainstem, which the non-specialists were surprised and delighted to find is considerably simpler than that of small mammals. Specifically, there is a neural circuit in the cochlear nucleus (CN) and lateral superior olive (LSO) in small mammals that is involved in calculating interaural level differences for sound localization. Globular bushy cells in the CN collect information from granule cells and project it directly to the ipsilateral LSO, and indirectly to the contralateral LSO via cells in the trapezoid body that invert the signal. It appears, however, that this circuit is primarily concerned with the orientation of the outer ears, or pinnae, which are mobile in small mammals, and the affect that they have on high-frequency sounds entering the ear. Humans have fixed pinnae and are low-frequency specialists. Perhaps for these reasons, we do not have granule or globular bushy cells in the CN or inversion cells in the trapezoid body, and we have at best a small LSO. Humans are sensitive to interaural level differences but they are not evaluated in the same way as for small mammals.

This means that in the human brainstem, there are primarily two pathways for ascending information from cochlear nerve fibers[1]: One involves multipolar and octopus cells that extract envelope and periodicity information from cochlear nerve fibers and project it to the contralateral inferior colliculus. Ian Winter indicated that the timing information in this pathway is often independent of loudness level over a surprisingly large range. The other pathway involves the spherical bushy cells in the CN which preserve detailed timing information and project bilaterally to the medial superior olive. Alan Palmer reported that interaural time differences are assessed in this pathway, and the information projects to the IC with sufficient temporal precision to support the detection of source motion in the IC (Ref. 2).

At the IC there is a dramatic reduction in phase locking which suggests that this is the point where the system converts the delicate phase-locking information into a more robust rate or place code (Roy Patterson, Cambridge, UK). It was argued that the system computes time intervals between neural spikes and constructs interval histograms, one histogram for each of the tonotopic channels set up by the cochlea. The array of histograms is referred to as an auditory image[3] and it was argued that this representation is much more like our initial perceptions of sounds than the neural patterns observed in the auditory nerve or the traditional sound spectrogram.

Advances in imaging techniques

Several talks and posters were devoted to how to overcome the problems of functional imaging in the auditory system. The first problem is that sub-cortical structures, which play an important part in the processing, are difficult to image because they are near the limits of imaging resolution. Moreover, whereas cortex is firmly anchored to the skull, the brainstem moves with the pulsing of the cardiac cycle over distances up to half the diameter of brainstem nuclei. This motion greatly reduces the sensitivity of techniques like PET where scans last 30 seconds or more and activity within that time is averaged by the technique. Functional magnetic resonance imaging (fMRI) has much better temporal resolution (tens of milliseconds) and this has led to gating techniques in which the initiation of a scan is synchronized to the cardiac cycle[4]. Jennifer Melcher (Boston, MA, USA) described how this technique can be used to image the IC and CN, and that a patient with unilateral tinnitus exhibited asymmetric activation at the level of the IC when the tinnitus was reported to be present.

The fMRI scanner produces a loud drumming noise right beside the ear, and it seems likely that the auditory effects of the scanner drumming are likely to interact with those of the test stimulus. This has led to 'sparse' imaging in which the test sound and the scanning occur in alternate intervals[5]. The test sound is presented on its own for about 10 seconds which is the time taken for the haemodynamic response to build up to its steady state level. Then the test sound is turned off and scanning proceeds for about 2 seconds. Although a session yields fewer scans, the sensitivity of sparse imaging is comparable to continuous imaging, and there is a much better chance that you are measuring the response to the test sound. There are also new high-fidelity, magnet-friendly headsets with carbon-fibre leads to replace the plastic tubes currently used.

The extended duration of the haemodynamic response is a serious

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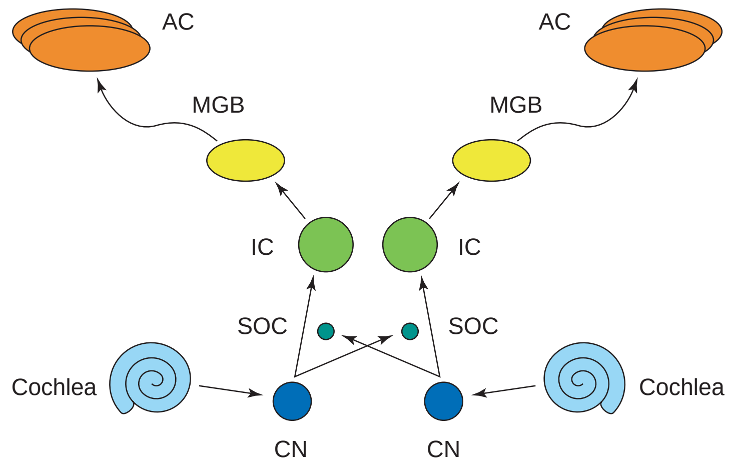

Fig. 1. Primary components of the auditory pathway. Shown in this schematic diagram are the cochlea (or inner ear), three brainstem structures [the cochlear nucleus (CN), the superior olivary complex (SOC) and the inferior colliculus (IC)], the auditory thalamus or medial geniculate body (MGB), and the auditory cortex (AC).

problem for designs in which sequences of different stimuli, like words, have to be presented with intervals of less that ten seconds. The responses of successive stimuli interact and in a non-linear way. Karl Friston (London, UK) described new analysis techniques that indicate that the interaction can be managed and the responses decomposed for stimuli as close in time as two seconds[6].

The improvements in spatial and temporal resolution of fMRI and MEG (magnetoencephalography), and techniques for single-unit recording in unanaesthetized monkey cortex, have provided a wealth of new information concerning the structure and function of auditory cortex. There is tonotopic organization for pure tone stimuli in primary auditory cortex, as would be expected, but it is not simple and there is much more there than just a frequency map. The tonotopic organization is duplicated in two separate crescents (Jennifer Melcher) and between the tuned cells are many that are not tuned (Xiaoqin Wang, Baltimore, MD, USA) indicating interleaved processing systems in primary cortex[7], as suggested previously by the anatomy (Jean Moore). Primary auditory cortex has been shown to be sensitive to most physical variables[8], like duration, intensity, and frequency range (Jeff Binder, Milwaukee, WI, USA). It also responds to 'delay-and-add noise' that produces a temporal pitch perception by manipulating the distribution of time intervals in the noise and creating a concentration of intervals at one particular delay[9] (Tim Griffiths, London, UK).

Auditory cortex

The second half of the meeting began with a review of thalamic and cortical anatomy by Jean Moore (Los Angeles, CA, USA). She emphasized that human auditory cortex consists of three separate subsystems that mature in distinct phases, the last of which occurs between the ages of 5 and 11! The brainstem is largely mature at birth, as are the axons of cells in the most superficial layer of the cortex (Layer I). This layer consists mainly of long backwards projecting axons that have been implicated in the control of arousal and sleep cycles, but it is also sufficient to enable infants to discriminate the basic categories of speech sounds. Phase Two of cortical development occurs between about six months and two years and involves maturation of neurons and axons in the deep cortical layers IIIc, IV, V and VI, which are the targets of thalamic input, and also the source of projections back down to subcortical structures. This period coincides with the development of speech and its onset is marked by the restriction of the child's speech to sounds of the language that they hear in their environment. The final phase of cortical development does not start until age five by which time most children have mastered speech and have language with complex syntax. The final phase of development continues to age 11 and involves maturation of neurons and axons in layers II, IIIa, and IIIb, a significant portion of auditory cortex which is, seemingly, not required for competent speech and language. These layers are the source and the target of cross-cortical connections including interhemispheric connections. The lexicon is not thought to reside in primary or secondary auditory cortex and so the anatomy suggests that the connections between sound and meaning remain flexible long after the lexicon develops.

Auditory cortex includes secondary areas surrounding primary cortex and a then a 'belt area' along the superior temporal gyrus. Joseph Rauschecker (Washington, DC, USA) provided evidence that neurons in the belt area of rhesus monkeys are sensitive to speech-like components of rhesus vocalizations; specifically, they were sensitive to the bandwidths of short noise bursts (analogous to fricative consonants) and the rate of change of frequency-modulated sweeps (analogous to diphthongs). In humans, the connectivity between primary auditory cortex and subsections of the belt area can now be established with fMRI techniques and it appears to parallel that in monkeys[10]. One of the main goals would be to locate the area responsible for word recognition. However as Jeff Binder noted, contrasts between the activation produced by meaningful and meaningless sentences have led to ambiguous results when the stimuli were carefully balanced for phonemic content. There are areas that show differences in activation between forward and reversed sentences but it seems that they are outside auditory cortex. Comparison of the two hemispheres reveals differences in terms of the efficiency with which they process temporal and spectral information[11] (Robert Zatorre, Montreal, Canada). Rapidly changing, broadband stimuli, like speech, seem to be processed more efficiently on the left while slowly changing stimuli that produce stable pitch perceptions are processed more efficiently on the right, particularly if they require pitch memory.

Christo Pantev (Muenster, Germany) emphasized that it is also important to be aware of individual differences associated with plasticity and acquired skills when dealing with adult humans. MEG studies show that following extensive practice skilled musicians have enlarged cortical representation of complex musical tones as compared with pure sinusoids. To assess permanent memory traces such as those used in speech and language, Risto Näätänen (Helsinki, Finland) advocated use of the 'mismatch negativity' component of event-related potentials. The mismatch negativity elicited by an unexpected vowel sound is much greater when it is a vowel from the listener's own language rather than a vowel from a foreign language. Developmental studies reveal that these traces are laid down in the infant brain between six and 12 months of age[12], which brings us back to the intriguing contrasts between the early onset of speech specific processing, the late development of layers II and II of auditory cortex, and the plasticity of cortex in response to training.

Summary

The meeting made the value of interdisciplinary auditory research clear to most of the participants – to understand the structure and function of one component of the auditory pathway requires knowledge about preceding and following components that in many cases can only be obtained through collaborative, interdisciplinary studies – but then, we were in large part preaching to the converted at this meeting. For the larger community, the most important conclusion, beyond the individual findings, is probably that many of the tools and techniques are now well established and encapsulated, so that scientists from complimentary areas can collaborate successfully. It was also clear that successful collaborations that extend your own research beyond its previous domain bring a special scientific pleasure.

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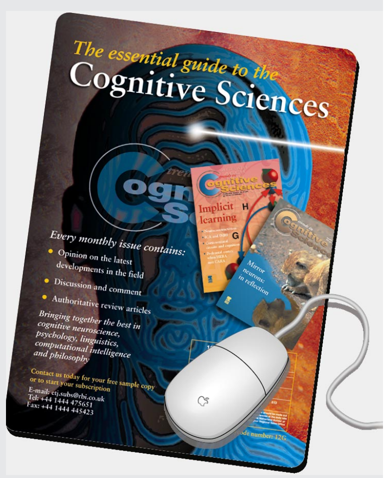

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