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*AJNR Am J Neuroradiol* 1997, 18 (4) 621-623

<http://www.ajnr.org/content/18/4/621.citation>

This information is current as  
of June 20, 2025.

# Functional Neuroimaging in the Study of the Human Auditory Cortex

Robert J. Zatorre, Associate Professor, Department of Neurology and Neurosurgery, Montreal (Quebec, Canada)  
Neurological Institute, McGill University

Functional neuroimaging has emerged as a major new scientific approach to the study of the central nervous system. The papers by Strainer et al (1) and Richards et al (2) in this issue of *AJNR* provide two examples of how such methods may be applied to furthering our understanding of functional aspects of the auditory cortex. These studies illustrate well the promise of these techniques for both experimental purposes and clinical applications; one must also be aware, however, of the limitations of such methods in order to interpret imaging findings appropriately. Past studies have demonstrated how positron emission tomography (PET) and functional magnetic resonance (MR) imaging can be used to study the distribution of cerebral hemodynamic changes associated with sensory stimulation in many modalities, including vision (3, 4), somatomotor function (5), olfaction (6), and audition (7–9). These methods have also been increasingly applied to investigate complex cognitive functions, such as speech and language processing (9–13). The tremendous importance of these imaging techniques is that they provide investigators with a tool to study how the pattern of activity in the human brain in vivo changes as a function of perceptual or psychological variables. Neuroscientists interested in behavior and cognition have welcomed these developments as a very significant complement to the more traditional lesion approach to the study of brain-behavior relationships.

To date, knowledge about the functional organization of the human auditory cortex has been quite limited. The studies by Richards et al and Strainer et al provide useful new knowledge that would be difficult to obtain with other techniques. The study of Strainer and collaborators (1) illustrates one application of functional MR, and demonstrates the feasibility of measuring

signal changes in the auditory cortex to acoustic stimuli, despite the inherent background noise produced by the echoplanar pulse sequences. Their study also demonstrates that the functional MR signal can be differentially sensitive in complex ways to various stimulus parameters, and thus highlights the necessity to perform careful, parametric studies of the relation between stimulus features and the observed signal.

This study also serves as a useful reminder of some of the issues that investigators must be aware of when interpreting findings with currently available functional MR techniques. For example, the presence of tonopcity in the auditory cortex is addressed in this study, but one must exercise caution in examining activation patterns from a single image section, since the presence of signal change in areas outside the area sampled are not available. This issue is particularly important in the case of a structure such as the gyrus of Heschl, which has a transverse course, and thus would not be fully sampled in a coronal section.

Another, related issue raised by the Strainer paper is that individual differences might exist in the functional MR response to a given input. For example, only half of the subjects in that study exhibited significant activation in response to a 4-kHz tone. This finding might be related to the limited field of view already mentioned, but could also be related to other factors, including differential sensitivity to habituation effects, for example. This variability might also reflect other, more complex sources of variation, including attentional or other cognitive processes. The latter variables would be of obvious importance when using more complex stimuli, such as speech. It is therefore clearly incumbent on the investigator to be cautious in interpreting a lack of signal in any given indi-

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Address reprint requests to Robert Zatorre, PhD, Department of Neuropsychology, Montreal Neurological Institute, 3801 University, Montreal, Quebec, Canada H3A-2B4.

**Index terms:** Hearing; Magnetic resonance, functional; Magnetic resonance, spectroscopy; Commentaries

AJNR 18:621–623, Apr 1997 0195-6108/97/1804-0621 © American Society of Neuroradiology

vidual, particularly in the situation of a clinical case study, unless ample normative information is available for the stimulus and task that are being used. Furthermore, since it has been shown in PET studies that the cerebral blood flow response to identical stimuli can change substantially as a function of the cognitive operations that the subject may be engaged in (9, 14), it is important to attempt to control for such task-related variables whenever possible.

The paper by Richards and colleagues (2) opens up another very interesting issue in the use of brain imaging techniques: the opportunity to study metabolic changes with specific biochemical markers. Although PET has the advantage of being able to trace many different chemical events by virtue of using different radioligands, the study of Richards et al illustrates how MR spectroscopy can also yield valuable insights into changes in metabolites as a function of different stimuli in a clinical population. Clearly, much more research will need to be done along these lines before a full understanding is achieved of the metabolic changes that can be induced in the central nervous system by a condition such as hearing loss, but this study shows the promise of the technique. Another useful feature of this study is that it provides a characterization of the spectral energy distribution of the acoustic noise produced by the pulse sequences used. This information is very helpful in being able to judge the effective signal-to-noise ratio of the stimuli used, and to evaluate the presence of any masking effects.

This paper, like the previous one, raises the issue of how complex stimuli, in this case music, are processed within the auditory cortices. It is of interest to note that a reduction in lactate accumulation was observed during music stimulation, implying possible decreases in neural activity. This finding highlights the complex interactions that may exist between a stimulus and the neural events that underlie its processing, and thus points to the need for carefully controlled experimental studies of these interactions. In the case of musical stimuli, research from our laboratory (14) has demonstrated cerebral blood flow increases in the right superior temporal cortex when healthy subjects were presented with tonal patterns, as expected based on lesion studies (15). But as mentioned above, activation patterns change substantially as a function of the instructions: when subjects were asked to listen to the stimuli and retain

pitch information in working memory, a complex network of regions was engaged, including temporal and frontal regions, as well as inferior colliculus, which had not been active under nondirected listening. Furthermore, decreases in cerebral blood flow were noted in the left primary auditory cortex in this condition. These findings thus demonstrate the difficulties involved in interpreting any given result in isolation, and point to the need for (a) careful control over both stimulus and task variables in any functional imaging study, and (b) converging evidence from other methods before coming to any definitive conclusions.

A final word should also be given about the anatomic specificity that brain imaging techniques offer. It is clear from the two papers in this issue, for example, that MR imaging can be quite accurate in delineating functional changes within a circumscribed anatomic region. However, apart from the problem of field of view, already mentioned, there are several other important issues that must be considered in this respect. First is the fact that there can be considerable anatomic variability in the position, size, and shape of a given structure across individuals. Selection of a region of interest therefore must be accomplished with care. One approach that has proven useful in the PET literature, and which has recently been applied to functional MR data as well (16), has been the use of stereotactic normalization, whereby a given brain volume is linearly scaled and transformed into a standardized coordinate system. This approach has several advantages, including the fact that it permits direct comparison of data sets across laboratories. In the case of the two studies discussed here, for example, both refer to the auditory cortex, but it is not clear whether the same brain regions were sampled; it would be of great help if one could compare the precise location of the functional MR and MR spectroscopic signals obtained via stereotactic coordinates.

Linear scaling of this type does not reduce interindividual anatomic variation to zero (17), of course, but it does allow one to develop consistent reference points, and permits the quantification of anatomic variability. For example, in a recent study from our laboratory (18), the region of Heschl's gyrus in healthy subjects was identified on structural MR images that had been transformed into the standardized stereotactic space of Talairach and Tournoux (19).

The resulting volumes were labeled using three-dimensional image processing software. The labeled region was superimposed across individuals, resulting in a probabilistic map of the structure of interest. This mapping not only quantifies the residual variations in anatomic location of Heschl's gyrus, but also allows one to examine any systematic interhemispheric differences in position and volume. In addition, the probability map provides a way to estimate the average position of a functional activation focus (from PET or functional MR as well as other techniques such as magnetoencephalography) relative to the structure of interest, and can also be used to describe the extent of encroachment of a lesion into the region of interest.

In summary, it appears clear that functional neuroimaging will continue to play a major role in both clinical and experimental neuroscience. It will be important for investigators and clinicians alike to develop expertise in the issues inherent to these techniques in order to maximize their enormous power while minimizing their limitations. I hope that the comments offered here will prove of some utility toward this goal.

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