Hearing: Cortical activation does matter

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Abstract

Lesion studies have suggested that the auditory cortex may not be involved in many aspects of hearing. A recent report casts doubt on this long-held view by showing that reversible inactivation of the auditory cortex leads to a transient impairment in tone detection and frequency discrimination.

Article Outline

Research into the association between brain lesions and behavioural changes has a long and chequered history. One major, and increasingly well-recognised challenge in this research is that neural plasticity dynamically reassigns function after a lesion is performed. Thus, as seen in stroke patients, a functional impairment can often resolve itself after long periods of recovery, despite the permanent loss of brain tissue that normally mediates the function. While this recovery is obviously good news for the patient, it can present difficulties for researchers trying to understand the role played by different parts of the brain. The possibility always exists that normal function following a lesion will be

mistakenly interpreted as a normal lack of involvement of the lesioned area in the function. Other brain structures will then, by default, be implicated. The functional 'snapshot' that is offered by behavioural studies can therefore be misleading, especially when limited data are available across time.

Several alternative strategies exist for eliminating or mod-ulating activity in specific brain areas (Box 1). A recent report [1.] based on the use of one of these approaches to examine the association between auditory cortical function and hearing looks set to consign some previously held beliefs to the waste bin or, at least, to turn a number of faces red. Talwar *et al.* [1.] employed muscimol inactivation of the primary auditory cortex (A1) in behaving rats to show that the basic tasks of tone detection and frequency discrimination are normally dependent on A1 function (Fig. 1). By developing very simple behavioural tests for assessing auditory function within 15–30minutes of muscimol application [2.], they were able to follow the time course of the deficits produced by the inactivation and their subsequent recovery. Performance on both tasks was severely impaired by 2–3hours after muscimol application began. However, the ability of the rats to perform the tone detection task recovered very rapidly, within 5–10hours, whereas performance on the frequency discrimination task recovered over a longer period of 10–20hours. Parallel physiological recordings revealed marked changes in surface-recorded auditory evoked potentials which followed a similar time course. Both tone detection and discrimination were thus reversibly impaired by the inactivation.

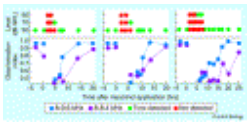 Full-size image (17K)

Fig. 1. Effect of muscimol application to auditory cortex on sound detection level and frequency discrimination in three rats. Tones were reliably detected at 50 dB SPL before, immediately after, and >5 hours after the muscimol (green points). Detection failed when tested 1–5hours after muscimol (red points). Discrimination

between two tones ('easy' – lighter blue, 'harder' – purple), measured by the A′ index, a function of hit and false alarm rates, followed a similar pattern, but recovery after muscimol took up to 25 hours.

Box 1 Strategies for inactivating the brain

Lesion studies have traditionally formed the basis for much of our understanding about the functions of particular areas of the brain. A variety of techniques have been used for this purpose, including aspiration, electrolytic and radio-frequency lesions, ischemia and injections of neurotoxic chemicals. Lesions are, however, irreversible and, depending on the method used, may lead to degeneration in brain areas that are either connected with or send axons through the lesion site. Other methods can be used to inactivate brain areas reversibly. For example, the brain can be temporarily inactivated by cooling, which, for surface structures, like the cortex or cerebellum, is relatively non-invasive but not really suitable for long-term studies. Chronic delivery of drugs for silencing or modulating the activity of specific brain areas can be achieved via a stereotaxically implanted cannula attached to an osmotic minipump or via the sustained-release polymer Elvax. Because they can be used to deliver drugs, such as the $GABA_A$ agonist muscimol, over relatively large areas and over periods of up to several months, Elvax implants are likely to be particularly suitable for behavioural studies. But most of these approaches involve surgical procedures from which the animal may take several days to recover fully. Consequently, transient changes in performance may be missed. The advantage of the approach used by Talwar *et al.*[1], in which muscimol was injected into a well implanted over cortical area A1, is that the hearing ability of their animals could be assessed straight away. Adequate controls are, of course, necessary for any of these methods, including sham-operated animals or the application of vehicle solution, such as saline. Moreover, reliable conclusions about the involvement of a given brain area in

perception and behaviour can be drawn only if the release characteristics of the drug, and the spatial and temporal extent over which it alters neural activity, are measured carefully.

Previous studies have generally found that the auditory cortex is unnecessary for sound detection and simple tone discrimination. Masterton and Berkley [3.] concluded in a 1974 review that “it is reasonably safe to bet that ablation of auditory cortex does *not* affect the capacity to discriminate sound versus silence, nor the intensity or frequency of tones in any mammal”. More recent studies have shown that, although cortically lesioned animals are able to relearn these tasks, they do so more slowly than during their initial training. Their ultimate performance, both in detection and discrimination tasks, remains below normal, with discrimination especially affected [4., 5., 6. and 7.]. Rodents [8.] seem to be less affected by the lesions than are carnivores [9. and 10.] and they are, in turn, less affected than primates [11.]. But there is considerable disagreement, and the variability produced by different behavioural tasks does not help the formulation of general principles. This raises the question of whether the results of Talwar *et al.* [1.] are specific to the rat or to the particular tasks they employed.
In common with several previous studies, Talwar *et al.* [1.] used a positively reinforced operant procedure to measure frequency discrimination. In contrast with some previous work, however, they did not attempt to determine detection or discrimination thresholds, and the detection task involved a qualitative, observer-based assessment of responses to three relatively high level tones (50, 70 and 90 dB SPL). But the tasks they used enabled hearing to be assessed quickly, within about 15 minutes — most conventional assessments of animal hearing take many trials over several hours (or days!). In studies involving brain lesions, or other forms of pharmacological inactivation, it is also common to allow at least a few days recovery from the surgery. Talwar *et al.* [1.] injected the muscimol into pre-implanted wells and were therefore able to assess the behavioural effects of this almost immediately (Box 1).

Persistent deficits in auditory localization have been reported following lesions of A1 [12., 13., 14. and 15.] — at least over the variable testing periods used in these studies — so it is not necessarily the case that sensory or perceptual impairments recover over time. Nevertheless, the study by Talwar *et al.* [1.] raises the possibility that any lesion-induced deficits in sound frequency or intensity discrimination may be transient in nature. Consequently, by the time conventional lesion studies have made their measures, the animals may well be on the way to functional recovery in these tasks.

The methods used by Talwar *et al.* [1.] do not allow a conclu-sion of 'normal' behaviour in the treated rats, as the baseline behaviour levels were undoubtedly supra-threshold. However, the main results of the study focus on the profound deficits exhibited by the muscimol-treated animals. Would those deficits have been observed with another method of behavioural assessment? In the human vision literature there has been great interest in the phenomenon of 'blind sight' — upon lesion of the primary visual cortex, patients lose all visual perception in the region of the space that corresponds to the site of the lesion, but they are still capable of responding to stimuli in this region when asked to execute forced-choice motor commands related to those stimuli [16. and 17.]. A similar phenomenon, 'deaf hearing', has recently been reported following bilateral temporal lobe lesions [18.]. Studies using forced-choice methods [7. and 19.] were among those that showed no effect of auditory cortical lesions on tone detection or discrimination in animals. Unfortunately, those studies also had a long delay between lesion and first post-operative test, so it is possible that the functional recovery discussed above could have occurred. Clearly, it would be of great interest to know whether animals treated with muscimol via a well implanted over A1, but tested using a forced-choice method, also show (transient) deficits. It would also be interesting to know whether longer-term muscimol inactivation leads to restored function, as the lesion studies seem to suggest.

Assuming that long-term inactivation of the auditory cortex leads to a transient loss of auditory function, what neural mechanisms might account for the reacquisition of hearing? A rapid reorganization of cortical function that occurs without further training is often attributed to unmasking of cortical connections [20. and 21.]. But it is difficult to imagine that unmasking, or any other cortical mechanism, can account for the retention of auditory function following massive lesions involving over half the cerebral cortex [19.]. An alternative is that sub-cortical processing, possibly responding dynamically to a release from cortical influence, may mediate the restored function. In any case, the study by Talwar *et al.* [1.] achieves what all quality science should strive for — intriguing results and the generation of exciting and testable hypotheses.

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