OPTICAL IMAGING OF INTRINSIC SIGNALS IN THE AUDITORY CORTEX

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Introduction

The central representation (topographic mapping) of the sensory epithelium is a fundamental feature of visual, somatosensory and auditory systems. The auditory system is organized with orderly projections from the cochlea resulting in cochleotopic maps at the brainstem, midbrain, thalamus and cortex. Such projections were originally elucidated using neuro-anatomical techniques (1) and subsequently confirmed by detailed electrophysiological mapping studies using sound stimuli (2). At the level of auditory cortex, tonotopic maps derived from electrophysiological studies have been revealed in numerous mammalian species for example: cat (3), ferret (4), chinchilla (5) and human subjects (6). In addition, a number of other methods (such as voltage sensitive dyes [7], scalp recorded evoked potentials [8] and neuromagnetic measurements [9]) have been refined for studying cortical patterns of neural activity and have revealed the tonotopic axis in auditory cortex. Refinements in the spatial resolution of medical imaging techniques (e.g. positron emission tomography [PET] and functional magnetic resonance imaging [fMRI]) have allowed for tonotopic mapping in human and non human subjects.

Another method for exploring patterns of central auditory activity is based on the detection of small changes to the optical properties of active neural tissue; optical imaging of intrinsic signals. The earliest investigations of such signals started decades ago (10) but only recently, with modern imaging technology, has useful application been possible (11, 12, 13).

There are a number of processes which accompany the activation of neurons and which can alter the optical properties of neural tissue, i.e. increasing the absorption of certain wavelengths of light. These processes include the transition of oxyhemoglobin to deoxyhemoglobin, local changes in blood volume and flow and physical changes to cell membranes and cell volume which accompany neural activation (11). These small (<1%) changes to the properties of neural tissue can be detected optically.

The vast majority of reports on the use of optical imaging of intrinsic signals are coming from studies in the visual cortex (e.g. 11, 14, 15). Somatosensory cortex has also been imaged successfully (16). Only a few preliminary reports have been made on the optical imaging of intrinsic signals from auditory cortex (18 - 22). We report here on acoustically evoked intrinsic signals arising from cortex.

Materials and Methods

Cortical imaging was carried out on anesthetized adult chinchillas (*Chinchilla laniger*) weighing between 500 - 700 g. All procedures were carried out within the standards of care of the local animal care committee and following guidelines of the Canadian Council on Animal Care.

The bone over the temporal lobe was removed (10 mm diameter) exposing the auditory cortex. The dura mater was kept intact. A well of Vaseline was build around the craniotomy, filled with silicon oil and covered with a glass cover-slip (see Fig. 1 for set up).

Intrinsic signals were recorded and analyzed using the IMAGER 2001 video acquisition system (Optical Imaging, Germantown, NY). Detailed descriptions of this system have been given elsewhere (11, 14 - 17). The essential operation of the system is that a reference (no stimulation) image is subtracted from video images of stimulated cortex and the resulting signal is amplified.

The cortical surface was illuminated with a monochromatic (green; 540 nm wavelength) light. Images of cortex were acquired with a CCD video camera. The camera was positioned and focused with its optical axis perpendicular to the cortical surface.

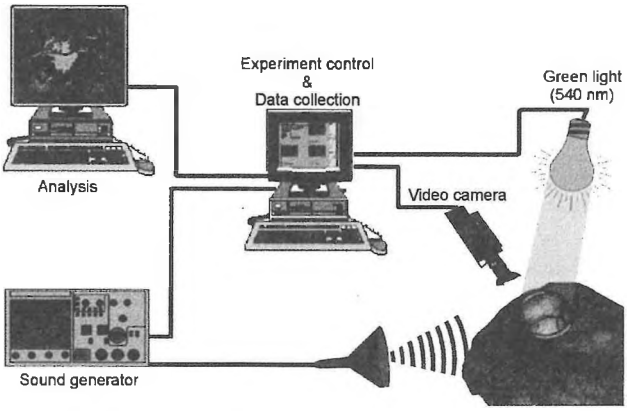

Fig. 1 Experimental setup for recording intrinsic signals

Images were collected for a 7.5 s period and stored as 15x500 ms data frames (repeated 8 - 16 times). Acoustic stimulation (10 ms rise/fall; 50 ms plateau; 10/s; frequencies 0.5, 1, 2, 4, 8, or 16 kHz and at a level between 0 - 80 dB SPL) was presented only during 4s of the data collection period (from 0.5 - 4.5 s; the initial 500 ms period provides a "no-stimulus" data frame). To allow for the relaxation of activity-dependent metabolic/vascular changes, each period of data collection was followed by a 12 s no-stimulus interval.

Results

Intrinsic signals in response to acoustic stimulation were found in a cortical area previously defined as primary auditory cortex in the chinchilla (5). The time course of the intrinsic signal is typically as shown in figure 2. The stimulus evoked intrinsic signal has an onset 0.5 - 1 s after stimulus onset and reaches a maximum after 3 - 4 s. After stimulation, the intrinsic signal decays at a slower rate. The graph quantitatively shows the changes in (540 nm) light absorption in three regions of the optically monitored area: an area (10 x 10 pixels) within the activated auditory cortex (A; solid line), and activity in two control areas: a non auditory cortical area (B; dashed line), and the bone on the edge of the craniotomy (C; dotted line).

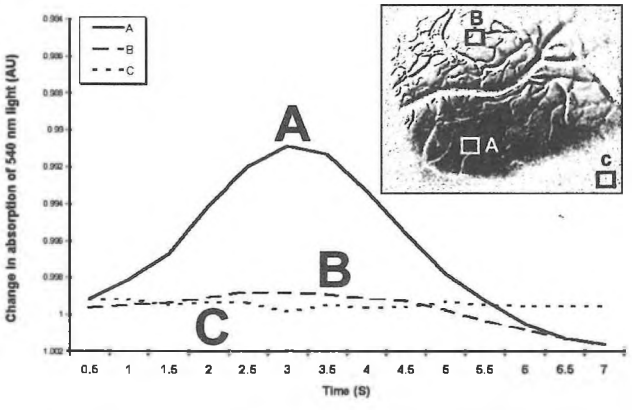

Fig. 2 Time course of intrinsic signal, see text for details

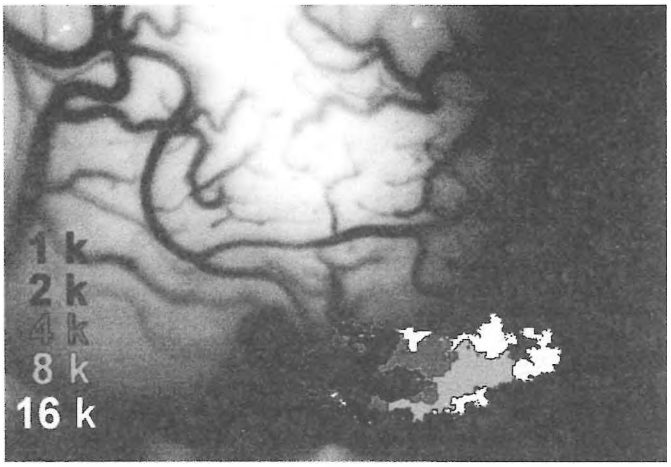

Fig. 3 A frequency (tonotopic) map of auditory cortex in the chinchilla derived by using optical imaging of intrinsic signals.

Tonotopic maps of auditory cortex were derived using pure tone stimuli (from 1 - 16 kHz; octave intervals) presented at 80 dB SPL (Fig 3). In randomly ordered experiments, areas of intrinsic signal activity were derived for each stimulus frequency. These areas are shown superimposed against the full grayscale reference image of the cortical surface. A clear shift in the region of activity in response to different stimulus frequency can be noted. The progression of low frequency anteriorly to high frequency posteriorly is fully consistent with the tonotopic axis in chinchilla AI cortex derived by single unit electrophysiological studies (5).

Discussion

In the present study we show that frequency specific suprathreshold stimuli produce intrinsic signal activity in different regions of auditory cortex such that tonotopic maps can be derived. Acoustically evoked intrinsic signals can be identified quite reliably using the time course (Fig. 2) of the signal as the main criterion. We have also found that in the absence of any acoustic stimulus one can often record apparently spontaneous waves of cortical activity.

We have found that the region of intrinsic signal origin coincides with the known position of primary auditory cortex in the chinchilla (5, 22). In addition, in one animal of the present study we have verified the position of AI cortex using surface recorded (ball electrode) auditory evoked cortical responses prior to optical imaging and found an accurate superimposition.

The potential of this method as a tool for exploring development and plasticity of auditory cortex lies in its relative non-invasiveness and speed. Under ideal conditions a tonotopic map can be derived in 30 minutes.

Acknowledgments

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