Spatial receptive fields of human auditory cortical neurons revealed by neuromagnetic recordings

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Previous work on the human auditory cortex has revealed areas specialized in spatial processing but how the neurons in these areas represent the location of a sound source remains unknown. We conducted magnetoencephalography (MEG) measurements to reveal the neural code of auditory space implemented by the human cortex. To this end, we used a stimulus-specific adaptation paradigm where the attenuating effect of a preceding adaptor on the brain responses to a subsequent probe sound is used as a measure of neuronal spatial selectivity. Utilizing both interaural time difference (ITD) cues and realistic spatial sounds we obtained results consistent with a population rate code of horizontal sound source location whereby spatial receptive fields are wide and laterally centered.

INTRODUCTION

Two alternative representation strategies of horizontal sound source location have been described in single unit recordings in animals and in theoretical studies (Fig. 2A). First, spatial location could be represented as a place code through narrow spatial receptive fields of auditory neurons (Joris *et al.*, 1998). Alternatively, two opponent populations of neurons could form a population rate code of auditory space, relying on wide spatial receptive fields spanning an entire hemifield (McAlpine *et al.* 2001, Stecker *et al.* 2005).

Single-unit studies on the mammalian auditory cortex have so far yielded results consistent with wide hemifield tuning (Brugge and Merzenich, 1973; Stecker *et al.*, 2005; Werner-Reiss and Groh, 2008). These studies have utilized two kinds of stimulation: free-field stimulation where all localization cues are present and stimuli where only the interaural level difference (ILD) is applied. However, when the interaural time difference (ITD) is used in isolation, support for both the narrow and the hemifield tuning has been found (Yin and Chan, 1990; McAlpine *et al.*, 2001).

Here, we describe MEG experiments performed on human subjects to map the auditory spatial tuning properties of cortex. To explore the potentially diverging coding strategies of different localization cues, we used realistic spatial sounds containing all localization cues as well as sounds where the ITD was the only spatial cue.
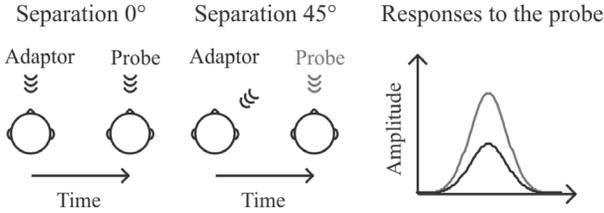
Fig. 1: The stimulus-specific adaptation paradigm. Sounds are presented as adaptor-probe pairs and brain responses to the probe are measured. The response amplitude depends on the location of the adaptor.

PARADIGM AND PREDICTIONS

Studying single-neuron tuning in the human brain is problematic as non-invasive measures collapse the activity of large populations into a compound signal. To overcome this problem, we used a stimulus-specific adaptation paradigm that capitalizes on the attenuation of the activity of individual neurons after the presentation of a preferred stimulus (Butler 1972; Ulanovsky *et al.*, 2003).

Sounds were presented in adaptor-probe pairs where the adaptor varied in sound source location but the probe remained constant. The attenuating effect of the adaptor on the non-invasively measured response to the probe could then be used as a measure of spatial selectivity (Fig. 1): The larger the overlap between the neuronal populations responding to the two sounds, the smaller the responses were expected to be in amplitude.

The two hypothesized coding strategies lead to distinct patterns of attenuation of the response to the probe (Fig. 2B). The narrow tuning of the place code predicts that strong attenuation occurs only when the adaptor and probe are identical (or very similar) in terms of sound source location. The hemifield tuning of the population rate code, in contrast, predicts that the attenuation is strong as long as the two sources are within the same hemifield.

EXPERIMENTAL PROCEDURE

The subjects took part in the experiments with informed consent and the approval of the Ethical Committee of Helsinki University Central Hospital. In Experiment 1 (11 subjects; Salminen *et al.*, 2010), ITDs were applied. For Experiment 2 (12 subjects; Salminen *et al.*, 2009), individual binaural recordings were conducted for each subject to create realistic spatial sound stimuli suitable for MEG measurements. The stimuli were 200-ms bursts of low-pass filtered (<3 kHz, Exp. 1) or wide-band noise (Exp. 2) and were presented in alternating probe-adaptor pairs with an inter-stimuli interval (ISI) of 1 s. The probe was always at -45° and the adaptors were presented at -90°, -45°, or 0° (Fig. 2B). MEG was acquired with a whole-head magnetometer (Vectorview 4D, Neuromag Oy, Finland). Data from the gradiometer pairs over the

right hemisphere yielding the largest amplitudes (i.e., vector-sum magnitudes) were selected for further analyses. The N1m response was identified as the amplitude peak in the 90-150 ms latency range. The N1m amplitudes were submitted to repeated-measures analyses of variance.
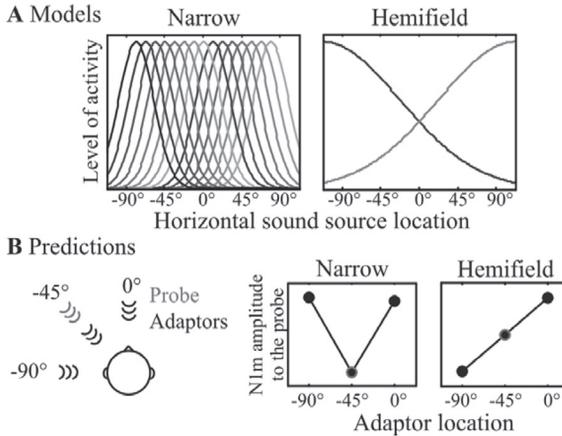
Fig. 2: **A**: Two alternative hypotheses on single-neuron spatial receptive fields were tested: narrow spatial receptive fields and hemifield tuning. **B**: The hypothetical receptive field properties lead to distinct predictions of MEG results (i.e., activity summed over all neurons).

RESULTS

For both spatial stimulus types, the response amplitudes measured to the probe depended on the location of the adaptor. When the ITD was used as the only localization cue, the attenuation was the stronger the further to the left the adaptor was (Fig. 2C; $F[2,20] = 5.9$, $p < 0.01$). For the realistic spatial sound, attenuation was strong whenever the adaptor was within the left hemifield and weaker when it was at the midline ($F[2,22] = 16.5$, $p < 0.001$).
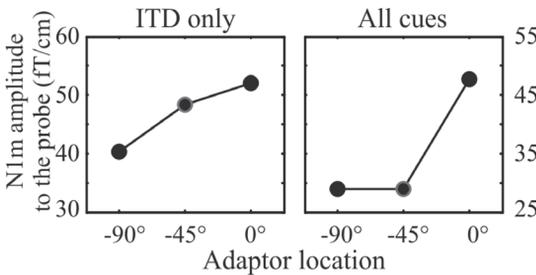
Fig. 3: MEG results obtained with two stimulus types: ITD only and realistic spatial sound with all localization cues. The results were more consistent with the hemifield tuning than with the narrow receptive fields.

DISCUSSION

Both the realistic spatial sound and the ITD sounds produced results consistent with the hemifield tuning to sound source location. The attenuation of the brain responses was determined by whether the adaptor was within the same hemifield as the probe or at the midline.

For the ITD stimulus, the leftmost adaptor (-90°) caused stronger attenuation than the adaptor being at the same location as the probe (-45°). For the realistic spatial sound, the attenuation was at the same level for these two adaptor locations. This could reflect the influence of the interaural level difference (ILD) which does not increase further when moving from -45° to -90°.

CONCLUSIONS

The spatial receptive field of neurons in the human auditory cortex are laterally centered, wide, and span an entire hemifield. Thus, two opponent populations, one tuned to the left and the other to the right hemifield, may form the representation of horizontal sound source location in human cortex.

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