Spatial representation of frequency-modulated tones in gerbil auditory cortex revealed by epidural electrocorticography

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Abstract – The present study investigated the topography of epidurally recorded middle latency components P1 and N1 evoked by spectrally dynamic stimuli (linearly frequency-modulated (FM) tones) with respect to the tonotopic structure of the right primary auditory cortex, field AI. Whereas the gross topography corresponded to the spectral content of the FM tones, specific tonotopic offsets were found between the potential distributions evoked by FM tones of different modulation direction (i.e. 'rising' vs. 'falling'). Potentials evoked by rising FM tones were located at tonotopic positions corresponding to higher frequencies compared with potentials evoked by falling FM tones. Data indicated that the magnitude of these offsets can be attributed to the local tonotopic resolution in AI and are not dependent on the modulation rate. © 2000 Elsevier Science Ltd. Published by Éditions scientifiques et médicales Elsevier SAS

frequency-modulation / electrocorticography / auditory cortex / non-stationary stimuli / topography

1. Introduction

Tonotopy, the topographic representation of sound frequency, is one of the most salient features of functional organization in auditory systems, including the auditory cortex [17, 25, 26, 30]. Tonotopic organization of a neuronal structure is usually probed by stimulation with pure tones of systematically varied frequency, i.e. stimuli of a stationary spectral composition. However, pure tones are practically never encountered in real environmental situations. In contrast, natural stimuli are characterized by a rich dynamic structure in spectro-temporal and amplitude features. It is generally not clear how the tonotopic organization of a neuronal structure pertains to the representational properties of neuronal activity evoked by such stimuli.

The present work therefore investigated the representation of a particular class of spectrally dynamic stimuli in the primary auditory cortex, namely linearly frequency-modulated (FM) tones, emphasizing the relation to its tonotopic organization. FM tones (also called 'glides' or 'sweeps') are an important element class of many natural stimuli including human speech and animal vocalization [5, 29, 33]. In behavioral learning experiments combined with auditory cortex lesions, we have previously shown that acquisition and retention of the ability to discriminate the modulation direction of linearly FM tones (i.e. 'rising' or 'falling') are dependent on the functional auditory cortex, whereas discrimination of pure tone frequencies is not [23]. Responses to FM tones are intensively studied at the single unit level [4, 6–10, 14–16, 24, 27] but little is known about the large scale organization of FM-tone-evoked activity. Based on our previous results on the large scale tonotopic organization of the primary auditory cortical field AI in the Mongolian gerbil (*Meriones unguiculatus*) obtained with epidural electrocorticography [22], the present work investigated in the same preparation the cortical representation of linearly frequency-modulated (FM) tones. Special attention is paid to stimuli of identical modulation range but differing modulation direction as such stimuli share a common long term spectrum while differing in their dynamic spectral composition.

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2. Materials and methods

Preparation, stimulation and recording procedures as well as data analysis have been reported

in detail elsewhere [22]. In short, four male adult Mongolian gerbils (*Meriones unguiculatus*) were implanted with epidural rectangular 3×6 microelectrode arrays (interelectrode distance: 600 µm) prefabricated from stainless steel wires (diameter: 100 µm). The gerbil was chosen because of its well investigated auditory cortex with respect to tonotopy [25, 26, 30] and spectral interactions [18–21, 27]. Arrays were centered over the primary auditory cortical field AI of the right auditory cortex. The right cortex was chosen because of the lateralized relevance for FM tone discrimination in the gerbil as was shown by lesion experiments [31]. FM tones covered one octave in five modulation ranges (cf. *table I*) in 250 ms and were free-field delivered at 70 dB SPL. Middle latency auditory evoked potentials (MAEPs) were monopolarly recorded from all electrodes against a mediofrontal reference using standard procedures, amplified (10 K), filtered (bandpass, 3 dB cutoff frequencies: 0.3 Hz, 100 Hz) and averaged ($n = 100$). Spatial patterns of activity distributions associated with the MAEP components P1, N1, P2 and N2 were determined by linear multiple regression analysis [1–3, 22] yielding a spatial pattern at the characteristic latency of each of the four components and a regression weight specifying the contribution of each pattern to the overall MAEP as a function of time. The assumption of a linear model is justified on the basis of its high degree of variance explanation ($\cong 95\%$) [1, 2, 22].

3. Results

We found FM-tone-evoked MAEPs to share the basic wave form and gross topography with pure-tone-evoked MAEPs notwithstanding subtler differences in their cortical topography as explained

below. In the present work, we have focused on the early MAEP components P1 and N1, as P2, N2 and later components are not tonotopically organized as was previously shown [22]. *Figure 1* shows typical results for the spatial patterns of activity distribution of the FM-tone-evoked early MAEP components P1 and N1 as obtained with linear multiple regression analysis (see Methods) with reference to the tonotopic structure of the primary field AI in the right auditory cortex.

3.1. Comparison of pure tone representation and FM tone representation

Generally, FM-tone-evoked spatial patterns at P1 latencies and P2 latencies were found to be located at cortical positions grossly corresponding to the tonotopic positions of frequencies traversed by the FM tone (*figure 1*). Typically, the spatial extent of FM-tone-evoked potentials exceeded the extent of pure-tone-evoked potentials both along the tonotopic axis (running in the rostro-caudal direction in *figure 1*) and (to a smaller degree) along the orthogonal (i.e. dorso-ventrally oriented) isofrequency dimension. The spatial extent of the FM-tone-evoked potentials however did not appear to be simply a union of the spatial extents of potentials evoked by pure tones of all frequencies between the start and stop frequencies of the FM tone. For example, in *figure 1*, the spatial extent of the P1 component evoked by an FM tone rising from 0.25 to 0.5 kHz showed only little overlap with the area corresponding to the 0.25 kHz pure-tone-evoked P1. Similarly, the P1 evoked by the FM tone falling from 0.5 to 0.25 kHz did not cover the rostral portion of the 0.5 kHz pure-tone-evoked isopotential contour. Analogous observations were made in other cases, although exceptions occurred in the mid-frequency range

Table I. Tonotopic offsets as a function of modulation rate for MAEP components P1 and N1.

MAEP component	mod. Range (kHz)	mod. Rate (kHz · s⁻¹)[1]	Mean	SEM
P1	0.25–0.5	1	0.55	0.03
	0.5–1.0	2	0.60	0.04
	1.0–2.0	4	0.60	0.04
	2.0–4.0	8	1.00	0.07
	6.0–12.0	24	0.48	0.06
N1	0.25–0.5	1	0.43	0.05
	0.5–1.0	2	0.65	0.03
	1.0–2.0	4	0.55	0.03
	2.0–4.0	8	0.85	0.06
	6.0–12.0	24	0.50	0.11

[1] These modulation rates all correspond to 4 octaves · s⁻¹.
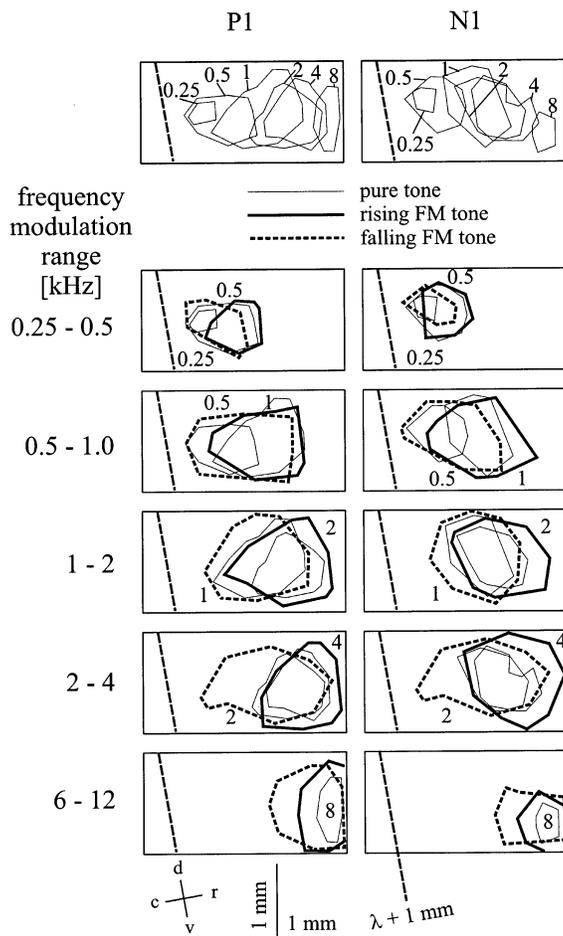
Figure 1. Topography of MAEP components P1 (left column) and N1 (right column) evoked by linear FM tones of rising and falling modulation direction in a representative case (gerbil # 1). Plotted are the 50% isopotential contours for P1 and N1 within a rectangle representing the spatial dimension of the 3 × 6 electrode array placed over field AI of the right auditory cortex. For orientation, the dashed lines mark the intersection of the parasagittal plane embedding the array surface with a frontal plane 1.0 mm rostral to landmark λ. The top two panels show the isopotential contours of the P1 and N1 component, respectively, of the MAEP evoked by pure tones from 0.25 to 8 kHz (inset numbers) defining the tonotopic frame of reference. The lower panels show the isopotential contours of the respective components evoked by FM tones traversing the frequency modulation range (indicated to the left of the panels) in a rising (full bold lines) or falling (dashed bold lines) manner. To facilitate reference to the tonotopic gradient the pure tone isopotential contours related to the frequencies matching the modulation range boundaries most closely are repeated in the lower panels; their frequencies are given by inset numbers. In the bottom panels (modulation 6–12 kHz) of the pure-tone-evoked potential only the 8 kHz case is shown due to lack of 6 and 12 kHz pure tone data.

(0.5–2 kHz) where the isopotential contours of FM-tone-evoked potentials tended to fully encircle those of pure-tone-evoked potentials.

3.2. Comparison of representations of rising and falling FM tones

The topographies of MAEP components P1 and N1 evoked by rising and falling FM tones, respectively, showed marked differences to each other. Potentials evoked by rising FM tones were generally located at more rostral positions (corresponding to higher frequency tonotopic positions) than potentials evoked by falling FM tones. Moreover, the rostral boundaries of isopotential contours associated with rising FM tones were typically located more rostrally than those associated with pure tones of the upper edge frequency of the FM tone. This was especially prominent for both P1 and N1 in the 1–2 kHz and the 2–4 kHz modulation experiments (*figure 1*). Conversely, the caudal boundaries of isopotential contours associated with falling FM tones were typically located more caudally than those associated with pure tones of the lower edge frequency of the FM tone (especially clear in the 2–4 kHz modulation experiment, *figure 1*). Thus, the experiments showed that the cortical localization of FM-tone-evoked potentials (for both P1 and N1) are shifted relative to each other along the tonotopic axis to tonotopic positions of higher and lower frequency representations for rising and falling FM tones, respectively. These 'tonotopic offsets' of the isopotential contours were manifest mainly at the stop frequency of the FM tone, i.e. at the higher edge frequency in rising FM tones and the lower edge frequency in falling FM tones (*figure 1*). Tonotopic offsets were quantified by the spatial distance between the amplitude maxima of the potentials evoked by rising and falling FM tones, respectively. This distance was defined positive when the amplitude maximum of the potential evoked by a rising FM tone was located rostrally to the maximum of the potential evoked by a falling FM tone, and negative in the reverse condition. This analysis was carried out separately for P1 and N1. We found in 100% of the cases (i.e. in each of the four animals and for each of the five frequency modulation ranges tested) P1 and N1 potential components evoked by rising FM tones to be located more rostrally (i.e. tonotopically shifted to higher frequency representations) than potentials evoked by falling FM tones (*table I*). There were no consistent differences between the tonotopic offsets in components P1 and N1 (Wilcoxon, $P > 0.27$).

3.3. Dependence of tonotopic offset on the rate of frequency modulation
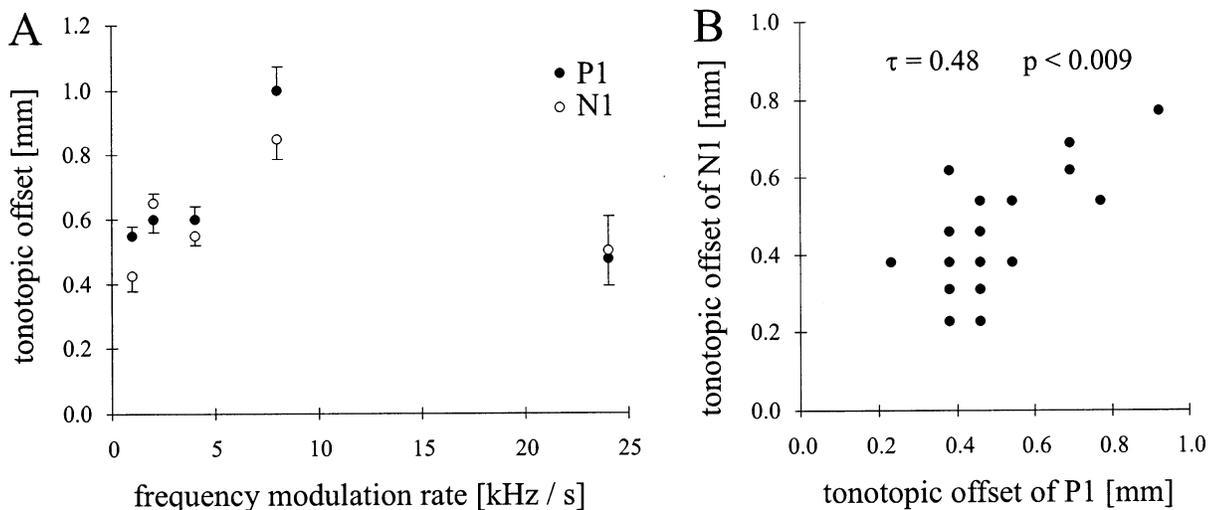
In *figure 2A*, tonotopic offsets were plotted against the rate of frequency modulation for P1 and N1. It can be seen that P1 and N1 tonotopic offsets covaried with each other and attained values between 0.3 and 0.5 mm for slower (1, 2 and 4 $kHz \cdot s^{-1}$) and fast (24 $kHz \cdot s^{-1}$) modulation rates and values between 0.6 and 0.8 mm for intermediate rates of frequency modulation (8 $kHz \cdot s^{-1}$). The covariation of the P1 and N1 tonotopic offsets was quantified by a rank correlation analysis yielding a correlation coefficient (Kendall's τ) of 0.476 ($P < 0.009$) (*figure 2B*).

4. Discussion and conclusion

Most studies on sensitivity to FM tone parameters in primary auditory cortex have focused on the single neuron level [4, 6–10, 14–16, 24, 27], although extrapolations to large scale spatial organization have been attempted from electrophysiological mapping studies [10, 16, 28]. In a number of instances on the single unit level sensitivity to FM tone parameters has been successfully related to receptive field properties. For example, sensitivity to the direction of frequency modulation (i.e. 'rising' or 'falling') could be at-tributed to the position of the modulation range relative to the unit's receptive field [24, 27] as well as to spectro-temporal summation of excitatory and inhibitory contributions [14, 15, 28]. Relatively few studies, however, have addressed the large scale spatial organization of cortical activity evoked by FM tones [11–13]. The present study, using an electrophysiological approach, compared the topography of the MAEP components P1 and N1 evoked by linearly frequency modulated (FM) tones with pure tones allowing the interpretation of the spatial representation of a spectrally transient stimulus with reference to the tonotopic structure of primary auditory cortex, field AI.

The gross correspondence between the tonotopic positions of FM-tone-evoked P1 and N1 and potentials evoked by pure tones of frequencies in the FM tone modulation range was expected on the basis of our previous demonstration of the tonotopic organization of these MAEP components in gerbil auditory cortex [22]. However, although the long term spectra of rising and falling FM tones are identical, the P1 and N1 components evoked by rising and falling FM tones were shifted relative to each other along the tonotopic axis into tonotopic representations of higher and lower frequencies, respectively. This tonotopic offset was manifest in the location of the amplitude maximum (*figure 2, table I*) as well as the borders of corresponding

Figure 2. (**A**) Tonotopic offsets plotted against modulation rate. Plotted are the means and standard errors separately for the MAEP components P1 and N1. (**B**) Rank correlation analysis revealing the monotonic relationship between P1 tonotopic offset and P2 tonotopic offset.

isopotential contours, most prominently at the border corresponding to the stop frequency of the FM tone (*figure 1*). Similar tonotopic offsets have been described in a 2DG study of the auditory cortex analogue of the chick [11]. This phenomenon can be explained by the finding that single neurons are usually stronger activated by an FM tone, when the modulation is towards its characteristic frequency than in the case when the modulation is away from it [24]. The latter asymmetry is suggested to result from the temporal summation of responses triggered by the input of successive frequency components traversed by the FM tone. Since responses to pure tones are triggered with increasing latency as the pure tone frequency is shifted away from the neurons characteristic frequency, an FM tone sweeping towards to characteristic frequency will recruit responses with higher synchrony than an FM tone sweeping away from the characteristic frequency [8, 9, 24]. Thus, a rising and a falling FM tone will activate tonotopically distinct regions, because both stimuli will stronger activate neurons tuned to the respective stop frequencies. In the aforementioned study on the chick auditory cortex analogue [11], this tonotopic offset was found to increase with increasing modulation rate. This is in contrast to the present data in which the tonotopic offset was maximal at intermediate modulation rates (*figure 2A*). Given that large scale activity patterns are however likely to depend also on the local spectral resolution of the tonotopic map, dependence of the tonotopic offset on the modulation rate might be accounted for this way. Specifically, the maximal tonotopic offsets found for the intermediate modulation rates with stimuli sweeping over the modulation range from 2–4 kHz could simply reflect the maximal tonotopic resolution of AI in gerbil auditory cortex in this frequency range [26, 30]. This interpretation is in correspondence with the finding that the frequency within an FM tone that triggers the response does not vary with the modulation rate [9, 27].

In conclusion, we have shown how for the simple case of linearly frequency-modulated tones, the spatial cortical representation of a spectrally non-stationary stimulus as assessed with epidural electrocorticography can be related to the tonotopic structure in the primary auditory cortex. This finding will assist the interpretation of FM-tone-evoked cortical spatial activity patterns found in animals trained to discriminate the modulation direction of FM tones [23, 32].

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