MEMRI reveals plasticity changes in the auditory midbrains of mice after two-tone rearing

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Introduction and Significance

Experience dependent developmental plasticity has been described in several regions of the mammalian cortex; however only a few studies have investigated developmental plasticity in subcortical regions and brainstem. In the cortex, environment cues influence nervous system development, but it remains to be determined whether the primary source of the plasticity is cortical or subcortical. Using Manganese-enhanced MRI (MEMRI), we observed a clear example of developmental plasticity in the mouse auditory midbrain induced by two-tone rearing. The defined rearing tones (simultaneous 16+40 kHz) specifically altered the functional architecture in the midbrain encoding the responses to 16 and 40 kHz pure tones, demonstrating large scale reorganization of the tonotopic map in the auditory midbrain. These results provide critical new insights on the origin of developmental plasticity in the auditory system.

Methods

Neonatal mice were exposed to a synchronous two-tone stimulus (16+40 kHz, 77dB SPL, peak value) from postnatal 9 days (P9) through P17. During this rearing period, mice were exposed to sound stimulation for 22-23 h per day, and were in the normal cage room environment for the remaining 1-2 h per day to accommodate veterinary health monitoring. At P17, the two-tone reared mice were kept in a quiet environment for 24 h. $MnCl_2$ was injected at P18 and the animals were exposed to a specific tone stimulus (16, 32 or 40 kHz) for 24 h. MRI images were acquired at P19 immediately after the sound exposure. Control studies were performed on mice maintained under normal rearing conditions. MRI was performed on a SMIS console interfaced to a 7T horizontal bore magnet with 250-mT/m actively shielded gradients (Magnex), using a custom mouse head holder and volume coil. MR images were acquired using a 3D T1-weighted gradient echo sequence (TE/TR=4/50ms, flip angle=65°) with 100-μm isotropic spatial resolution and an acquisition time of 2 hours [1]. 3D images of the IC were co-registered and analyzed with Amira (Mercury Computer Systems). Voxel-based statistical parametric mapping was performed to compare the sound stimulated and quiet control image groups (n>8) using Matlab [2].

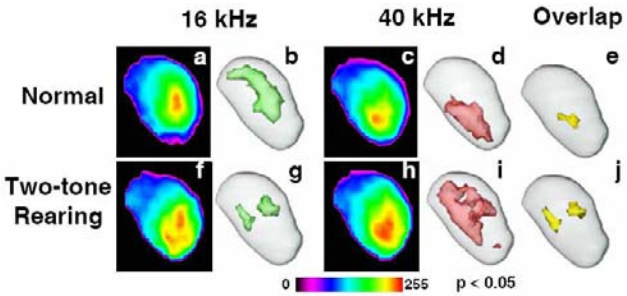

Fig. 1. Two-tone (16+40 kHz) rearing induced changes in both the 16 and 40 kHz IC activity patterns. 2D coronal slices from averaged images and 3D p-maps of normal (a-d) and two-tone reared mice (f-i) demonstrated marked differences in both the 16 (green) and 40 kHz (red) activity patterns ($p < 0.05$; $n \geq 8$ in each group). The activity maps showed significant overlap (yellow) between 16 and 40 kHz patterns in two-tone reared mice (j) compared to normal controls (e).

Results

Two-tone (16+40 kHz) reared mice were tested with either 16 kHz or 40 kHz stimulation. MEMRI activity patterns were analyzed statistically by comparing images from stimulated animals to images from mice kept in a quiet environment. After both 16 and 40 kHz stimulation, the 3D p-maps showed overlapping activity regions corresponding to the 16 and 40 kHz frequency coding areas in the two-tone reared mice (Fig 1) . These altered activity patterns in the two-tone reared mice suggest that the rearing environment induced aberrant functional connections. Although the 16 and 40 kHz spatial patterns were clearly altered in the two-tone reared mice, it was not clear whether the effect was limited to the rearing tones, or whether the entire IC tonotopic organization had been altered. Therefore, we examined the activity pattern of a third frequency (32 kHz) in control and two-tone reared mice. The 32 kHz coding area in the mice reared in the normal condition was located between the 16 kHz and 40 kHz coding regions, in excellent agreement with the tonotopic maps previously established by electrophysiology [3]. A similar pattern of 32 kHz evoked activity was observed in the two-tone reared mice (Fig 2), indicating that the effect of two-tone rearing was specific to afferent activity recruited by 16 kHz and 40 kHz.

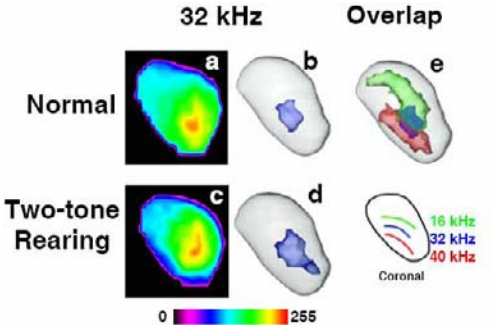

Fig. 2. The changes in IC activity patterns were specific to the tones used in rearing. Similar activity patterns (blue) were observed following 32-kHz stimulation of normal (a, b; $p < 0.05$, $n \geq 8$) and two-tone (16+40 kHz) reared mice (c,d; $p < 0.05$, $n \geq 8$). Superimposed p-maps show the relative positions of the 16 (green), 32 (blue) and 40 kHz (red) activity patterns in normal mice (e). The corresponding electrophysiological tonotopic map is also shown for reference (inset).

Conclusions

Our results indicate that synchronous activation of afferents responding to 16 or 40 kHz leads to an alteration of functional connectivity in the auditory midbrain. The functional alteration could represent the local or upstream auditory nuclei afferent reorganization. It also remains possible that a substantial descending projection from auditory cortex could contribute to the observed plasticity changes. Therefore, future studies will examine the functional patterns of auditory cortex ablated mice under two-tone rearing conditions. (This research was supported by NIH grants NS038461 and DC006892)

References

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