Functional mapping of the auditory pathway in adult mice by manganese-enhanced MRI

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Introduction

Manganese-enhanced MRI (see ref. [1] for review) is now increasingly used for a functional characterization of animal brain. Recent work attempted to map sound-evoked activity in the inferior colliculus of developing mice [2]. The purpose of this study was to examine whether such evoked activity can be observed in other structures of the auditory system by exposing adult mice to intense stimuli for a long period of time. The primary aim was to develop an optimal method for the detection of activation-dependent enhancements of the auditory pathway in mice, with particular emphasis on its morphological delineation.

Methods

Animals. Eight female mice (NMRI, 8-12 weeks old, 28-38 g) received manganese chloride (0.5 mmol/kg body weight) dissolved in distilled water via subcutaneous injection. Animals were returned to a chamber with unlimited access to food and water. For a period of 48 hours before MRI, four mice were kept in a quiet chamber, while four animals were exposed to continuous acoustic stimuli. Ultrasonic stimuli involved 25-50 kHz noise bursts with an acoustic pressure of 110 dB.

MRI. MRI measurements were carried out at 2.35 T using a MRBR 4.7/400 mm magnet (Magnex Scientific, Abingdon, UK). Radiofrequency excitation and signal reception were accomplished with use of a Helmholtz coil (inner diameter 100 mm) and an elliptical surface coil (inner diameter 20 × 14 mm), respectively. 3D gradient-echo MRI data sets (rf-spoiled 3D FLASH, TR/TE 17/7.6 ms, flip angle 25°, measuring time 99 min) were acquired at 117 µm isotropic resolution.

Results

As reported previously [1-3], systemic administration of manganese led to a generalized unspecific signal enhancement in the brain of all mice. While there were no differences between the two groups in the forebrain, the brainstem revealed marked differential enhancements. Figure 1 compares parasagittal images of the brain of (left) a mouse kept in a quiet chamber and (right) a mouse exposed to the acoustic stimuli. Specific enhancements are seen in the ventral part of the inferior colliculus (white arrow). Figure 2 compares coronal sections through (top) the inferior colliculus and (bottom) the cochlear nucleus of mice (left) kept in a quiet chamber and (right) exposed to the stimuli. The images show a different degree of enhancement not only in the inferior colliculus (white arrow) and the cochlear nucleus (white arrowhead), but also in the lateral lemniscus (black arrow) and the superior olivary complex (black arrowhead). The Table summarizes the signal-to-noise ratio (SNR) in selected structures confirming the qualitative findings. While there is no difference between groups in non-auditory cerebral cortex, the SNR is higher by 11-20% in lower auditory centers. Nevertheless, higher auditory centers such as the medial geniculate body or the auditory cortex cannot be distinguished from surrounding tissue.

Discussion

The present results clearly indicate stimulus-dependent signal enhancements due to the local accumulation of manganese in structures known as auditory pathway. In agreement with previous work in developing mice [2], the present results demonstrate enhancement in the inferior colliculus of adult animals. In addition, however, the data reveal for the first time a stimulus-dependent enhancement in the lateral lemniscus and the superior olivary complex, which are the relaying centers of the auditory pathway between the cochlear nucleus and the inferior colliculus. This new finding may be ascribed to the used long and intense activation of the neural circuit formed by these four lower auditory centers. The fact that higher auditory centers could not yet be distinguished may be explained by insufficient delivery of manganese to these structures. In conclusion, functional mapping of the auditory pathway by manganese-enhanced MRI is expected to open new ways in assessing genetically modified mice as models of human brain disorders. Further improvement of the method is currently in progress.

References

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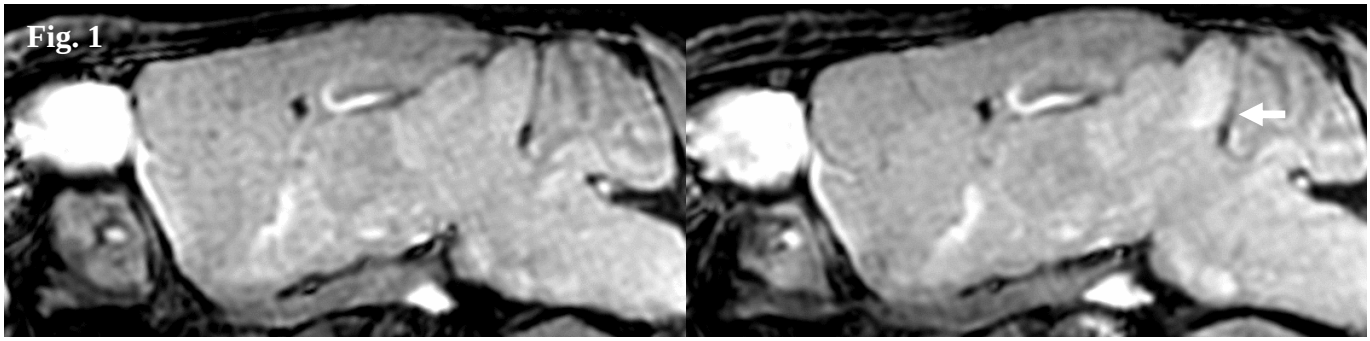

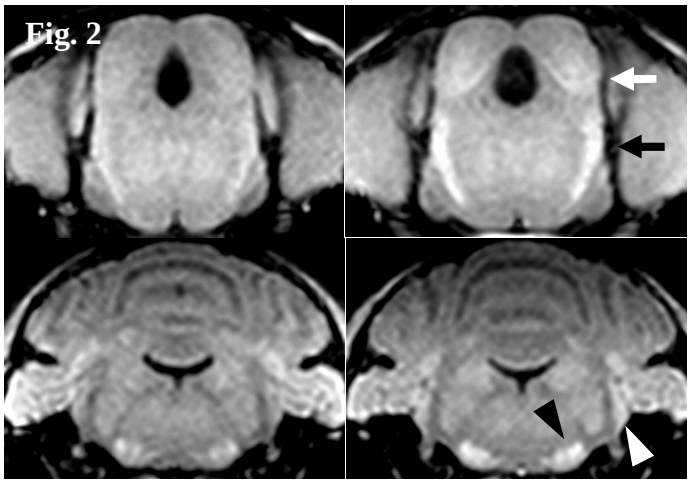

Region		SNR	
		Quiet (n=4)	Stimuli (n=4)
Cerebral Cortex (Non-Auditory)	L	31.5 ± 2.5	31.3 ± 2.7
	R	31.6 ± 2.9	30.9 ± 4.0
Inferior Colliculus	L	32.9 ± 2.1	38.1 ± 1.8**
	R	33.1 ± 1.8	38.8 ± 2.5*
Lateral Lemniscus	L	34.8 ± 1.4	40.9 ± 1.1**
	R	34.7 ± 2.0	41.4 ± 1.4**
Superior Olivary Complex	L	36.6 ± 0.6	42.0 ± 2.2**
	R	37.4 ± 2.3	41.8 ± 2.6*
Cochlear Nucleus	L	34.2 ± 1.1	41.0 ± 0.5**
	R	34.6 ± 1.3	40.5 ± 1.2**

Values are given as mean ± SD; *p<0.05, **p<0.01 (unpaired *t* test vs. Quiet)