Odorant stimulation manganese enhanced MRI for olfactory pathway after intranasal manganese administration

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Introduction

Olfaction plays important roles in reproduction and learning in many mammalian species [1]. To understand how odorants are processed and encoded in the central nervous system is critical to determine the neural basis of these behaviors. Although there were some olfactory MEMRI studies [2,3], these MEMRI studies focused on the manganese delivery at olfactory bulb. Therefore, the aim of this study is to investigate the manganese delivery response to different olfactory stimulants at brain structures along olfactory pathway following intranasal administration from the nasal passage to whole olfactory system.

Material and Methods

Thirty Sprague-Dawley rats (8-10 weeks old and 150-200 g weight) were anesthetized with 5 % isoflurane. After the pre-contrast image was obtained, 0.02 ml of 1 M $MnCl_2$ solution was injected into each nostril using a 24-gauge medicut syringe inserted at a depth of 19mm into the nostril. The contrast was infused through the side holes of medicut, and the tip of medicut was obliterated by silicone in order to avoid the accumulation of the contrast into the mucosal tissue of nasal cavity. After manganese injection, the animals were placed back into the anesthesia chamber under 2 % isoflurane for an additional 5 min, allowing the manganese to be absorbed. The animals were then returned to their home cage and the post-contrast image was acquired approximately 6hour, 24hour, 48hour after $MnCl_2$ exposure. After 24hour, 0.02 ml acetone (N=6), linalool (N=6), formic acid (N=6) and normal saline (N=6) were infused into nasal cavities of rats. T1-weighted images were obtained on a 1.5-T MR scanner (Signa, GE, Milwaukee, WI) using a custom-made rat brain volume coil and a 2D-spin Echo pulse sequence. Sequence parameters were as follows: field of view of 5 × 5 cm, matrix size of 192 × 192, 0.9 mm slice thickness, no gap, repetition time (TR) = 500 ms, echo time (TE) = 15 ms, number of acquisitions (NEX) = 10 and scan time = 16 min 18 sec. The protocols were approved by the Institutional Animal Care and Use Committee of University.

Results and Discussion

The MEMRI exhibited increase in signal in the olfactory bulb along with enhancement throughout the olfactory tract, 48hour after intranasal manganese administration by injection into the nasal cavity of normal rats (Fig. 1). After odorant stimulation, MEMRI showed different patterns of Mn^{2+} uptake according to different odorants (Fig. 2 shows representative subtraction images between pre-(24 hr) and post-odorant (48 hr) stimulation at each brain region). That is, olfactory bulb (R1) showed increased signal intensities after intranasal stimulation of linalool and formic acid ($P<0.05$). However, olfactory bulb (R1) showed decreased signal intensities after intranasal stimulation of saline and acetone ($P<0.05$). Brain regions of olfactory tubercle (R2), amygdala (R3), pons (R4) and cerebellum (R5) showed increased signal intensities after intranasal stimulation of saline, acetone, linalool and formic acid ($P<0.05$). Among odorants, formic acid showed strongest signal enhancements at all brain regions (Fig. 3). Furthermore, our MEMRI data revealed signal enhancement in regions outside the conventional olfactory pathway such as pituitary gland, which has no direct connection with olfactory bulb. These findings therefore suggest that MEMRI showed two routes of entry into the central nervous system: (1) one associated with the olfactory system connecting the nasal passages with olfactory bulb and (2) the peripheral trigeminal system connecting the nasal passage with brain stem and spinal cord. In sum, the current MEMRI study revealed different Mn^{2+} uptake on olfactory pathway according to different odorants, which suggest olfactory activity-dependent manganese signal enhancement.

References

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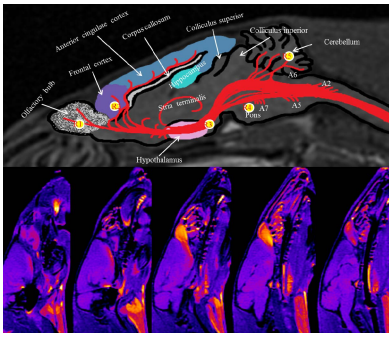

Fig. 1 Dynamic Mn^{2+} uptake measured in each region of interest (R1: Olfactory bulb; R2: olfactory tubercle; R3: Amygdala; R4: Pons; R5: Cerebellum)

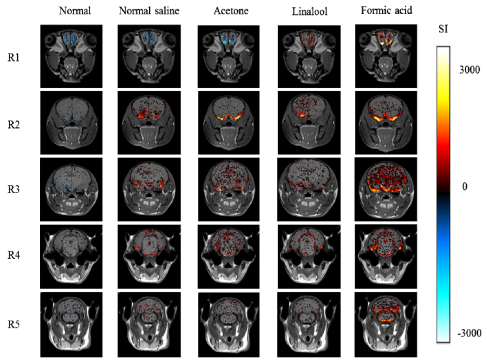

Fig. 2 MEMRI of before and after odorants stimulations subtraction imaging

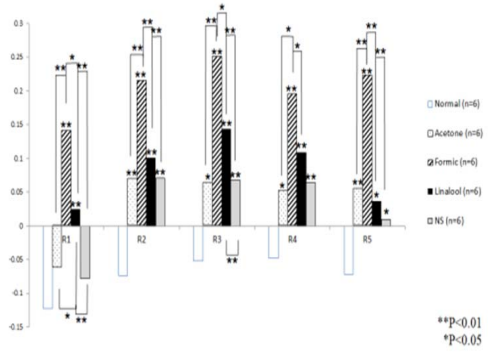

Fig. 3 Comparison of change of signal intensities on olfactory pathways according to different odorant stimulations