Topographical Projection from Olfactory Epithelium to Olfactory Bulb in Rat Studied by Dynamic Manganese-Enhanced Magnetic Resonance Imaging

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Introduction: In olfaction, information of odor is first passed to olfactory sensory neurons located in the olfactory epithelium (OE) and then sent to glomeruli in the glomerular layer (GL) of olfactory bulb (OB) for further processing. Previous studies have shown that there is, to some degree, a regional topographical organization in the relationship between the OE and the OB in mammals[1-4]. It is suggested that the topographical relation between the OE and the GL follows the principle of "zone to zone" projection[3]. In this study, dynamic manganese-enhanced magnetic resonance imaging (MEMRI)[5] was used to monitor accumulation of Mn^{2+} in the olfactory system of urethane anesthetized rat after intra-naris application of $MnCl_2$ solution and to trace anterogradely the topographical connections between the OE and the GL.

Materials and Methods: 28 Female Wistar rats (160-200g) were anesthetized by i.p. injection of urethane (100 mg/ml saline solution; 1.5 ml/100g body weight). 2 μl of 400 mM $MnCl_2$ saline solution was pipetted into the right naris of each rat using a precision microliter pipette. The rat was then transferred to an animal bed and placed in the magnet for imaging. The rat breathed room air voluntarily inside the magnet. MRI was performed on a Bruker Biospec 4.7 T/30 cm spectrometer equipped with a 20-cm diameter gradient insert. A 12-cm diameter Helmholtz volume coil was used for excitation and a 2.5-cm diameter surface coil for reception. Images of the OE were acquired using a T_1-weighted spin echo sequence with FOV 1.5×1.5 cm^2, matrix size 128×128, slice thickness 1 mm, TR 400 ms, TE 15 ms, and 4 averages. Images of the OB were acquired using an inversion recovery spin echo sequence with FOV 1.5×1.5 cm^2, matrix size 128×128, slice thickness 0.8 mm, TR 5 s, TE 20 ms, TI 450 ms, and 4 averages. The OE images acquired about 1hr after Mn^{2+} application and the OB images acquired 2.5-3.5hrs after Mn^{2+} application were used for tracing the topographical connections between the OE and the GL. The OE and the GL on the images were segmented into sub-regions according to their anatomy (Fig. 1a and b), among which those with Mn^{2+} deposition were identified for each rat by visual inspection and signal intensity comparison. The sub-regions had average signal intensities 50% higher (for OE) or lower (for GL) than those of the corresponding sub-regions at the contralateral side were considered to have Mn^{2+} deposition. A binary code was then applied to mask the sub-regions, with the sub-regions without Mn^{2+} deposition represented by "0" and those with Mn^{2+} deposition represented by "1". Cross correlation was carried out between the masks of the OE and the GL across all rats to examine the topographical connections among the sub-regions of the OE and the GL.

Results: Figure 1 shows images of the OE and the OB from two typical rats demonstrating the topographical connections between the OE and the GL. When Mn^{2+} was deposited on ectoturbinate 1 and dorsal recess (areas with hyperintensity, Fig. 1a), Mn^{2+} was observed anterogradely on the dorsal and the dorsolateral parts of the GL (areas with hypointensity, Fig. 1b). The data also show that endoturbinates II/II' (Fig. 1a and d) have topographical projection to the medial and the ventromedial parts of the GL (Fig. 1b and e), endoturbinates III/IV together with ectoturbinate 3 project topographically to the ventral and the ventrolateral parts of the GL, and ectoturbinates 2/2' correspond to the lateral part of the GL. No diffusion or transportation of Mn^{2+} among the different sub-regions was found in the OE. However, the sub-regions in the GL with Mn^{2+} deposition expanded with time to the adjacent regions (Fig. 1b and c) and to the opposite side of the GL (Fig. 1e and f).

Discussion and Conclusion: There are two major findings in this study. First, the results confirm the previous observation that olfactory sensory neurons locating in a specific sub-region in the OE terminate in topographically corresponding sub-regions in the OB. Secondly, it was found that, the area with Mn^{2+} deposition in the GL increases with time (Fig. 1c and f). There are two possible explanations for this observation: 1) interneuronal connections might exist among the glomeruli located in different sub-regions of the GL; 2) within a specific sub-region of the OE, there may exist sub-populations of olfactory sensory neurons, different in either the number of neurons or the transportation rate for Mn^{2+}, projecting to different parts of the GL, causing time-dependent Mn^{2+} deposition in the sub-regions of the GL. Nevertheless, the results from this study demonstrate that dynamic high spatial resolution MEMRI can be used to study anterogradely topographical projection in the olfactory system in rat.

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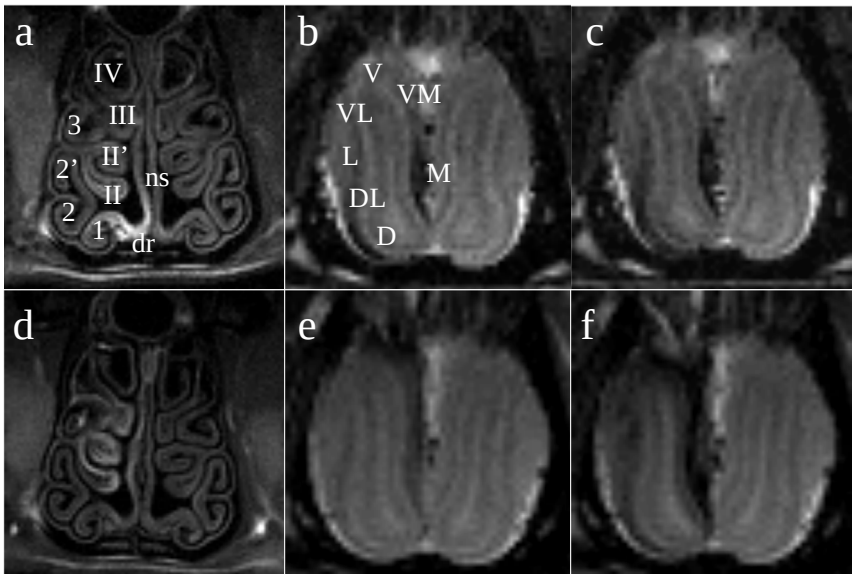

Figure 1. (a) T_1-weighted image of a coronal slice of the OE 1hr after intra-naris application of Mn^{2+}. Ectoturbinates are labeled by 1, 2, 2' and 3, and endoturbinates are labeled by II, II', III and IV. ns: nasal septum; dr: dorsal recess. In this rat, Mn^{2+} was applied to ectoturbinates 1, endoturbinates II and dr. (b and c) inversion recovery images of a coronal slice of the OB in the same rat as that in (a) 2.5 and 5.5hrs after intra-naris application of Mn^{2+}, respectively. The GL of the OB is segmented into different sub-regions: D: dorsal region, DL: dorsolateral region, L: lateral region, VL: ventrolateral region, V: ventral region, VM: ventromedial region and M: medial region. (d-f) Similar data from another rat in which Mn^{2+} was applied to endoturbinates II, II' and III (d).