Activity mappings in olfactory bulb of newborn rabbits elicited by odor stimulation using quantitative manganese enhanced MRI

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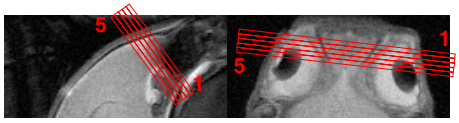
INTRODUCTION/PURPOSE

The Mammary Pheromone (2-methylbut-2-enal, MP) is a pheromonal signal emitted by lactating female rabbits. MP triggers the orocephalic movements allowing the blind new-born to find their mother's nipples (1). This model constitutes an original model to explore the neural pathways recruited by a single molecule in a developing mammal. Odor signals enter the brain through the olfactory bulb where glomeruli contain the first central olfactory relay. Using 2-deoxyglucose (2-DG) radioautography, it has been shown that MP induces a specific pattern of activity, with a higher labelling in the posterior part of the olfactory bulb (2). Here, we present a preliminary work using the non destructive functional manganese-enhanced MRI (MEMRI) for the localization of olfactory responses. After its injection in the nostrils, the Mn^{2+} tracer is selectively taken up by the activated neurons, thus allowing MEMRI to reveal the olfactory pathways selectively involved. When compared to the blood oxygenation level dependent (BOLD) image contrast, MEMRI has the advantages of allowing odor stimulation outside the magnet, on conscious freely moving animals. This avoids the depressing effects of anesthetics on neural activity, probably responsible for the low BOLD responses (3) and its bad reproducibility (4). In addition, due to the latency of Mn^{2+} distribution, activity maps provided by MEMRI have a higher spatial resolution than the one derived from fast T_2* sequences used for BOLD.

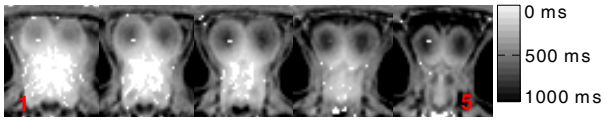
MATERIALS AND METHODS

Awake 3 day-old (P3) rabbits received two consecutive administrations of 0.1 ml $MnCl_2$ (0.1 M) to each nostril using a Burgener nebulizer. They were subsequently exposed 8 times to MP at 10^{-6} or 10^{-2} g/ml, concentrations known to be inactive and active respectively, on their sucking-related behavior (5). Animals were sacrificed 4h later, a delay long enough for the tracer to be transported along the whole olfactory bulb (see 6 and results). Imaging was performed on a Biospec 4.7 T MRI horizontal system (Bruker) with a 12-cm diameter fast gradient hardware. Five contiguous slices (0.6 mm thick) were analyzed per olfactory bulb with an in-plane voxel size of 0.3 x 0.3 mm^2. For improving the MEMRI sensitivity as proposed in (7), T1 mapping was performed by acquiring multiple images at 19 different inversion times (TI) with an inversion-recovery prepared RARE.

RESULTS/DISCUSSION



Parasagittal (left) and horizontal (right) views of the anterior brain showing the position of the slab (red lines) through the rabbit olfactory bulb between the eyes. The five 0.6 mm thick coronal slices imaged using the IR-RARE sequence yield a high-resolution T1-map covering the whole extent of the olfactory bulb.



The five coronal sections through the olfactory bulb (1: rostral most, 5: caudal most), illustrate a high Mn^{2+} labelling in the nasal cavity (central part of the lower half of the figures). In the olfactory bulb (symmetrical circular structures in the upper part of the figures) the decrease of this signal unmasks the ventral medial labelling of the peripheral layer (best seen in 4-5). This labelling was markedly heavier than the one observed under control conditions (Mn^{2+} without olfactory stimulus, data not shown), suggesting that at this location the olfactory stimulus MP might induce specific patterns of activation.

CONCLUSIONS & PERSPECTIVES

Our preliminary results strongly suggest that MEMRI labels heterogeneous areas within the olfactory bulb, in agreement with previous results of 2-DG radioautography. The exploration of other brain regions raises the problem of the anatomical identification of activated areas. In this purpose, we are currently generating average, high-resolution three-dimensional anatomical models from histological sections of P3 rabbit brain. The combination of MEMRI and 3D modeling should ultimately provide a means of exploring the brain regions involved in the MP processing.

REFERENCES

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