

Blood volume functional MRI of the mouse whole brain

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Target Audience: neuroscientists

PURPOSE: Olfaction is one of the most important sensory systems, particularly for rodents [1]. When stimulated by an odor, the brain first receives signals in the olfactory bulb from the olfactory epithelium, which then sends the signal up to specific brain areas in the olfactory pathway. While several fMRI studies of the olfactory bulb in rodents have been performed [2-4], similar fMRI studies of olfaction in the rodent brain have not been reported to our knowledge. The aim of this study was to investigate fMRI responses to odor stimulation from the olfactory bulb to the brain in mice.

METHODS: *Animal models:* Mice (n=4, C57BL/6J, male, 15-19 weeks old), were anesthetized initially with ketamine (100 mg/kg) and xylazine (2.5 mg/kg) by intraperitoneal injection and were administered with supplemental ketamine (100 mg/kg/hr) and xylazine (~0.3 mg/kg as needed). The rectal temperature, respiration rate, heart rate and arterial oxygen saturation were monitored. Magnetic iron oxide nanoparticles (MION; 20 mg/kg) were injected into the tail vein. Iso-amyl-acetate diluted to 5% in mineral oil was used as the odor delivered to the mice by nose cone. The odor stimulation consisted of 3 min OFF, 2 min ON, 3 min OFF, 2 min ON, 3 min OFF, 2 min ON, 3 min OFF. This whole stimulation protocol was repeated 3 times in each animal.

MION MRI: The MRI scans were performed on an 11.7T/16 cm Bruker system with a 1 cm diameter surface coil. A 3D FLASH sequence was used: TE=3.6 ms; TR=10 ms (15 s/image); FOV=12.8*12.8*12 mm; matrix=64*64*30; resolution=0.2*0.2*0.4 mm. For reference, high-resolution anatomical images were also acquired using 3D FLASH: TE=4.7 ms; TR=14 ms; NA=4; FOV=12.8*12.8*12 mm; and matrix=128*128*30.

Data analysis: For each animal, images were realigned in SPM8 and the images from the 3 repeats were averaged. FSL was used to register all the images and do group analysis to calculate the z-score maps.

RESULTS: Figure 1 shows the group activation map due to the odor stimulation of the brain from 4 mice. The strongest activation was located in the olfactory bulb. The odor also activated the olfactory tubercle, anterior olfactory nucleus, tenia tecta, dorsal endopiriform nucleus, piriform cortex, areas of the amygdala, insular cortex and entorhinal cortex.

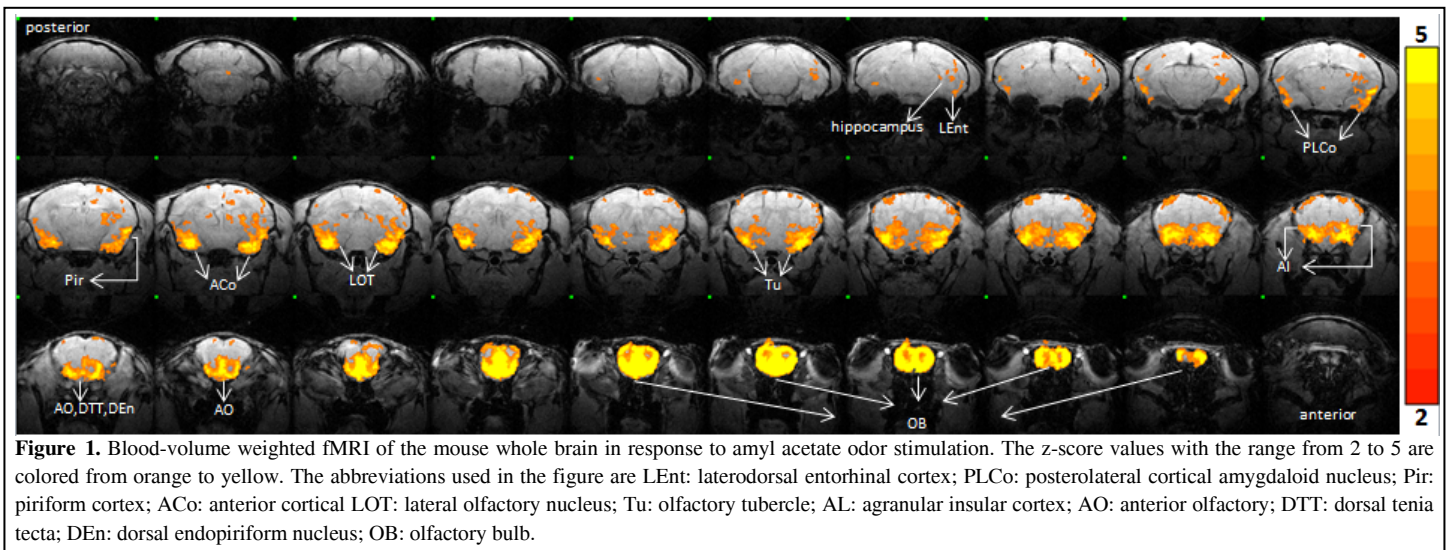


Figure 1. Blood-volume weighted fMRI of the mouse whole brain in response to amyl acetate odor stimulation. The z-score values with the range from 2 to 5 are colored from orange to yellow. The abbreviations used in the figure are LEnt: laterodorsal entorhinal cortex; PLCo: posterolateral cortical amygdaloid nucleus; Pir: piriform cortex; ACo: anterior cortical LOT: lateral olfactory nucleus; Tu: olfactory tubercle; AL: agranular insular cortex; AO: anterior olfactory; DTT: dorsal tenia tecta; DEN: dorsal endopiriform nucleus; OB: olfactory bulb.

DISCUSSION and CONCLUSION: Blood-volume weighted fMRI robustly detected activations in the mouse olfactory bulb and the olfactory network in the brain. Previous non-MRI studies have implicated multiple brain regions to be involved in olfaction, including the olfactory tubercle, anterior olfactory nucleus, tenia tecta, dorsal endopiriform nucleus, piriform cortex, areas of the amygdala, insular cortex and entorhinal cortex [5]. We detected activations in essentially all of these olfactory brain circuits. Although previous work has reported the involvement of the hippocampus and thalamus in olfaction, we did not detect activations in these regions. We only detected sparse activations in entorhinal cortex (only anteriorly, involved with odorant memory) and orbitofrontal cortex (involved with odorant pleasure). These minor discrepancies might be due to the anesthetized status of the animals or unfamiliarity with the odor. Activations of most of these structures are consistent with data reported in human olfactory fMRI [6], suggesting conservation of homologous functions. In conclusion, this approach offers a non-invasive means to probe of the entire olfactory circuitry from the bulb to the brain in healthy animals and animal models of neurological disorders such as Parkinson's and Alzheimer's diseases.

Reference: 1) Wall et al. *J Mammal* 2003; 487:496. 2) Xu et al. *PNAS* 2003; 100:13735. 3) Xu et al. *J Comp Neuro* 2005; 489:491. 4) Poplawsky and Kim. *ISMRM* 2013; #0296. 5) Baum et al, *Horm Behav* 2009; 579-588. 6) Barresi et al. *J Neurophysio* 2012; 16:24.