

# High-throughput manganese enhanced magnetic resonance imaging in newborn rabbits for olfactory response to nitric oxide stimulus

Y. Yang<sup>1</sup>, A. Drobyshesky<sup>1</sup>, X. Ji<sup>1</sup>, L. Yu<sup>1</sup>, and S. Tan<sup>1</sup>

<sup>1</sup>Department of Pediatrics, NorthShore University HealthSystem and University of Chicago, Evanston, IL, United States

## Introduction

Different nitric oxide (NO) level in olfactory nerves may affect the activity of neurons.  $Mn^{2+}$  will move along appropriate neuronal pathways in an anterograde direction. The function of olfactory neurons can be monitored in vivo by manganese enhanced magnetic resonance imaging (MEMRI). To observe manganese enhanced process, MRI experiments need several hours or even several days. Therefore, multi animal imaging strategy is needed to provide an efficient way to perform experiments and acquire data with enough statistical power. This abstract presents a high-throughput MEMRI method to determine whether nitric oxide can affect olfactory neuronal function in newborn rabbits.

## Method

1000  $\mu M$  Spermine NONOate (NO donor) or JI5 600 (NO inhibitor) were administered into both nostrils of newborn rabbits on day 1 (P1). Control groups consisted of newborn rabbits receiving expired Spermine NONOate or saline. After 1 hour incubation of these chemicals, the kits were administered 25  $\mu L$  0.1M  $MnCl_2$  in each nostril and received odor stimulation (amyl acetate) for half an hour. Animals were sedated and placed in a low-cost small animal shelf (Figure 1) which can hold 4x2 small animals. Imaging was performed at 4.7T Bruker magnet. T1-weighted images (Figure 2) were acquired with RARE sequence (TR/TE 800/10 ms, NEX 2, 1 mm slice, 0.2 mm in plane resolution) every 40 sec. Time course of image intensity of the glomerular layer of olfactory bulbs normalized by the signal of vitreous chamber, were obtained. Time of the contrast arrival and slope of enhancement curve were calculated.

## Results

The dose response experiments showed that 1000  $\mu M$  Spermine NONOate was significantly different from expired Spermine NONOate. The time of  $Mn^{2+}$  arrival in NONOate group (98 $\pm$ 12 minutes, N = 23) was significantly less ( $P < 0.05$ ) than that in expired NONOate group (100 $\pm$ 2 minutes, N = 21). The slope of the enhancement curve in JI5 600 group (184 $\pm$ 42 a.u., N=24) was significantly greater ( $P < 0.05$ ) than that in saline group (100 a.u., N = 27).

## Conclusion

Nitric oxide stimulates the neuronal transduction of the olfactory neurons in newborn rabbit kits. It increases the speed of calcium transport as well as the intensity of the neuronal transport. The high-throughput MEMRI method may allow us to investigate molecular mechanisms of in vivo neuronal function.



Figure 1. Multi-animal imaging shelf for Bruker RF coil

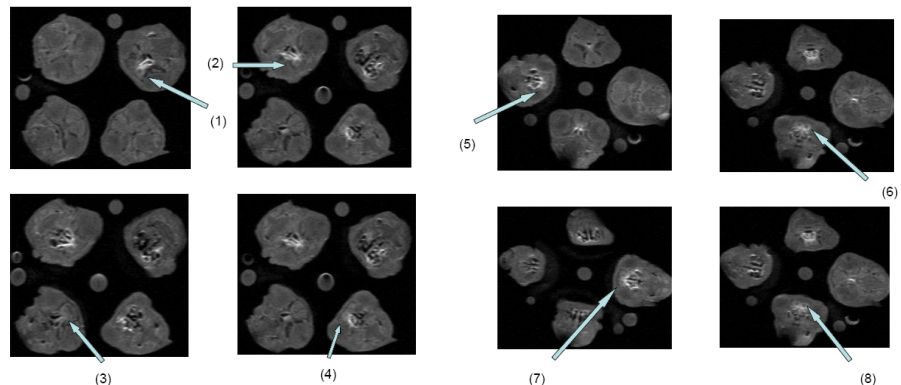


Figure 2. T1-weighted images showing Manganese enhancement in 8 animals' olfactory bulbs