High resolution 3D functional images of the human olfactory bulb using passband SSFP at 3T

T. B. Parrish[1], Y. Chen[1], W. Li[2], J. Howard[2], and J. A. Gottfried[2]

[1]Radiology and Biomedical Engineering, Northwestern University, Chicago, IL, United States, [2]Neurology, Northwestern University, Chicago, IL, United States

Introduction: fMRI studies of the human olfactory system have successfully highlighted many of the critical brain areas involved in the detection and perception of smells. However, functional imaging of the human olfactory bulb has not yet been achieved, due to its slender size and the high susceptibility artifact resulting from adjacent air sinuses. These technical difficulties present formidable limitations in trying to delineate human olfactory function, because the olfactory bulb is the very first recipient of odor inputs from olfactory receptors in the nose. Moreover, animal studies strongly suggest that considerable signal processing and odor feature extraction already occurs at this first synaptic point in the olfactory hierarchy. The present inability to measure fMRI signal from the human olfactory bulb is equivalent to the problem that would arise if (in the visual system) fMRI data from primary visual cortex (V1) could not be obtained. Therefore, developing new imaging techniques to overcome this challenge has become imperative. Methods to date have been developed for EPI fMRI techniques to limit the artifact from the sinuses with limited temporal and spatial resolution [1-4].

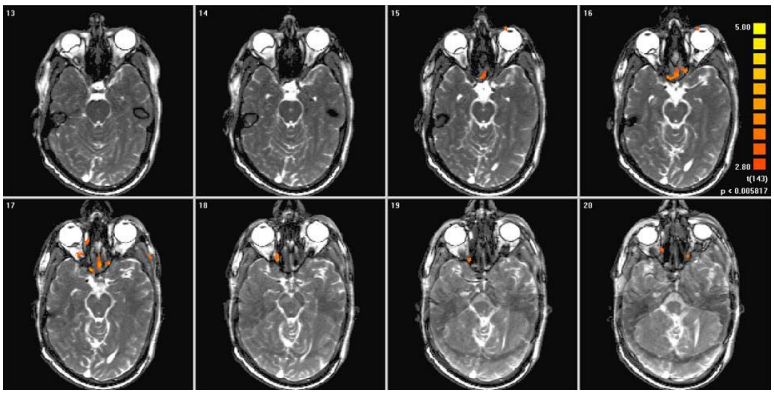
The advent of better imaging hardware and higher magnetic fields has fueled the quest for higher resolution fMRI data. As a result, researchers have turned to Steady State Free Precession (SSFP) sequences [**5-8**]. This family of imaging sequences maintains the transverse magnetization which provides a strong T2 contrast. More importantly, they do not require the susceptibility weighting, which makes them ideal for use around regions with poor magnetic homogeneity. Initially, the transition band (tbSSFP) was used to detect the differences in frequency shift in the oxy- and deoxygenated blood [**5-6**]. In this work, we explore the use of a novel passband SSFP (pbSSFP) sequence [**7-8**] to provide high resolution, artifact-free functional images of the human olfactory bulb at 3T.

Methods: A 29 year old, right handed male subject was imaged using a 3T scanner (Siemens TIM Trio, Erlangen, Germany) and a twelve-channel receive-only head coil. A 3D FISP sequence was used with imaging parameters of TR_{pe}=4ms, TE=2ms, flip angle= 30 degrees, pixel bandwidth=685 Hz, and parallel imaging acceleration using GRAPPA with a factor of 2 and 24 reference lines. The inplane resolution was 1.1 mm with a slice thickness of 2mm. The acquisition matrix was 137x192x20 covering a field of view of 165x220x40mm. The TR_{3D} for the entire 3D volume was 4 seconds. A total of 151 volumes were acquired with scan duration of 10 minutes and 4 seconds. An olfactory stimulus delivery system [**9**] was synchronized with the start of the scan.

The paradigm consisted of a simple odor detection task using 3 different pleasant odorants. A total of 24 trials was used, including 12 "odor" trials (4 trials per each odorant, randomized) and 12 "odorless" (air only) trials. Each trial began with 12s of fixation, then 7s of odor delivery, and ended with 5 s of fixation during which time the subject responded by pushbutton indicating whether odor was present or absent. During odor delivery, the subject was given two 2s visual cues to sniff, with an intervening 3s of rest between sniffs. The long sniff period was used because of the 4s TR_{3D} employed in the pbSSFP sequence.

The pbSSFP data were imported into Brain Voyager V1.9 for analysis using a general linear model of the sniff events (7s duration) convolved with a canonical hemodynamic response function. The data were first 3D motion corrected, spatially smoothed using a 4mm FWHM Gaussian kernel (twice the largest voxel dimension) and then temporally smoothed with an 8s (twice the TR_{3D}) FWHM Gaussian kernel. The odor trials were directly compared to the air-only trials (see figure).

In order to characterize the sensitivity to activation induced blood flow changes, a 25 year old female subject was studied with an auditory cued motor task at 8 Hz. This experiment used identical parameters as outlined above except the TR_{3D} for the volume was reduced to 3 seconds by limiting the number of slices to 16. The paradigm used 30 seconds of rest followed by 2 cycles of 45s active/45s rest. The data were analyzed in a similar fashion as described above with the model of the active periods. An analysis of the signal change of the significantly active voxels in the motor cortex was conducted to determine the magnitude of the signal change.



Results: The image to the right is the functional map resulting from the direct comparison of odor versus odor-free air, overlaid on the raw pbSSFP image. The raw image quality in the sinus and around the olfactory bulb is exceptional and without artifact. The statistical threshold was set at t>2.8 for this single subject with 12 long trials per condition. Robust functional signal in the bulb is clearly evident bilaterally.

The signal change measured in the motor task demonstrated a 1.0 - 1.3% change in the primary motor cortex. This is similar to a standard EPI BOLD acquisition with TE=20ms and a 3.4x3.4x3mm voxel at 3T.

Discussion: The images presented here represent exquisite functional and anatomical detail of the human olfactory bulb. The images of the olfactory bulb are the first reported functional data of this small structure that resides within the sinus space, which has severely limited its ability to be imaged with conventional BOLD imaging methods. The method described here demonstrates the benefits of using non-EPI based functional imaging alternatives such as passband SSFP sequences in regions of high susceptibility. The high SNR combined with the high spatial resolution results in a new class of highly sensitive functional imaging methods. Such techniques will have far-reaching implications for understanding the functional organization of the human olfactory system.

References:

1. Constable RT, Spencer DD. MRM 42(1) 110, 1999.**2**. Glover GH MRM 42(2) 290, 1999. **3**. Weiskopf N, Hutton C, Josephs O, Deichmann R. Neuroimage 33(2) 493, 2006. **4**. Deichmann R, Gottfried JA, Hutton C, Turner R. Neuroimage 19 (2) 430, 2003.**5**. Miller KL, Smith SM, Jezzard P, Pauly JM. MRM 55(1) 161, 2006. **6**. Zhong K, Leupold J, Hennig J, Speck O. MRM 57(1) 67, 2007.**7**. Miller KL, Smith SM, Jezzard P, Wiggins GC, Wiggins CJ. Neuroimage 37(4) 1227, 2007. **8**. Bowen C, Menon R, Gati J. ISMRM 119, 2005. **9**. Li W, Luxenberg E, Parrish T, Gottfried JA. Neuron 52 1097, 2006.