Hemodynamic Response in Human Central Olfactory System

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Introduction

The hemodynamic response function (HRF) to odors is expected to be significantly different from those to visual and other sensory stimuli because of a rapid habituation. Characterization of this phenomenon unique to olfaction is important for olfactory fMRI paradigm design and data analysis. We performed an olfactory fMRI study with a paradigm designed to specifically investigate this question.

Methods

Human Subjects Eight normal subjects (28.6 years ± 6.6, 5m, 3f) screened with the University of Pennsylvania Smell Identification Test with an average score of 36.1 ± 3.0.

fMRI protocol The subjects were trained to breathe following audio instructions at a rate of 10 cycles / min (3 s: "Breathe In" and 3 s: "Breathe Out") to synchronize the respiration with odorant delivery and image acquisition to ensure accurate onset and duration of stimulation. The respiration was closely monitored. During fMRI, lavender odor (Quest International) was delivered to the subject´s nostrils through Teflon tubing at a strength of 0.32% and flow rate of 8 L / min. After a 60 s baseline, the stimulation lasted for 21 s and then repeated for 3 times which interleaved with 45 s recovery periods. A series of T_2*-weighted EPI images (TR / TE / FA = 1500 ms / 35 ms / 90°, FOV = 230 × 230 mm^2, matrix = 80 × 80, 25 axial slices, 4 mm slice thickness with no gap, SENSE factor = 2) were acquired on a Philips 3.0 T system during execution of the olfactory paradigm.

Data processing and analysis The fMRI data were processed with SPM2 [1]. The hemodynamic response was modeled with different length of stimulations (15 s, 18 s, and 21 s). Group analyses were performed utilizing student t-tests and ANOVA.

Results

Statistical analysis with standard hemodynamic model (21 s) detected activations in the primary olfactory cortex and other secondary brain structures (i.e. hippocampus, amygdala, insula, orbitofrontal cortex) (uncorrected, $p < .001$, extended threshold = 4). However, when the hemodynamic response was modeled with shortened length of stimulations (15 s and 18 s), stronger activation maps were yielded at the same confidence level. This is quantitatively demonstrated by the activation volume in the primary olfactory cortex (POC) and the entire brain shown in Table 1 and 2 and Figure 1. These analyses clearly indicate a rapid decay of hemodynamic signal responding to the odor after onset of stimulation.

Discussion and Conclusion

The fMRI activation map is generated by fitting the MRI temporal signal to a hemodynamic response function (HRF) convolved with the stimulation paradigm used. The current HRF for statistic parametric mapping is modeled based on the experimental data obtained from other stimulations (auditory, motor and visual) than olfaction. Although widely successful, the current HRF model does not take habituation effect into consideration. Habituation effect is notoriously strong in olfaction. Therefore, the current HRF model is less than optimal for olfactory fMRI data analysis. These data demonstrated that in olfactory fMRI, a) a habituation factor should be incorporated in the HRF model, and b) olfactory stimulation paradigm should be built based on brief stimulations with precise synchronizations with data acquisition and respiration. The study of the HRF in olfactory system leads to a better understanding of the dynamic behavior of fMRI signal under other stimulations (e.g., pain) involving habituation.

HRF Model	Total Activation Volume (voxel)
15 s	451
18 s	228
21 s	127

Table 1. The total activation (uncorrected, $p < .001$, extended threshold = 4).

HRF Model	Activation Volume (voxel)	T value
15 s	70	9.26
18 s	57	8.67
21 s	37	7.70

Table 2. The average activation at the left POC (-26, 6, -20 mm) (uncorrected, $p < .001$).

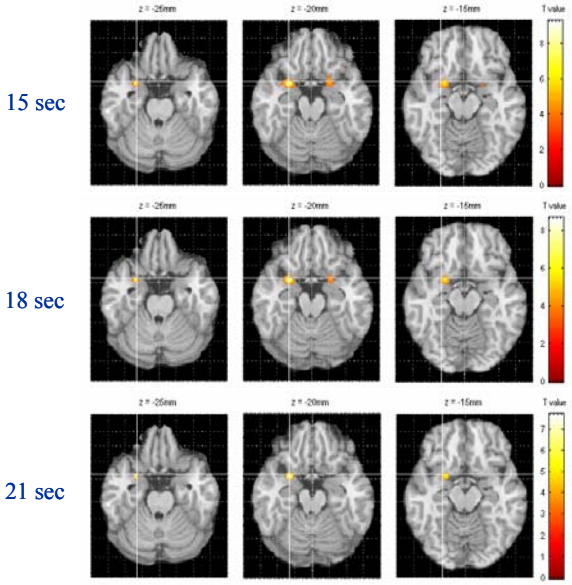

Figure 1. With the HRF modeled using shorter duration than actual stimulation paradigm (15 s or 18 s), activation at the POC was increased under the same statistical threshold.

References

1. Friston KJ, et al. Human Brain Mapp 1: 153-171; 1994.