

# Dynamic Behavior of BOLD Signal and the Associated Olfactory Neural Networks: A Functional Magnetic Resonance Imaging Study

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## Introduction:

Investigating olfaction in terms of underlying networks has received considerable attention in recent years [1, 2]. Using fMRI data, we present a novel approach capable of revealing the olfactory network that subserve a four-strength fMRI paradigm. The method entails combining unified Structural Equation Modeling (uSEM) and group independent component analysis (ICA) to investigate the network connectivity associated with olfactory processing [3, 4].

**Materials and Methods:** Ten healthy subjects (mean age  $24.7 \pm 1.8$  years) completed two identical runs of a four-strength olfactory fMRI paradigm at 3.0T [5]. Using an olfactometer (with a flow rate of 8 L/min and synchronized with image acquisition and visual cues), three rounds of each odorant concentration (6s per stimulation) were presented to the subject's nostrils sequentially, interleaved with a 30s period of odorless air between each stimulation.

The olfactory function of all participants was assessed using The University of Pennsylvania Smell Identification Test (UPSIT) [6], and found to be within the normal range ( $37.1 \pm 1.5$ ). The study had the Penn State College of Medicine IRB approval, and all volunteers provided written informed consent prior to taking part in the study.

MR images of the entire brain were acquired using EPI (with an acceleration factor of 2) on a Siemens Trio 3.0 T system with the following parameters: TR / TE / FA= 2000 ms / 30 ms / 90°; FOV =  $220 \times 220$  mm<sup>2</sup>; acquisition matrix=  $80 \times 80$ , 30 slices; slice thickness= 4 mm, and the number of repetitions= 234.

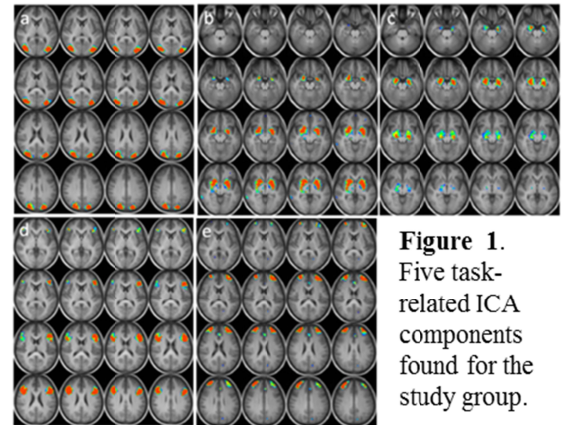
The group ICA analysis was based on FastICA algorithm and performed according to the methods outlined elsewhere [3]. We used individual IC time courses as input to estimate the uSEM(s) at the subject as well as the group level in order to examine the effective connectivity in the olfactory network for this task [4].

**Results and Discussion:** Fig. 1 shows five task-related group ICA maps that subserve the four-strength olfactory fMRI task. These networks encompass: (a) parietal-occipital junction; (b) Primary Olfactory Cortex (POC), amygdala, hippocampus, and insula; (c) striatum; (d) dorsolateral prefrontal cortex; and (e) PFC and cingulate. Presence of different cortical regions in the same ICA map implies that these regions are functionally connected. Fig. 2 shows the associated averaged time courses for the first three task-related networks shown in Fig. 1.

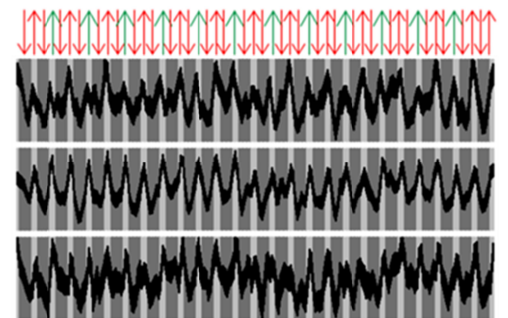
The optimal unified SEM, that best describes the underlying olfactory network across subjects, derived using the Group Iterative Multiple Model Estimation (GIMME) technique is shown in Fig. 3. Based on this model, we hypothesize that IC b and c subserve primary olfactory-related functions. A detailed analysis of the group model on individuals revealed that IC c and b appear to be highly correlated. Additionally, IC c influences b in two different ways: both in a lagged and contemporaneous manner. Similarly, IC b also had a lagged effect on c. IC b appears to have a central role: with contemporaneous effects on IC d and a.

**Conclusion:** Unlike previous GLM analysis of this task [5], ICA provided both the spatial and temporal information and laid the foundation for a comprehensive network analysis of the four-strength olfactory fMRI task. A significant finding of this study is the identification of two networks (IC maps) presumed to be related to primary olfactory processing [5, 6]. Additionally, it also identified other olfactory networks signifying the importance of secondary level olfactory processing for this fMRI task. Thus, the approach presented and described in this paper highlights the advantage of analyzing olfaction in terms of cognitive modules based on underlying network structure(s).

**References:** [1]. Gottfried J.A., *et al.*; Nat Rev Neurosci 2010; 11(9): 628-41. [2]. Yeshurun Y., *et al.* Annu Rev Psychol. 2010; 61:219-41. [3]. Karunanayaka et al., NeuroImage 2010; 51:472-87; [4]. Kathleen M. Gates., *et al.*, NeuroImage 2011; 54(2):1151-58; [5]. Weitekamp *et al.* at ISMRM 2010; [6]. Doty R., *et al.*; Physiol Behav 1984; 32: 489-502;

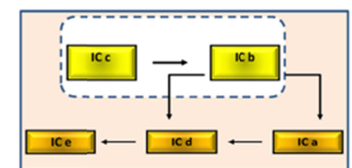


**Figure 1.** Five task-related ICA components found for the study group.



**Figure 2.** Associated IC time courses for the first three independent component maps shown in Figure 1.

↑ = "Rest" + fresh air, ↑ = "Smell?" + fresh air, ↑ = "Smell?" + odor.



**Figure 3.** The SEM for the olfactory network based on the 5 ICA maps, shown in Figure 2.