

A Novel Data Processing Method for Olfactory fMRI Examinations

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Introduction:

Unlike other sensory central nervous systems, the olfactory brain structures have only limited number of functional magnetic resonance imaging (fMRI) studies, partially due to imaging difficulty of the inferior frontal-temporal olfactory territory, and technical difficulties in reliable odorant delivery. Recently several MRI compatible olfactometers for accurate odorant delivery and monitor have been developed [1-4]. However, few of those devices would handle the irregularity of examinees' respiration and the problem of olfaction habituation [5, 6]. Because of the habituation effect inherited in the olfactory system, traditional boxcar design produced poor fMRI results. Thus in most of the recent olfactory fMRI studies, the research subjects were trained to follow either visual or audio instructions for respiration to synchronize the olfactory stimulation. Such method not only involves multiple central nervous systems besides olfaction, but also limits the application of olfactory fMRI in studying neurological and psychiatric diseases as patients are not able to follow the breathing instructions. Here we present an olfactory fMRI data processing method that can significantly improve the data processing quality when the patients' respiration pattern is not controlled and does not synchronize with olfactory stimulation paradigm.

Methods:

Theory We suppose that olfactory activation intensity is linearly correlated with the amount of odorant stimulant. When the air flow and odorant concentration are consistent, the amount of odorant stimulant received by the olfactory system is linearly correlated with the amount of air inhaled during the odorant delivery period. Thus we developed a program (written in IDL 7.1) that are able to calculate the amount of odorant received by the patient from the recorded respiration data during olfactory fMRI experiment. The program reads in respiration data and preprocessed by smoothing and low pass filtering and then finds all the inhalations. After validating the respiratory data by calculating the inhalation volume (integral under the inhalation curve), each inhalation volume will be normalized with the maximum inhalation volume during the entire experiment. A lower threshold of 30% is set-upped empirically to exclude the irregular shallow inspiration period from fMRI data processing.

Odor Stimulus paradigm The olfactory stimulation paradigm was executed by a highly integrated olfactometer, which can deliver up to six different odorants to the patients' nostrils accurately without any optical, acoustic, thermal, or tactile cues to the subject. Four concentrations of lavender odorant (Quest International Fragrance Co.) were prepared via dilutions in 1, 2-propanediol (Sigma) to generate weak (0.032%), medium (0.10%), strong (0.32%), and very strong (1.0%) concentrations that were previously determined from psychophysical study of a large cohort of healthy adults.

fMRI Study Protocol fMRI images of the entire brain were acquired from a healthy 39 year old male subject with normal olfaction function (The University of Pennsylvania Smell Identification Test (UPSIT) [7] score = 38) on a Siemens 3 T system. T₂*-weighted EPI sequence was used with an acceleration factor of 2, TR / TE / FA = 2000 ms / 30 ms / 90°, FOV = 220 × 220 mm², acquisition matrix = 80 × 80, 30 axial slices with a slice thickness = 4 mm, number of repetitions = 234. Three presentations of each odorant concentration (6s per stimulation) were presented to the subject's nostrils sequentially with a 30s period of odorless air between each stimulation. The odorant was delivered with a flow rate of 8 L / min. The odorant delivery and image acquisition was synchronized by TTL pulses from the scanner. The subject's respiration was monitored and recorded with the commercial software in the Siemens 3 T system. There were no cues for smell or instruction for respiration provided to the subject, and the subject was not asked to provide any response during the scan protocol.

Data Processing and Analysis The respiration data was processed with qMRI (<http://www.pennstatehershey.org/web/nmrlab/resources/software/qmri>). The fMRI data were normalized to the Montreal Neurological Institute brain template [8] and olfactory activation maps were processed with the original olfactory stimulation paradigm and the adjusted stimulation with respiration data by SPM5 [9].

Results: During the execution of olfactory paradigm, the subject's respiration was irregular from time to time (Figure 1) interfering the olfactory paradigm. Processed with the original stimulation paradigm, besides left orbitofrontal and bilateral insular cortex, there was no significant activation in the primary olfactory cortex (POC) from the statistic parametric map processed (Figure 2). After correction with the subject's respiration using our method, in addition to the much stronger activation in

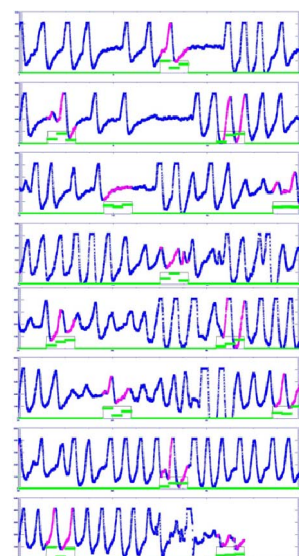


Figure 1: respiration (blue) and odorant stimulation paradigm (pink).

Discussion: Our data demonstrates that it is critical to consider the subject's respiratory modulation on the olfactory stimulation paradigm. The presented olfactory fMRI data processing method was simple and effective in generating robust olfactory fMRI results. In addition to the example of real time respiration data, subjective response data (not provided here) can also be convolved with odor delivery data for more improved fMRI data processing. This experimental set-up will be useful in the olfactory fMRI study of neuropsychiatric and neurologic patients that are not cooperative or be able to follow the breathing instructions.

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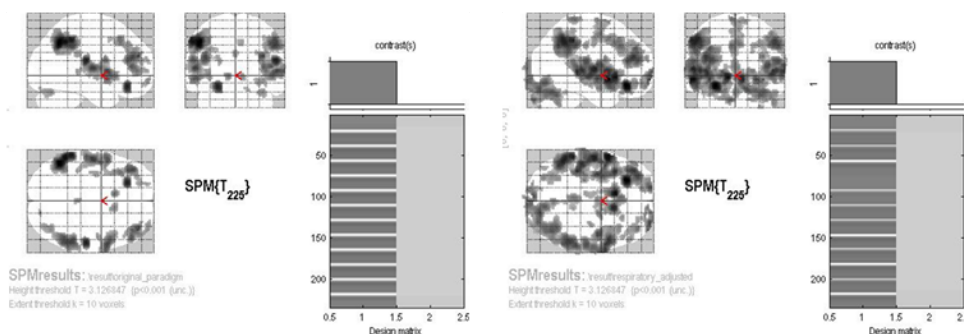


Figure 2: SPM results processed with original stimulation paradigm (left) and with adjusted stimulation by subjects respiration data (right) (uncorrected, p<0.001).