FUNCTIONAL MRI OF HUMAN OLFACTION; PRELIMINARY REPORT FOR TECHNIQUE, PARADIGM, AND BRAIN MAPPING

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INTRODUCTION

In spite of many trials with various techniques, there is still little quantitative information available about human olfaction. Initial trials to obtain this information used EEG, but results failed to define specific olfactory responses. More sophisticated EEG techniques had been introduced, but quantification of olfactory responses was not significantly improved. PET techniques in human improved sensory localization with detailed cerebral localization of visual, auditory, and cognitive function and memory. Studies using PET revealed decreased olfactory responsed in patients with Alzheimer disease patients and schizophrenia. Increased cerebral blood flow was demonstrated at pyriform cortex, amygdala, and orbitofrontal cortex in normal human during olfactory stimulation.

Functional MRI (fMRI) is a recently designed imaging method, which shows neuronal activation in response to various stimuli on sectional image. Initially, there was little reliable results due to insufficient support of instrument and technique, but now sophisticated system for fMRI is available. It is based on the BOLD (blood oxygen level dependant) theory; when regional blood flow in brain increases according to the regional brain activation, amount of oxygen influx exceeds required amount of oxygen, producing increased oxyhemoglobin and decreased deoxyhemoglobin in draining veins. Because deoxyhemoglobin is paramagnetic substance, Its reduction brings about decreased magnetic susceptibility effect, producing increased signal intensity on T2* image. With use of sensory stimuli with fMRI, localization of CNS activity was observed for visual, auditory, and somatosensory stimuli and mentality. However, there have been little reports for olfactory stimulation, which is probably due to difficulties in objective transmission of odor to the person lying in MR gantry and designing proper paradigm. So, it will be valuable to study for the paradigm and methods for objective odor transmission. In this study, we demonstrate quantification of brain activation in normal human in response to olfactory stimuli with consistent localization in orbitofrontal cortex, other areas of frontal cortex, entorhinal cortex, amygdaloid, and hippocampal brain regions.

MATERIALS AND METHODS

Selected 20 subjects were included, aged 17-40 years (M:F=15:5). Before examination, we explained the purposes and methods of this study, and consensus of subjects were obtained. MR brain scans were obtained using a 1.5 T superconducting magnet unit with a quadrature head coil (Signa horizon and LX; GE medical system, Milwaukee, Wisconsin, USA). First, fast spin echo T2 weighted axial images of brain were obtained to rule out abnormalities of brain. Functional imaging was acquired using EPI sequence (FA: 90o, TR: 1500 msec, TE: 80 msec, FOV: 24x24 cm, 128x128 matrix, 5 mm thickness with 2 mm interslice gap). Total 3 sets of scans with each 3 sections of images were obtained; 2 axial scans for inferior frontal area, 1 sagittal scans for temporal area. Olfactory stimultion was obtained by placement of hard paper rod, to the tip of which was placed a gauze saturated with orange odored perfume, 1-2 cm above the subject's nose for stimulation period. Paradigm for fMRI was 40 seconds resting and 20 seconds stimulation with 5 times of repetition (total scanning time: 5 minutes). Data processing was done at functool - specified software for fMRI. Activated signal was determined with statistical analysis using t-test. The location and intensity of activating signals was evaluated on processed fMRI images.

RESULTS

Each subjects identified odor correctly, but fMRI signal with concordance to cycles of resting and activation was demonstrated only in 10 subjects. No subjects reported any change in respiration, muscle tension, or other abnormal physical and mental changes. In 10 subjects showing activating signal, it was demonstrated at frontal and temporal area including orbitofrontal cortex (n=5), septal area (n=5), periamygdala (n=4), entorhinal area (n=7), limen insulae (n=6), and hippocampus (n=4). But activating signal of frontal area was thought to be underestimated due to susceptibility artifact of EPI sequence in 6 subjects. The degree of susceptibility artifact showed individual difference. Unexpected signals were noted at brain stem (n=3), occipital lobe (n=1), and posterior portion of temporal lobe (n=1). The intensity of activating signal was variable in each subject. The percent change of signal intensity at activating site ranged from 10% to 40%. In 3 subjects, intrapersonal signal difference during same scanning was demonstrated. We did not estimate pixel number of activated site because of variable p-value for activation display. Because of variable intensity of activating signal as mentioned above, using consistent p-value in the statistics for image processing was impossible in each case

CONCLUSION

Our results demonstrated semiquantitative responses in normal human brain to olfactory stimulation. Activating sites were consistent with previously reports using EEG and PET. But our data did not show functional lateralization of in the orbitofrontal cortex and entorhinal area for olfactoion, reported in previous studies. Unexplained activating areas were also noted in our results, whose mechanism was not clear. Variability of change in signal intensity was a limiting factor for precise quantification of olfactory response in human brain. Although there are limiting factors for precise data acquisition, it is believes that fMRI will be a good modality in the researches for human olfactory processing in brain.