The sensitivity of olfactory fMRI in quantifying olfactory performance during normal aging

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Target Audience Scientists and trainees interested in olfactory function, fMRI techniques, and the effect of aging on sensory processes.

Purpose Olfactory deficits have been identified as an early symptom associated with several neurodegenerative diseases[1]. In particular, olfactory dysfunction measured using olfactory fMRI has gained prominence as a potential early diagnostic marker of disease progression. However, many studies have also observed a general effect of aging on olfactory function, with older healthy subjects having significantly decreased function compared to younger individuals[2]. In order to establish the use of olfactory fMRI as a diagnostic marker, the effect of normal aging on of fMRI measurements must be taken into account. The purpose of this study is to quantitatively evaluate the effect of aging on olfactory system function using fMRI and to establish its relationship with olfactory behavioral results.

Methods Young (n=21, mean age = 26.8 ± 4.7 years, 13 females) and older (n=37, mean age = 69.2 ± 9.6 years, 18 females) healthy subjects underwent fMRI on a 3T Siemens system with EPI (GE) sequence for functional data acquisition (TR = 2s, TE = 30 ms, FA = 90°, FOV = 230 x 230 mm^2). Figure 1 illustrates the olfactory fMRI paradigm that was used. The University of Pennsylvania Smell Identification Test (UPSIT) was used to evaluate olfactory performance. SPM 8 was used for both individual and group analyses. The SPM extension MarsBaR was used to extract BOLD response values relative to all odor conditions from each region of interest (ROI) for post-hoc analysis. The ROIs included the primary olfactory cortex (POC) and insular cortex.

Results A one-way ANOVA analysis found significantly greater activation in younger subjects in the POC and insula for odor conditions ($p < 0.001$, unc). Age was negatively correlated with the BOLD response in the older population in the POC and the insula for both odor (Fig. 2a) and no odor conditions. This was not seen in the young population, though a positive trend was observed. This finding was further supported by linear regression analysis of the older population with age as a covariate, which revealed a significant negative correlation between age and activation in the POC and insula for both odor (Fig. 2b) and no odor conditions. UPSIT scores were also found to be positively correlated with the BOLD response to odor conditions in the left POC and insula across all subjects (Fig. 2c).

Discussion There is a significant negative effect of aging on olfactory function in central odor processing. Younger subjects were found to have significantly greater activation during the olfactory paradigm in olfactory-related areas, specifically the POC and insula during odor conditions. Furthermore, a significant age effect was observed even within the older population. UPSIT scores were found to be positively correlated with olfactory-related activation, establishing a direct relationship between BOLD response and behavioral testing. Finally, our data provide normative aging data that are essential for using olfactory fMRI as a diagnostic marker for detection of disease-related olfactory changes in the brain. Using olfactory stimuli provides the unique opportunity to observe disease-related pathology due to the lack of susceptibility of the olfactory system to compensatory mechanisms, a typical confound of fMRI studies. Subsequent research on validation of olfactory fMRI as a biomarker for neurodegenerative diseases should aim to include the differentiation between normal aging and disease pathology.

Conclusion Age clearly has a strong effect on olfactory-related brain activation. Younger subjects showed significantly higher olfactory-related activation when compared to older subjects, particularly in the POC. Therefore, when evaluating olfactory fMRI as an early diagnostic marker for neurodegenerative diseases, the effect of age must be taken into account in order to correctly identify the difference between disease pathology and normal aging deficits in olfaction.

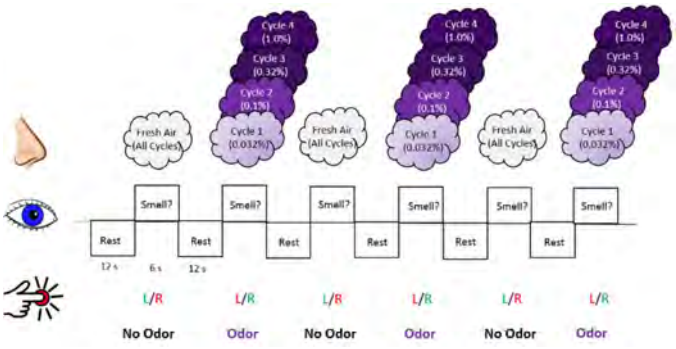

Fig 1. Olfactory fMRI Paradigm. The cycle is repeated 4 times. Each concentration of lavender is presented 3 times. Every time the visual cue "Smell?" appears on the screen, the subject is instructed to respond with a right button press if they do smell lavender and a left button press if they do not.

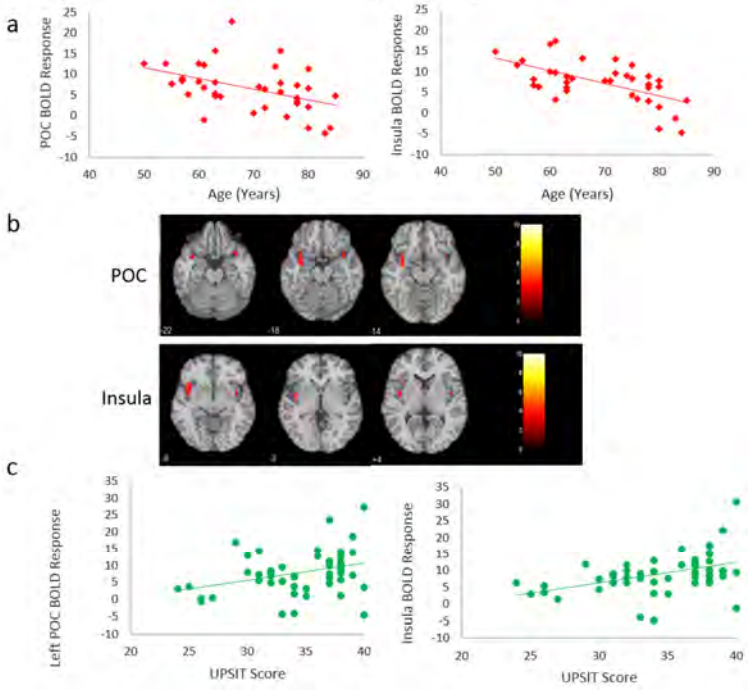

Fig 2.Age effect on olfactory fMRI activation. (a) BOLD response to odor conditions was found to be negatively correlated with age in the older population in the POC ($r = 0.443$, $p < 0.05$) and insula ($r = 0.608$, $p < 0.001$). (b) Linear regression analysis showing that regions in the POC and insula are negatively correlated with age ($p < 0.001$, unc.). (c) BOLD response to odor conditions was found to be positively correlated with UPSIT scores across all subjects in the left POC ($r = 0.331$, $p < 0.05$) and insula ($r = 0.436$, $p < 0.05$).

References

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