Odor-related Functional Deficits in the Primary Olfactory Cortex in Early-stage Parkinson's Disease

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INTRODUCTION Olfactory dysfunctions occur in up to 96% of Parkinson's disease (PD) patients [1] with deficits in odor identification, discrimination and detection threshold [2, 3]. The central olfactory system is known to be highly affected by the PD pathology (Lewy body deposition) that initiates in the olfactory bulb (OB) and anterior olfactory nucleus (AON) [4]. However, the study of functional deficits in the primary olfactory cortex (POC) is challenging [5-8]. The POC processes two intimately coupled functions: odor perception and sniffing function. In the previous study, we have demonstrated that the BOLD signals in the POC from odorant stimulation can be separated and quantified from those by sniffing. In this abstract, we will demonstrate with this technique the functional deficits in the POC of early-stage PD.

METHODS

Human Subjects 27 early-stage idiopathic PD patients (H&Y stage 1, age 55.8 ± 4.3 years, 9 females) and 22 age-/gender-matched healthy controls (HC) (age 54.4 ± 6.2 years, 13 females). There was no significant difference in age (two-sample *t*-test, $p = 0.24$) or gender ($\chi^2 = 3.25$, $p = 0.07$) distributions between the two groups. All subjects gave written informed consent, which was approved by the local Institutional Review Board.

Data Acquisition The olfactory function of subjects was assessed with the University of Pennsylvania Smell Identification Test (UPSIT). The fMRI study was conducted on a Siemens 3 T scanner with an 8-channel head coil and a BOLD-sensitive EPI sequence: TR/TE/FA = 2000 ms/30 ms/90°, image resolution = 2.9 mm×2.9 mm, 34 4-mm-thick oblique slices, number of acquisition = 239.

Odor Stimulation paradigm The sniffing-odor stimulation paradigm contained 6 s of visual prompted sniffing of either odorized air (0.10% of lavender oil in 1,2-propanediol) or odorless air, with each condition repeated twelve times and interleaved with 22-38 s odorless air at a constant air flow of 6 L/min. The subjects were instructed to sniff when they saw the word 'SNIFF' on the screen. The subjects' sniffing and respiration patterns were monitored via a pneumatic respiration sensor and recorded together with the odor delivery and imaging data.

Data Processing and Analysis The respiration data were processed with ONSET [9]. There was no significant difference in the respiration rate and volume during the odor-sniffing or odorless-sniffing periods for each subject. The fMRI data were processed with SPM8. The odor-induced activation map was generated by subtracting odorless-sniffing activation from odor-sniffing activation. Activation differences between cohorts were detected by a one-way ANOVA. Statistical analysis of BOLD signal was conducted with SPSS.

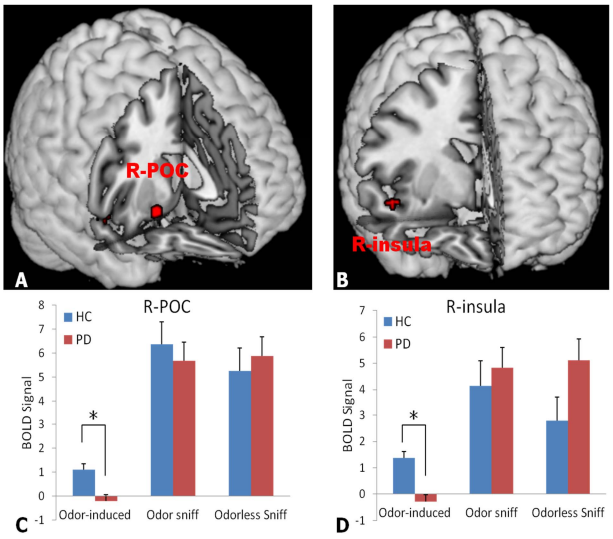

Fig. 1. The odor-induced BOLD signal in the PDs was significantly weaker than the HCs. *, p ≤ 0.001.

RESULTS There was significant olfactory dysfunction in PD subjects (UPSIT score of 21.7 ± 9.5, which was significantly lower than the HCs (34.9 ± 2.7, $p < 0.001$ with age as a covariate). fMRI shows both odor-sniffing and odorless-sniffing induced significant POC activation in both PD and HC subjects, however, compared to the HCs, the odor-induced activation in PD was significantly reduced in the right POC and right insular cortex (Fig. 1).

CONCLUSION In early-stage PD patients, odor-induced activation in the primary and secondary olfactory cortex was significant lower compared to the HCs. The observed POC dysfunction was consistent with the impairment of smell identification function in these patients that was detected by the psychophysical test. Conversely, the sniffing function in the POC was less affected at the early stage of disease. In conclusion, olfactory deficits in the early-stage PD are dominantly odor-related.

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