Olfactory Habituation in the Human Brain

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Introduction:

Study of human olfaction using fMRI is of great clinical interest since olfactory deficits have been associated with many neurological and psychiatric disorders (AD, PD and PTSD). As the brain's BOLD signal is strongly modulated by habituation and respiration, quantitative assessment of neurofunctional deficit using fMRI is complex; published fMRI studies on human olfactory habituation have been limited [1, 2]. A thorough understanding of the dynamic behavior of the BOLD signal due to habituation in the central olfactory system is essential for clinical applications of olfactory fMRI. In this study, we characterized the dynamic behavior of the BOLD signal in the primary olfactory cortex (POC) and related structures when subjected to odor habituation.

Methods:

To induce habituation, a long odor stimulation paradigm was used which consisted of 4 repetitions of an extended odorant presentation (60-s exposure to 0.10% of lavender oil in 1,2-propanediol) followed by a long baseline (98-s exposure to odorless air) at a constant airflow of 6 L/m. The subjects were instructed to breathe normally. Their respiration patterns were monitored via a pneumatic respiration sensor and recorded temporally along with odorant delivery and image acquisition timing. Twelve healthy volunteers with normal olfactory identification and threshold functions completed the fMRI study. T_2*-weighted EPI was used for fMRI image acquisition on a 3 T MRI system with an acceleration factor of 2, TR / TE / FA = 2000 ms / 30 ms / 90°, FOV = 220 × 220 mm^2, acquisition matrix = 80 × 80, 30 axial slices with a slice thickness = 4 mm. The respiratory data were processed with qMRI (http://www.pennstatehershey.org/web/nmrlab/resources/software/qmri) for the stimulation onset vectors. The fMRI data were processed with SPM5 (University College London, UK) following the standard procedures.

Results:

Under the prolonged odor stimulation, BOLD signals in all the activated structures exhibited a striking, dynamic pattern of habituation: at around 6-8-s after stimulation onset, a steep initial peak emerged with an intensity of about 0.3-0.8%, clearly in response to the first inhalation of odorant; then at around 18-20-s after onset, the signal quickly decreased down to the baseline (Fig. 1). Most interestingly, in POC (right), shortly after the initial activation peak, a prolonged activation signal re-emerged, with a reduced intensity of about 0.3%, which then started to return to the baseline shortly after the odorant stimulation stopped. This second, prolonged activation was significantly weaker than the initial peak (paired t-test, $p = .034$), but stronger than the baseline (paired t-test, $p = .042$). Of the four repetitions of 60-s odorant presentation periods over the entire paradigm, BOLD signals in the last session were significantly lower than in the first three (paired t-test, $p < .021$), indicting a long-term habituation effect. The activated areas included bilateral POC, insular cortex, precuneus cortex, occipital cortex, anterior and posterior cingulate cortex, right supramarginal cortex, right orbitofrontal cortex, and right dorsolateral prefrontal cortex.

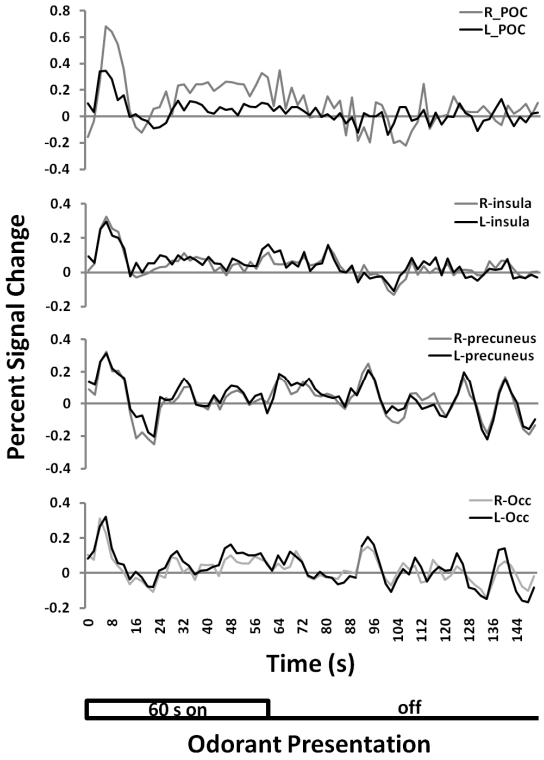

Fig. 1. Average BOLD signal-time courses of the four odorant presentation periods in the bilateral POC, insula, precuneus, and occipital cortices (Occ).

Discussion:

In this study, we observed a detailed olfactory BOLD signal habituation pattern in the POC of subjects presented with our odorant paradigm. The POC revealed a rapid olfactory activation habituation within the 6-s odor onset, clearly in response to the first inhalation of odor, which was then followed by a significantly attenuated activation prolonged till odor disappeared. This dynamic behavior is the first observed in humans with fMRI and almost identically matches the electric recording data in the anterior piriform cortex of freely-breathing, anesthetized rats responding to prolonged single odorant presentations (50-s) [3]. In that animal study, a strong transient activation occurred at odorant onset for a few seconds, returned to baseline briefly, and was then followed by a much weaker (about 70% weaker than the initial peak activation), but prolonged, activation until the end of odorant stimulation.

Another significant finding is that the BOLD signal in the structures beyond POC (e.g., insula, precuneus, and calcarine cortices) all followed a similar time-course as in the POC. No reports of such significant activation habituations in these structures have been made previously. In prior human fMRI studies, rapid activation habituation was observed, similar to the activation observed in our study, but limited to POC only; while in other areas, such as lateral orbitofrontal cortex, the activation remained high throughout odor stimulation [1, 2]. Such an anatomically-dependent, temporal behavior is difficult to interpret. The BOLD signal is known to last for a long time (minutes) under sustained stimulation. For example, activation in the calcarine cortex triggered by visual stimulation can last as long as 15 minutes with no habituation [4]. Therefore, the BOLD signal habituation phenomena shown here are specific to the olfactory network. Olfactory habituation in the olfactory network is quite plausibly synchronized with the secondary olfactory structures directly or indirectly receiving and/or responding to the output of activations in the POC.

References:

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