Heterogeneity of orbitofrontal cortex with reference to hypothalamus

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**Background**: The orbitofrontal cortex (OFC) is involved in cognitive functions, and is also closely related to autonomic functions. The OFC is densely connected with the hypothalamus, a heterogeneous structure that contains several nuclei related to the autonomic functions. The hypothalamus, although it contains several nuclei, can be classified into two major parts: the lateral and the medial. Resting-state functional connectivity has allowed us to parcellate the cerebral cortex into putative functional areas based on the changes in the spatial pattern of connectivity in the cerebral cortex when a seed point is moved from one voxel to another. In the present high spatial-resolution fMRI study, we investigated the functional architecture of the OFC with reference to the hypothalamus.

**Methods**: Twelve healthy right-handed subjects (aged 20–39 years; seven males and five females) participated in the experiments after written informed consent was obtained. The procedures of fMRI experiments were approved by the Institutional Review Board of The University of Tokyo School of Medicine.

The MRI scanning was conducted using a 3T MRI scanner (Philips Achieva X 3T Rel. 2.6, Best, The Netherland). Functional imaging used gradient-echo echo-planar sequences (TR = 9.0 s, TE =35 ms, flip angle =90 deg, resolution = 2.0 x 2.0 x 2.0 mm³, 75 slices). The data were sampled using the cubic voxels of 2 mm to minimize signal contamination from the other bank of the sulcus. During the functional imaging, the subjects were instructed to passively view a fixation point on the screen.

In the present high spatial-resolution fMRI study, to investigate the functional architecture of the OFC with reference to the hypothalamus, the OFC was parcellated using resting-state functional connectivity (Margulies et al., 2007; Cohen et al., 2008) in an individual subject approach (Hirose et al., 2013). The functional connectivity was then examined between the parcellated areas in the OFC and the lateral/medial hypothalamus.

**Results**: The functional double dissociation was found in the OFC. The lateral OFC contained more areas with greater connectivity with the lateral hypothalamus \( t(11) = 2.7, P < .05 \), whereas the medial OFC contained more areas with greater connectivity the medial hypothalamus \( t(11) = 3.1, P < .01 \). The OFC-by-hypothalamus interaction in a two-way ANOVA was also significant \( F(1,11) = 34.0, P < .001 \).

**Conclusions**: These results reveal the neuroanatomical basis of the OFC-hypothalamic functional interaction, and provide an essential step toward understanding mind-body interaction.