White matter connectivity between superior temporal sulcus and amygdala is associated with empathetic ability in normal humans

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Introduction
In patients with autistic spectrum disorders (ASD) and schizophrenia, severe impairment in social functions such as reduced communication skills and empathetic concern are reported. Recent neuroimaging studies have indicated that empathetic ability in normal humans is subserved by a neural circuit involving the superior temporal sulcus (STS), amygdala (AMG), and medial prefrontal cortex. Functional alterations in the STS and AMG have been observed in patients with ASD and schizophrenia by using functional magnetic resonance imaging (fMRI) and face processing tasks. In the present study, we investigated whether neural connectivity between these regions would associate with empathetic ability in normal subjects. For this purpose, diffusion tensor imaging (DTI) and fMRI experiments were conducted to delineate white matter connectivity between the STS and AMG. The volume of connectivity was computed in each subject and correlated with the empathetic ability as measured by a standard questionnaire.

Methods
DTI (b-value, 3000 s/mm²; TR/TE, 6200/116 ms; direction, 64; voxel size, 2.5 × 2.5 × 2.5 mm; slices, 42) and fMRI (TR/TE, 2000/24 ms; voxel size, 3 × 3 × 3.75 mm; slices, 39) were performed using a 3 T MRI scanner (Siemens, Tim Trio) in 30 volunteers (14 men and 16 women; mean age, 22 years). We conducted fMRI when the subjects were performing passive tasks such as viewing faces, abstract shapes (Slotnick, 2004), and words. After the scan, the subject was asked to complete the Interpersonal Reactivity Index (IRI): a questionnaire consisted of 4 subscales (perspective taking, PT; fantasy, FS; emotional concern, EC; personal distress, PD) that was designed to assess empathy (Davis, 1983).

fMRI experiment was conducted in a block design consisted of face (F), word (W), and shape (S) blocks. During each 15s-block, 25 different items were presented for 300ms each followed by fixation for 300ms. Each block was repeated 4 times in a fixed-order (FWSFWSFWSWF) and interleaved by 15s-fixation block. Each scanning run consisted of 190 image volumes (380s). The run was repeated twice with the order of items randomly intermixed in each block. The subject passively viewed the items and did not make any decision or response.

Group analysis of functional imaging data with SPM8 defined the face-specific activation in the right STS and AMG (contrast of face versus shape + word; p < 0.001, uncorrected). The activated clusters in the Montreal Neurological Institute (MNI) coordinate system were saved as binary mask images by using the MRicro software.

During DTI analysis using FSL (ver. 4.1), probabilistic tractography was performed to determine the connectivity between STS and AMG mask images. This procedure yielded a probabilistic image that showed connectivity between the functionally defined regions associated with face processing in each subject. The volume of connectivity images was computed for each subject. Finally, the Spearman’s rank order correlation coefficients between these values and each IRI subscale were computed (threshold at p < 0.05).

fMRI results
The result of random-effects group analysis at p = 0.01, FDR corrected, and k = 20 voxels is shown.
White arrows indicate face-selective activation in the AMG (x, y, z = 24, 4, 40) and STS (x, y, z = 52, 54, 16).
Mask images of these clusters were created by using MRicro (p = 0.001, AMG, 4112 mm³, STS, 2096 mm³).

Discussion and conclusion
The present study reveals that white matter connectivity between the STS and AMG associated with face processing correlates with empathetic ability in normal human subjects.
A negative correlation between these values indicates that the larger the connectivity, the less the fantasy score of IRI which is a measure of ability for emotional identification with characters.
The inverse relationship implies that a person with low fantasy score may have compensatory increase in white matter connectivity between the AMG and STS.
A combined fMRI and DTI study contributes to elucidate neural substrates of human emotion and cognition that have not been revealed by fMRI or DTI alone.

References and notes
2Slotnick SD, Schacter DL, 2004, Nat Neurosci, 7, 664-672
3SPM8: http://www.fil.ion.ucl.ac.uk/spm/
4FSL ver. 4.1: http://www.fmrib.ox.ac.uk/fsl/index.html

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