

A combined study of functional magnetic resonance imaging and diffusion tensor imaging revealed neuronal tract associated with autistic tendency

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Introduction

Individuals with autism spectrum disorders (ASDs) show limited social relatedness and limited ability to communicate with others both verbally and nonverbally. Dysfunction of the mirror neuron system (MNS), which allows recognition of the goal of perceived action for imitation, may underlie ASD symptoms (Jacoboni M et al. *Nat Rev Neurosci* 7, 942–, 2006). On the other hand, amygdala (AMG) is also known to play a key role in the perception of social signals such as faces and expressions (Sabatinelli D et al. *Neuroimage* 54, 2524–, 2011). Since MNS is distributed in the superior temporal sulcus (STS), premotor cortex, and intraparietal sulcus, it is important to consider functional alterations in the STS observed in patients with ASD. In the present study, we investigated whether neural connectivity between these key regions of the human MNS and face processing are associated with autistic traits in healthy subjects. DTI and fMRI experiments were combined to delineate white matter connectivity between the STS and AMG.

Methods

DTI (b value = 3000 s/mm², TR/TE= 6200/116 ms, 64 direction, 2.5³mm voxel, 42 slices) and fMRI (TR/TE = 2000/24 ms, 3×3×3.75 mm voxel, 39 slices) were performed using a 3-T MRI scanner (Siemens, Tim/Trio) in 30 volunteers (14 men and 16 women; mean age, 22 years). fMRI was conducted during the passive viewing task of faces, shapes, and words. After the scan, the subject was asked to complete the Japanese version of Autism-Spectrum Quotient (AQ; Baron-Cohen S, et al, *J Autism Dev Disord*, 31, 5-17, 2001): a questionnaire consisting of 4 subscales (communication, social, imagination, local details, attention switching). In a group analysis of functional imaging data with SPM5, face-specific activation in the right STS and AMG was defined (contrast of face versus shape + word, $p < 0.001$, uncorrected). In the DTI analysis using FSL ver. 4.1, probabilistic tractography was conducted to delineate the connectivity between the STS and AMG mask images. The volume of the connectivity images were computed for each subject. Finally, the Spearman's rank order correlation between these values and AQ scale were computed ($p < 0.05$).

Results

The mean total AQ score for 30 subjects was 21.2 (range, 9–34). Two subjects (6.7%) exceeded the cut-off point. The mean AQ score of the male subjects (22.8±6.9) was greater than that of the female subjects (19.9±5.5); however, the difference was not statistically significant (Kruskal–Wallis test, $p=0.23$). fMRI data showed significant activation associated with face processing in the STS ([52, -54, 16]; $T = 5.11$) and AMG ([24, 4, -20]; $T = 6.30$) of the right hemisphere. DTI analysis showed connectivity between the STS and AMG in each subject. The volume of STS–AMG connectivity correlated positively with the total AQ score across the subjects ($p<0.05$). Among the AQ subscales, the imagination score significantly correlated with the connectivity volume ($p<0.05$), whereas the other subscales did not ($p>0.05$). BOLD signal change in the STS and AMG for the face condition measured against the mean of the shape and word conditions also did not correlate with the total AQ score ($p>0.05$).

Conclusion

The present study shows that white matter connectivity between the STS and AMG associated with face processing correlates with autistic traits in healthy human subjects. A positive correlation between this connectivity and the AQ score indicates that the larger the connectivity the greater the autistic tendency with respect to imagination subscale. Combined fMRI and DTI can reveal the neuroanatomical substrates of autistic traits in healthy subjects. Subjects with high AQ scores tended to have increased connectivity between the regions involved in the putative MNS as compared to subjects with low AQ scores. Because autistic traits related to social function are continuously distributed in the general population and ASD patients, a future study involving both the groups of subjects may help in determining a specific biomarker for ASD.

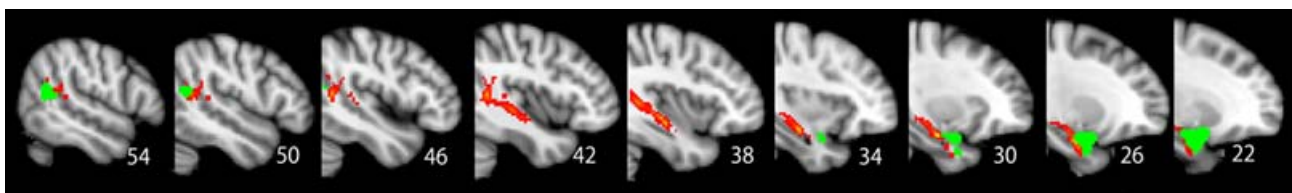


Figure: White matter connectivity between the right STS and AMG in a single representative subject is shown in red. Green areas are the face selective regions in the STS and AMG as defined by fMRI group analysis.