A Diffusion Spectrum Imaging Study on Mirror Neuron System in Schizophrenia

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**Introduction** First discovered in the ventral premotor cortex of the macaque, mirror neurons fire both while a monkey performs goal-directed actions and while it observes the same actions performed by others. This observation-execution matching system is thought to provide a neural mechanism by which others' actions and intentions can be automatically understood [1]. So far, mirror neurons have been identified in two cortical areas in humans — the inferior frontal gyrus (IFG) and the inferior parietal lobule (IPL) [2]. MNS deficits have also been reported in schizophrenia. The primary cognitive deficits in schizophrenia lie within the domain of social cognition, while the primary structural and functional abnormalities are located within the corresponding cortical networks [3]. Therefore, we aimed to investigate the white matter integrity of IFG and IPL in patients with schizophrenia, and analyze the association of the white matter integrity with the scores for the social withdrawal provided by the Positive and Negative Symptom Scale (PANSS).

**Materials and Methods** Thirty-three schizophrenic patients and matched neurotypicals were examined using diffusion spectrum imaging (DSI). Images were acquired on a 3T MRI system with a 32-channel head coil (Siemens, Erlangen, Germany). DSI was performed using a twice-refocused balanced echo diffusion EPI sequence, TR/TE = 9600/130 ms, matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm^2, and slice thickness = 2.5 mm. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity b_{max} = 4000 s/mm^2 were sampled on the grid points in the 3D q-space with $|q| \leq 3.6$ units [4]. DSI analysis was performed based on the relationship that the echo signal S(q) and the diffusion probability density function P(r) were a Fourier pair, i.e., S(q)=FT{P(r)}. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction. The intravoxel fiber orientations were determined by decomposing the original ODF into several constituent ODFs [5]. Generalized fractional anisotropy (GFA) at each voxel was quantified from the original ODF [6] to represent an index of white matter integrity. Tractography was reconstructed using a streamline-based algorithm and the targeted tracts were selected by specific regions-of-interest. The tracts interconnecting IFG to IPL were tracked on both hemispheres for each subject. A method that projected the GFA onto a single mean path of a specific white matter tract was used to analyze local changes along the individual tract bundles [7]. Comparison of GFA between patients and neurotypicals was performed using an independent sample t-test. The fourth negative symptom score (N4: Passive/apathetic social withdrawal) was correlated with the GFA values using a 2-tailed Spearman's correlation test.

**Results** No significant difference in mean GFA values was found between patients and neurotypicals. Significant positive correlation was found between the scores for social withdrawal and the GFA values of the left and right IFG-IPL tracts (left: r=0.535; p=0.001 and right: r=0.441; p=0.01). [Figure]

**Discussion** Previous fMRI studies of MNS dysfunction in autism found that activation in MNS area was inversely related to symptom severity in the social domain [1]. Our results further provide a possible modulation of white matter integrity compensating for difference in the cortical activation. Increase in white matter integrity is required to make up for cortical hypoactivation, whereas the compensation is less required if the cortical activation is nearly normal. Future studies including correlation with fMRI results are warranted to test our hypothesis.

**References** [1] M. Dapretto, _et.al._, Nature Neuroscience, 2006. [2] M. Iacoboni, M. Dapretto, Nature Reviews, 2006. [3] J. Burns, World Psychiatry, 2006. [4] V.J. Wedeen, _et al._, Magn Reson Med. 2005; 54:1377-86. [5] F.C.Yeh, _et al._, Proc ISMRM, 2008. [6] D.S. Tuch, Magn Reson Med, 2004. [7] W.Y. Chiang, _et al._, Proc ISMRM, 2008.
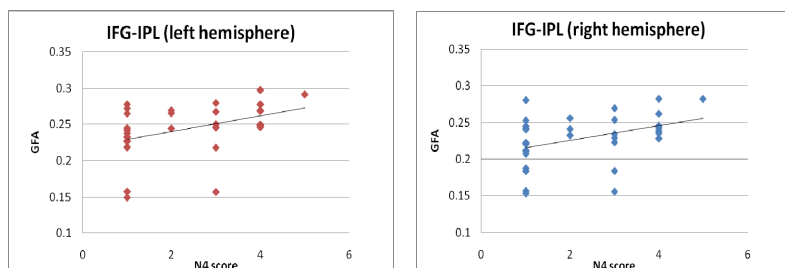
Figure. Positive correlation between the scores for social withdrawal (N4 score) and the GFA values of the left and right IFG-IPL tracts (left: r=0.535; p=0.001 and right: r=0.441; p=0.01).