# Acute Impact of Antipsychotic Treatment on Patient with Schizophrenia: A tract-based automatic analysis (TBAA) with diffusion spectrum imaging (DSI).

Su-Chun Huang[1], Chih-Min Liu[2], Tzung-Jeng Hwang[2], Hai-Gwo Hwu[2], Yung-Chin Hsu[1], Yu-Chun Lo[1], Yu-Jen Chen[1], and Wen-Yih Isaac Tseng[1,3]

[1]*Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan,* [2]*Department of Psychiatry, National Taiwan University Hospital, Taipei, Taiwan,* [3]*Molecular Imaging Center, National Taiwan University, Taipei, Taiwan*

## *Introduction*

Schizophrenia is a complex psychiatric disorder which influences around 1 % of the population world-wide.[1] Researchers have speculated that schizophrenia is a result of failure in the integration of structural and functional connectivity in the brain.[2] Medications have been proven to be able to reduce the clinical symptoms of schizophrenia, however, the mechanisms of how the medications work in the brain, i.e. how the medications affect the structural and functional connectivity in the brain, is still unclear. Structural connectivity can be evaluated *in vivo* by diffusion spectrum imaging (DSI), a high-angular resolution diffusion imaging (HARDI) technique with is capable to solve the crossing fiber problem.[3] Here we employed a novel analysis theme called tract-based automatic analysis (TBAA) which is capable to reconstruct 74 major fiber tracts in the brain and map the quantification parameters for white matter property along the fiber tracts.[4] We recruited 18 drug-naïve subjects who were experiencing their first episode of schizophrenia. DSI scans were taken pre- and post- treatments of 4 weeks. Structural connectivity changes of the whole brain 74 major white matter tracts were evaluated by TBAA.

## *Materials and Methods*

***Subjects:*** Eighteen drug-naive subjects with schizophrenia were recruited in the study (seven females; age = 26.94 ± 5.96 years; two left-handed, Edinburgh handedness inventory score = 62.43 ± 53.00). All subjects were treated with 15mg Abilify/day. MRI scans were performed before treatment and after four weeks of medication. ***MRI Data acquisition:*** All images were acquired on a 3T MRI system with a 32-channel head array (TIM Trio, Siemens, Erlangen, Germany). DSI experiment was performed with a pulsed-gradient spin-echo diffusion EPI (TR/TE=9100/142 ms, isotropic resolution=2.5 mm, bmax=4000 s/mm$^2$, 102 diffusion gradient vectors). ***MRI Data analysis:*** The flow chart of TBAA was shown in Figure 1. The individual DSI images of all the subjects were first co-registered to form a study-specific template (SST) through large deformation diffeomorphic metric mapping (LDDMM), the SST were further normalized onto the NTU-DSI-122 template, a high resolution HARDI template based on 122 healthy individuals. [5] The coordination of the whole brain 74 major tracts on the NTU-DSI-122 template was then transferred to the SST, then to the individual dataset. The quantification parameter for white matter property, generalized fractional anisotropy (GFA), was sampled in individual's native space along the coordinates of the tracts. Each tract was further divided into 100 steps, GFA within the same step were averaged. ***Statistics:*** Threshold-free cluster enhancement (TFCE) was used to increase the statistical power and to select the steps of the tracts which GFA differ more pre- and post- treatments. Paired t-tests were performed on the steps. The significance level was set at 0.05.

## *Results*

Seven tracts were selected by TFCE with difference between pre- and post- treatment scans. Three of them showed significant difference. They were left superior longitudinal fasciculus (SLF) II (p = 0.029), left SLF III (p = 0.014), and left medial lemniscus (ML, p = 0.006). The pre- and post-treatment GFA were shown in Figure 2.

## *Discussion and Conclusion*

In the present study we found that after 4 weeks of treatment, GFA value was significantly increased in left SLF II, SLF III, and ML. The increase was not presented along the whole tract, but limited to discrete segments. Since all the patients reported reduced severity of symptoms after treatments, these results suggest that the medication can modulate the integrity of white matter tract, and further influence the clinical symptoms. Notably, all the differences were found in tracts related of sensory input and integration, implying that the core pathology of schizophrenia may be related to sensory integration.

## *Future Works*

We also collected pre- and post- treatment resting-state fMRI data of all the subjects, which can supply us information about the changes in functional connectivity due to treatment. The fMRI data will be analyze before the end of 2014. By combining both structural and functional results, we can have a better understanding of the effects of anti-psychotic medicine on brain structure and function in schizophrenia.

## *References*

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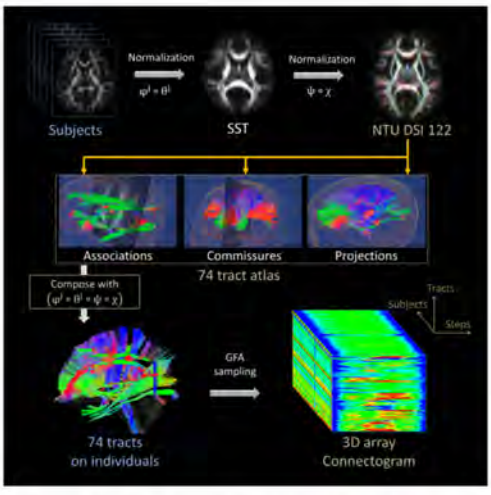


**Figure 1** The flowchart of tract-based automatic analysis (TBAA).

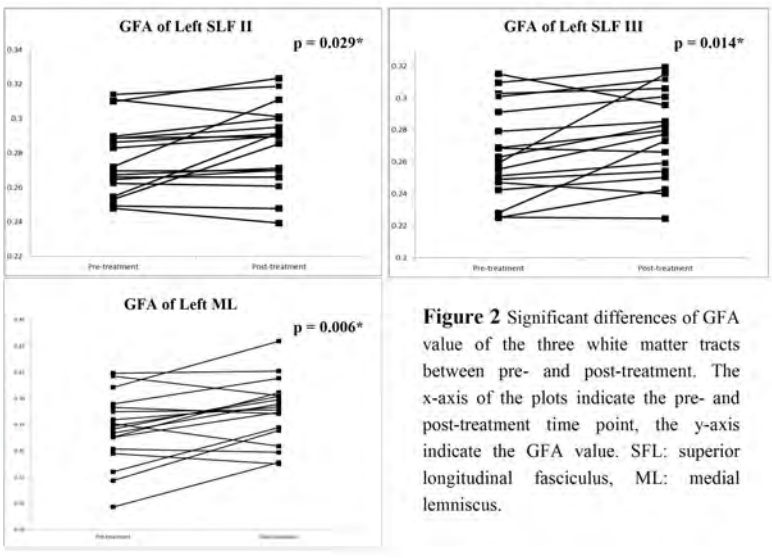


**Figure 2** Significant differences of GFA value of the three white matter tracts between pre- and post-treatment. The x-axis of the plots indicate the pre- and post-treatment time point, the y-axis indicate the GFA value. SFL: superior longitudinal fasciculus, ML: medial lemniscus.