Disrupted white matter connectivity revealed by diffusion tensor imaging in children with Tourette syndrome

X. Huang[1], J. Sun[2], X. Li[1], F. Li[1], M. Huang[2], L. Guo[2], and Q. Gong[1]

[1]Huaxi Magnetic Resonance Research Centre, Department of Radiology, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of,

[2]Department of psychiatry, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of

Introduction

Tourette syndrome (TS) is a childhood-onset neurobehavioral disorder characterized by motor and vocal tics[1]. To date, the neural basis of TS is not fully understood yet. Previous studies suggested the anatomical and functional disturbances in sensorimotor pathways of cortico-striato-thalmo-cortical (CSTC) circuits as core pathophysiology for the disease. Diffusion tensor imaging (DTI) is an MR technique sensitive to reveal the microabnormality of brain white matter connectivity, and it had been used to investigate neuropsychiatric disorders [1]. Studies using DTI had reported changes of basal ganglia [2] and corpus callosum [3] in TS. Present study aimed to perform the whole brain voxel-wise DTI analysis and to explore the abnormalities associated with CSTC circuits in children with TS.

Method

The study was approved by the local ethical committee and written informed consent was obtained from the legal custody of all subjects. Ten TS patients with a mean age of 95 ± 31.5 months, range from 72 to 168 months and diagnosed according to the criterion of DSM-IV and ten age and sex matched controls were recruited. MRI scanning was performed using a 3T MR imaging system (EXCITE, General Electric, Milwaukee, USA). DTI was acquired using a single shot spin echo EPI sequence (TR/TE = 10000/70.8 ms; slice thickness, 3 mm, matrix = 128×128, b value = 1000s/mm2). FA maps were generated from each participant's DTI scan using DTIstudio (http://cmrm.med.jhmi.edu/). The b = 0 images of all control subjects and patients were first normalized and averaged to construct a study-specific template, to which all raw b=0 images were re-normalized. Then the derived mapping parameters for each subject were applied to the FA maps which were finally smoothed using 8 mm FWMH isotropic Gaussian kernel to reduce errors related to intersubject variability. The first stage whole brain comparison was performed using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/software/) on a Voxel-based analysis way. The second stage fiber comparison was done by load the normalized FA maps to RoiEditor (http://cmrm.med.jhmi.edu/) and calculates the FA value to each fiber track.

Results

At defined threshold value of t>2.55(p<0.01at voxel level) and cluster voxel>100, significant reductions of FA value in TS patients were found in bilateral middle cerebellar peduncle(MCP), bilateral posterior limbs of internal capsule(PLIC) and genu [fig 1]. Further comparison of FA value for separate tracks extracted from RoiEditor revealed that only left CST (cortico-spinal track) showed a trend of reduced FA in TS patients, although this did not reach statistical significance(P>0.05, table 1).

Conclusion

Impairment of cerebellum and sensorimotor cortex in TS children had been demonstrated by past PET [4], structural[5] and functional MRI[6] studies. FA reduction in bilateral MCP suggested that the dysfunction of neural circuit involving cerebellum played an unique role in the pathology of TS. PLIC is mainly composed of superior thalamic radiation and long corticofugal pathways, such as CST. So it is the mainly pass way for thalamo-cortical part in CSTC. Obvious FA reduction in this particular area showed the disruption of CSTC as expected. Present study demonstrated brain connectivity disruption in both CSTC circuit, interhemisphere connectivity and the involvement of cerebellum in TS children. Further larger cohort study is warranted to provide further insight into the underlying psychopathology of the TS.

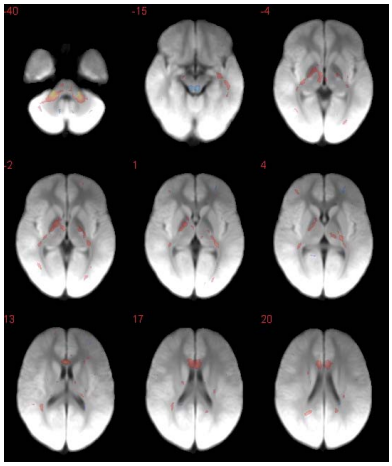

Fig 1. Reduction of FA values(t>2.55) in TS children compared to controls showing on averaged aDWI maps of all subjects. (red indicate reduction, and blue indicate increase)

Table 1. Comparison of FA values for fiber tracks in TS children and normal controls.

	TS group (N=10)		Control group (N=10)		P
	FA Mean	SD	FA Mean	SD	
ATRL	0.349	0.022	0.359	0.022	0.32
ATRR	0.331	0.026	0.341	0.021	0.36
FMINOR	0.383	0.045	0.395	0.026	0.48
FMAJOR	0.371	0.026	0.352	0.028	0.13
CGHL	0.265	0.038	0.286	0.020	0.14
CGHR	0.275	0.028	0.278	0.016	0.77
CGCL	0.296	0.027	0.307	0.025	0.35
CGCR	0.259	0.026	0.266	0.023	0.53
CSTL	0.404	0.026	0.424	0.021	0.07
CSTR	0.405	0.029	0.418	0.019	0.26
IFOL	0.352	0.033	0.361	0.016	0.45
IFOR	0.352	0.027	0.361	0.011	0.35
ILFL	0.323	0.031	0.34	0.026	0.20
ILFR	0.332	0.032	0.351	0.023	0.15
SLFL	0.291	0.028	0.303	0.021	0.30
SLFR	0.299	0.027	0.307	0.018	0.45
TSLFL	0.31	0.032	0.323	0.027	0.34
TSLFR	0.315	0.025	0.328	0.020	0.22
UNCL	0.333	0.042	0.343	0.020	0.50
UNCR	0.316	0.040	0.324	0.016	0.57

Reference

1. Taylor WD, et al. *Biol Psychiatry* **55**:201-7.
2. Makki MI, et al. *Mov Disord(in press)*
3. Plessen KJ, et al. *J Child Psychol Psychiatry* **47**:1013-22.
4. Lerner A, et al. *Neurology* **68**:1979-87.
5. Sowell ER, et al. *Nat Neurosci* **11**:637-9.
6. Bohlhalter S, et al. *Brain* **129**:2029-37.