Diffusion tensor imaging findings associated with cognitive performance in hydrocephalus patients

HongWei Cheng, MD, *WenMing Hong,* MsC, *XiaoJie Wang,* MD, *XiaoPeng Hu,* MD.

Hydrocephalus patients often manifest a mental decline or dementia in addition to the neurological signs, creating a heavy burden for the family and the health care system. Therefore, it is critical to identify the mechanism and early manifestations of hydrocephalus cognitive dysfunction. The mechanism of hydrocephalus leading to cognitive impairment is controversial; many consider cortical and subcortical fiber bundle connection damage a possible pathogenesis, and imaging findings will become the focus of attention. Conventional MRI technology is limited in the study of hydrocephalus cognitive function changes, because of limitations in resolution and difficulties in distinguishing pathological changes. Diffusion tensor imaging (DTI) is a recently developed water diffusion imaging technique, which has very high sensitivity to cerebral white matter fiber tract changes. Water molecular diffusion can quantitatively reflect the brain microstructure, providing information on small pathological changes and analyze white matter and gray impairment, which appears normal on traditional MRI. The aim of this study was to research hydrocephalus cognitive dysfunction in patients with brain fiber bundle damage by using DTI technology to explore the process of cognitive dysfunction and to provide a useful index of early clinical evaluation in the region of cognitive impairment for clinical guidance of the early treatment of hydrocephalus.[1]

Our study was carried out in the Department of Neurosurgery, First Affiliated Hospital of AnHui Medical University from January 2008 to December 2012. Thirty patients (41.20±6.82 years) with cognitive dysfunction, and 30 healthy volunteers (41.65±6.50 years) were included. The patients and control groups were collected from patients admitted to the internal medicine polyclinic for routine check up examination. All data were collected prospectively and recorded in Excel data collecting system. All patients provided signed informed consent before undergoing DTI examination. The study was conducted in accordance with the Declaration of Helsinki, and the local ethics committee approved the study.

Inclusion criteria. Patients diagnosed with hydrocephalus by conventional MRI completed an assessment of cognitive function and then underwent DTI examination. Cognitive function was assessed using the Montreal cognitive scale (MoCA). The scale comprised 6 test projects including visuo-spatial and executive ability, 5 words in immediate and delayed recall, which was performed after 5 minutes. A total score ≥26 indicated normal cognitive function, while the <26 mean cognitive scores. The hydrocephalus patients with cognitive dysfunction underwent ventriculoperitoneal shunt insertion following DTI and neuropsychological evaluation. The patients were followed up for one year, when they again underwent DTI and neuropsychological evaluation. Twenty-six patients completed follow-up and reevaluation, and fractional anisotropy (FA) value and made a contrast analysis with the preoperative patients.

Exclusion criteria. (1) None hydrocephalus factors such as inflammation, multiple sclerosis, vascular lesions, or tumors causing white matter lesions; (2) Infarction of functional brain areas causing aphasia, hearing loss, and cognitive impairment (3) Other clear causes of cognitive impairment, such as Parkinson's disease, or thyroid dysfunction; (4) A Hamilton Depression Evaluation Scale (HDRS) score ≥18 points in the 17 items (5) Patients with hypertension and (or) hyperglycemia, especially in elderly patients.

Post-processing of the DTI image data was carried out using DTI tracking software for DTI imaging reconstruction, thus obtaining the fractional anisotropy (FA) value, average value of b0, and eigenvalue of graphs. Head motion correction was used for the automated image registration. We extracted each patient's ROI and excluded non-brain tissue, and used FSL software to calculate FA value, then extracted white matter's fractional anisotropy, axial diffusivity and radial diffusivity with the standard of JHU White Matter Atlas. They were imported to SPSS for model establishment and statistical analysis. The processed data were repeated with measurements taken by the same imaging practitioner at different times.

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 12.0, and a p-value of <0.05 was

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considered statistically significant. The measurement data were recorded as mean ± standard deviation and count data indicated the actual cases. Comparison of measurement data between the 2 groups was assessed by t-test of 2 sample means, and the count data between the 2 groups were compared by chi-square test. The correlation between the index of DTI and MoCA scale was analyzed using the Pearson test.

A total of 30 patients with cognitive dysfunction were included in this study, and their results were compared with those of 30 healthy controls. The characteristics of the patients and controls are shown in **Table 1**, and there is no statistically significant differences in age, percentage of males, years of education, blood sugar, and systolic blood pressure. There is statistically significant difference in the duration of disease, with the study group having a significantly longer duration of disease than the control group.

All subjects underwent neuropsychological evaluation, and the result show that the scores of the hydrocephalus cognitive dysfunction group were lower than the control group. Scores in execution of vision and space, name, attention, abstract power, and delay memory were statistical significant, while scores in language and orientation between the 2 groups did not reach statistical significance. The hydrocephalus group with cognitive dysfunction underwent insertion of a ventriculoperitoneal shunt, and results of the neuropsychological evaluation on follow-up of one year later, shown that the execution of vision and space, name, attention, and abstract power are obviously improved in patients after operation treatment ($p<0.05$), but improvements of memory delay were not obvious ($p>0.05$). Significance was considered at the level $p<0.05$ and 95% confidence interval. The MoCA scores in each item were recorded as following: execution of the vision and space: 5 points; name: 3 points; attention: 6 points; language: 3 points; abstract power: 2 points; memory delay: 5 points; orientation: 6 points.

Analysis of the DTI data between the hydrocephalus cognitive dysfunction group and the control group, showed a significant reduction in FA value in the frontal and semi-oval region ($p<0.01$), and in the temporal and parietal lobe ($p<0.05$) of the hydrocephalus cognitive dysfunction group, while there was no statistically significance difference in the occipital lobe between the 2 groups. After one year follow up in the hydrocephalus group with ventriculoperitoneal shunt insertion, the FA values in the frontal and semi-oval region had an obvious rise ($p<0.05$), however, the temporal and parietal lobe values did not obviously rise ($p>0.05$). Fractional anisotropy is a value between 0 to 1, 1 was the largest anisotropic, 0 was maximal isotropic, and the fiber bundle damage more seriously. The smaller value of FA means the fiber bundle damage more seriously.

Table 1 - Comparison of basic clinical features between 2 groups of hydrocephalus patients.

Basic features	Cognitive dysfunction group (n=30)	Control group (n=30)	*P*-value
Age (year)	41.20 ± 6.82	41.65 ± 6.50	0.7143
Male (rate%)	15 (50)	13 (43)	0.727
Years of education (years)	6.80 ± 1.15	7.00 ± 1.29	0.5677
Duration of disease (month)	58.30 ± 6.09	35.55 ± 9.08	<0.01
Blood sugar	5.72 ± 1.59	5.87 ± 1.59	0.5867
Systolic blood pressure	127.0 ± 13.73	128.9 ± 12.00	0.3569

The Pearson correlation coefficient of MoCA total scores and frontal FA value was 0.953, and revealed the presence of significant correlation ($p<0.0001$).

The study results show that hydrocephalus cognitive dysfunction is related to the duration of disease, indicating duration of illness a basic factor of cognitive dysfunction. Data showed a number of patients with long-term high blood glucose, and hypertension, which could impair cognitive function by causing neuronal damage, indicating hypertension and hyperglycemia as risk factors for cognitive impairment.[1]

Hydrocephalus cognitive dysfunction was classified into cortical dementia, wherein the frontal dysexecutive syndrome was a dominant clinical manifestation. A detailed characterization is required to identify hydrocephalus cognitive dysfunction and other types of dementia. Previous researchers compared hydrocephalus cognitive dysfunction with senile cognitive impairment, and found that hydrocephalus patients with frontal lobe dysfunction for more than 50% performance in executive function, while Alzheimer's disease was over 50% performance in memory.[2] Many early studies on hydrocephalus cognitive function focused on attention, memory, and executive function however, in recent years, research directions have been aimed at posterior cortical functions, such as visuospatial and visuoperceptual functions.[2] In addition, cerebral white matter damage of patients has played a very important role in impaired cognitive function, which is confirmed in a study of cerebrovascular disease, epilepsy, and hypertension.[3] Diffusion tensor imaging, which can evaluate the integrity of descending white matter tracts, is a non-invasive imaging technique that can analyze cerebral white matter in microcosmic view, such as the quantitative analysis of tissue water molecular diffusion

movement in three-dimensional space, and using tissue water molecular diffusion anisotropy to infer tissue ultrastructural characteristics and pathological changes. Therefore, DTI is an effective means for the early study of cerebral white matter lesions.[4]

For the choice of ROI, we read relevant literature and found that in the study of patients' cerebral white matter the centrum semiovale white matter was often selected as the ROI, with some researchers also detecting the whole brain FA values. In our research, we choose the frontal, temporal, parietal, and occipital lobe and the semi-oval area as the ROI to obtain the DTI data. One previous study showed that frontal lobe damage was an important cause of cognitive dysfunction.[2] The study was through examination of DTI on the frontal lobe, temporal lobe, parietal lobe, occipital lobe, and semi-oval region, and collected the corresponding brain regions' FA value. Meanwhile, there was no any statistical difference between the 2 hemispheres in the same patients. Morphological changes of fiber bundles in different brain regions were also observed. The statistical analysis found that the FA value of patients with hydrocephalus cognitive dysfunction decreased significantly in the frontal, parietal, semi-oval region, which is consistent with previous study, which also showed that whole brain average FA values were reduced in patients with cognitive impairment.[5] The study also found that the FA values in the frontal lobe and centrum ovale increased significantly after insertion of a ventriculo peritoneal shunt and after follow-up of one year, suggesting that the function of nerve fibers had some improvement. On the neuropsychological evaluation, we found that the abilities of the execution of vision and space, name, attention, and abstract power were obviously improved, which also confirmed the restoration of nerve function.

This pilot study has several limitations. First, some cases were lost to follow-up, which influenced the data integrity of the postoperative patients. Secondly, as our study group included only 30 patients, we cannot be certain regarding the reliability of the results, and a larger number of patients would provide more certainty. Therefore, further studies of the specific mechanism causing changes in hydrocephalus cognitive dysfunction and the specific pathological physiology are required.

In conclusion, the use of DTI technology for the acquisition of FA values is beneficial in detecting early hydrocephalus brain damage. This will provide guidance for the individualized treatment of hydrocephalus, which is very important in improving cognitive function in hydrocephalus patients and further improving patient quality of life.

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From the Department of Neurosurgery (Cheng, Hong), Department of Pathology (Wang), and the Department of Radiology (Hu), First Affiliated Hospital of AnHui Medical University, Hefei, China. Address correspondence and reprints request to: Dr. HongWei Cheng, Department of Neurosurgery, First Affiliated Hospital of AnHui Medical University, No. 218 JiXi Road, Hefei, AnHui 230032, China. Tel. +86 (139) 55173701. E-mail: 524594636@qq.com

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