MRI Diffusion Tensor Imaging (DTI) in Assessment of White Matter Tracts in Primary Dystonia

HAITHAM M. FODA, M.Sc.*; AHMED F. YOSSEF, M.D.**; AMANEY M. EL-KHARBOTELY, M.D.* and SHERIF A. MOUSTAFA, M.D.*
The Department of Radio-Diagnosis, Faculty of Medicine, Benha University

Abstract

Background: Diffusion tensor magnetic resonance imaging (DTI) is the only noninvasive technique that can be used to assess micro-structural integrity of white matter structures and depict brain connectivity in vivo. This study was undertaken to evaluate white matter changes in primary dystonia using DTI-FT.

Methods: We evaluated 24 patients with primary dystonia and 24 age-and sex-matched controls. Conventional non-contrast MRI followed by MR diffusion tensor imaging and fiber tractography were acquired in all of the studied population; we collected diffusion-weighted images along twelve different directions with a b value of 1000s/mm². We measured the Mean Diffusivity (MD) and Fractional Anisotropy (FA) from voxels of interest. We compared measurements in patients and controls with the high-resolution MR imaging, as well as clinical data.

Results: DTI has 100% sensitivity in detection of micro structural changes in studied cases of primary dystonia, while conventional MRI was normal in all patients.

Conclusion: This analysis visualized group level white matter tract differences between dystonia patients and normals. This analysis can be useful in understanding the pathophysiology of primary dystonia.


Introduction

IN the last decade, advances in the field of Magnetic Resonance Imaging (MRI) have led to the design of different innovative imaging techniques. Diffusion Tensor Imaging (DTI) is one such MRI technique that has generated great interest in clinical studies. DTI attempts to analyze the magnitude and orientation of random microscopic motion of water molecules in the brain tissue. This technique provides details on the tissue microstructure and organization. With DTI, diffusion anisotropy can be quantified and subtle white matter changes not normally seen on conventional MRI can be detected [1].

The two main parameters derived from DTI data are Mean Diffusivity (MD) and Fractional Anisotropy (FA) [2,3]; MD reflects the average magnitude of molecular displacement by diffusion. FA reflects the directionality of molecular displacement by diffusion. A disruption of brain micro-structural environment in various neurologic conditions will lead to the changes of MD and FA values. This technique has been used to detect pathological changes in the nervous system in various neurological conditions including cerebral ischemia, multiple sclerosis [4] and brain tumor [5,6].

DTI relies on thermally driven random motion of water molecules also known as Bronwian motion, to supply tissue micro structural information in vivo (Le Bihan et al., 1986; Chenevert et al., 1990). In unconstrained water molecules in a pure liquid environment free of impediments diffusion is equal in all directions. The situation is referred to as ‘isotropic’. In brain tissue, however, water diffusion is considerably reduced due to numerous barriers such as myelin sheaths, cell membranes, and white matter tracts. Diffusion of the water molecules is less restricted along the long-axis of a group of aligned tissue fibers than perpendicular to it. The condition of directionally dependant diffusion referred to as ‘anisotropic’. In Diffusion Weighted Imaging, (DWI) diffusion is described using a scalar parameter, the diffusion coefficient D. In the presence of anisotropy, diffusion can be characterized by a tensor D, which described the mobility of the molecules in each
direction and the correlation between these directions. Quantities related to diffusion can be determined from the tensor (matrix). The two most commonly used DTI metrics are Fractional Anisotropy (FA) and Mean Diffusivity (MD). FA (equation 1) measures the degree of directionally of diffusion while MD (equation 2) measures the magnitude of diffusion [1].

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FA(\lambda_1, \lambda_2, \lambda_3) = \frac{1}{\sqrt{2}} \sqrt{\frac{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}
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MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}
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Primary Torsion Dystonia (PTD) is a chronic movement disorder manifesting clinically as focal or generalized sustained muscle contractions, postures, and/or involuntary movements [7].

PTD is thought to be a neuro-developmental disorder affecting motor circuits (particularly striato-thalamic and cerebellar pathways), but the details are not yet worked out. Diffusion Tensor Imaging (DTI) has exquisite ability to visualize the white matter pathways and may be useful in understanding the underlying pathology in this disease [8].

Patients and Methods

Twenty-four patients (18 females, 6 males) with idiopathic dystonia (mean age, 52 years) and 24 age-and sex-matched controls (18 females, 6 males; mean age, 53 years, \(p > 0.05\)) were enrolled in this study between August 2014 and February 2016 in Mansoura University Hospitals referred from outpatient clinic.

Acquisition of MR images:

A 1.5-T MR unit (ingenia; Philips Medical Systems) was used. The following sequences were acquired: T2 weighted sequences, Fluid Attenuated Inversion Recovery (FLAIR), T1-weighted sequences. DT imaging data were acquired by using a single-shot echo-planar imaging sequence with the sensitivity-encoding, or SENSE, parallel-imaging scheme (reduction factor, 2). The imaging matrix was 128 X 128, with a field of view of 220 X 220mm. Transverse sections of 2.75mm thickness were acquired parallel to the anterior commissure-posterior commissure line. A total of 50 sections covered the entire hemisphere and brainstem without gaps. Diffusion weighting was encoded along 12 independent orientations, and the b-value was 1000mm²/sec. Other imaging parameters were as follows: Echo time=70msec, repetition time=6,599-8,280msec, number of acquisitions=two.

Data processing:

We transferred the diffusion-tensor imaging data to an offline workstation (extended work space “EWS”) (Release 2.6.3.5; Dell, Round Rock, Tex); Pride software (Philips Medical Systems) which is based on the Fiber Assignment by Continuous Tracking (FACT) method which is an algorithm depends on the direction of anisotropy (the principal eigenvector of the diffusion tensor) and proceeds from an initially determined point (or set of points) in the direction of the principal eigenvector from pixel to pixel (continuously updating the direction as it assesses each new pixel). This process continues until a predetermined lower FA threshold is encountered, often an FA value of 0.3 or greater than 70º for the trajectory angles between the ellipsoids, at which point the fiber path is terminated. This pixel of lower FA would no longer be dominated by white matter, thus indicating the termination of the tract. Anisotropy was calculated by using orientation-independent Fractional Anisotropy (FA), and diffusion-tensor MR imaging-based color maps were created from the FA values and the three vector elements. The vector maps were assigned to red (x element, left-right), green (y, anterior-posterior), and blue (z, superior-inferior) with a proportional intensity scale according to the FA.

Estimation of DTI indices:

Fractional Anisotropy (FA) and Mean Diffusivity (MD), which is also termed Apparent Diffusion Coefficient (ADC), are measures by placing ROI (Region of interest) on the preferred place on the anatomical diffusion map. FA and MD measured at genu, body, and splenium of the corpus callosum, posterior limb of internal capsule, and the subcortical white matter of the cerebellar hemispheres, as well as on grey matter structures including the caudate head, putamen, globus pallidum, thalamus, and Supplementary Motor Area (SMA).

We first examined the conventional MRI images searching for any signal abnormality. Then we started to examine color-coded DTI maps, followed by tractography of individual tracts.

Results

Twenty-four patients with dystonia (mean age 52 years) were enrolled in this study. The mean disease duration was 13.4 years (SD 10.4) and the mean age at disease onset was 37.1 years (SD 15.2).
Conventional MRI failed to detect abnormalities in dystonia patients, while DTI measurements revealed statistically significant reduction in FA and increase in ADC in caudate, lentiform nuclei as well as thalamus, prefrontal area, cerebellar hemispheres and cerebellar vermis when compared to age matched controls. Tractography revealed no significant changes of selected white matter tracts as compared to the control subjects.

Measuring FA and MD values in of patients with dystonia revealed statistically significant ($p < 0.05$) reduction in FA and increase in MD in the affected side as compared to the normal age-and sex-matches controls. The mean FA value of the diseased side was 0.29 as compared to 0.7 of normal. The mean MD value of the lesion side was $1.13 \times 10^{-3} \text{mm}^2/\text{s}$ as compared to $0.98 \times 10^{-3} \text{mm}^2/\text{s}$ of the normal.

Fig. (1): 5 years old female child known to have dystonia. (A) Axial FLAIR image at the level of the basal ganglion shows no significant abnormalities. (B, C and D) Are DTI color maps measuring FA and ADC value in prefrontal, caudate, thalamus, lentiform, cerebellar hemispheres and vermis. These measures are compared with age matched control. The significant findings are reduced FA and increase ADC values of the left caudate nucleus (FA 0.29 and ADC $1.958 \times 10^{-3} \text{mm}^2/\text{s}$) as compared to the right one (FA 0.33 and ADC $0.964 \times 10^{-3} \text{mm}^2/\text{s}$). The rest of measurements are not significant when compared to both sides but show significant difference when compared to the control. (E, F) Are DTI tractography images for the thalamoprefrontal tracts and middle cerebellar peduncles respectively show normal pattern. Accordingly diffusion tensor findings are going with the clinical diagnosis of dystonia and give special predilection to the left caudate nucleus.
Fig. (2): 16 years old female patient with dystonia. (A) Axial FLAIR images show no significant abnormalities. (B, C and D) ARE colored diffusion maps with selected ROIs at prefrontal, caudate, thalamus, lentiform, cerebellar hemispheres and vermis measuring FA and ADC values. These measurements are compared with age matched control. There is reduced FA and increase ADC values of the left caudate nucleus and the cerebellar vermis as compared to age matched control. Patient's FA of left caudate 0.255, right caudate 0.342 and vermis 0.276 compared to control, FA of left caudate 0.425, right caudate 0.37 and cerebellar vermis 0.387. ADC values of patient's left caudate = 1 X 10^{-3} \text{mm}^2/\text{s}, right caudate 0.88 X 10^{-3} \text{mm}^2/\text{s} and vermis 1.17 X 10^{-3} \text{mm}^2/\text{s} compared to control's left caudate 0.745 X 10^{-3} \text{mm}^2/\text{s}, right caudate 0.801 X 10^{-3} \text{mm}^2/\text{s} and vermis 0.817 X 10^{-3} \text{mm}^2/\text{s}. The rest of measurements are not significant when compared to both sides but show significant difference when compared to the age matched control. (E and F) Are tractography of the CSTs and MCPs show that patient had increased diffusivity of left MCP (1.13 X 10^{-3} \text{mm}^2/\text{s}) and both CSTs (right 0.95 X 10^{-3} \text{mm}^2/\text{s} and left 1 X 10^{-3} \text{mm}^2/\text{s}) as compared to control subject (left MCP 0.98 X 10^{-3} \text{mm}^2/\text{s}, right CST 0.86 X 10^{-3} \text{mm}^2/\text{s} and left CST 0.81 X 10^{-3} \text{mm}^2/\text{s}). These data show decreased integrity of white matter tracts as compared to control and supported the clinical diagnosis of dystonia.
Discussion

This study, aimed to evaluate white matter changes in primary dystonia patients using DTI. The study was conducted on 24 patients with clinical manifestations of dystonia to demonstrate how DT mapping further elucidate white matter changes. The majority of the studied cases were above 30 years, and mostly female (75%).

Colosimo et al., [9] studied 15 patients with primary cervical dystonia and analyzed the FA and MD at genu, body, and splenium of the corpus callosum, PLIC, and the subcortical white matter of the cerebellar hemispheres, as well as on grey matter structures including the caudate head, putamen, globus pallidum, thalamus, and Supplementary Motor Area (SMA) and found that conventional MRI were normal in all patients, however patients with cervical dystonia had higher FA values than controls in the putamen and lower FA values in the genu and body of the corpus callosum. Patients also had lower MD values than controls in the globus pallidum, putamen and the caudate. The rest of measurements showed no significant difference between the patients and control.

In the current study, conventional MRI failed to detect abnormalities in primary dystonia patients, while DTI measurements revealed statistically significant reduction in FA and increase in ADC in caudate, lentiform nuclei as well as thalamus, prefrontal area, cerebellar hemispheres and cerebellar vermis when compared to age-sex matched controls. Tractography revealed no significant changes of selected white matter tracts as compared to the control subjects.

In conclusion, DTI provides a powerful noninvasive tool to study complex brain tissue architecture. The previous results showed that primary dystonia patient that had previous normal appearing conventional MRI has significant changes in white matter tracts using DTI, these findings can be useful in understanding the pathophysiology of primary dystonia.

So, despite its limitations and potential pitfalls, DTI has proven to be the only method of demonstrating the disease effect on white matter tracts in vivo even if there is no abnormality detected in conventional MRI images.

References


الملخص العربي

يعتبر التصوير المغناطيسي باستخدام الانتشار الجزيئي للمسار عصبى وسيلة حديثة تمكنتنا من معرفة اتجاهات وسلامة الآليات العصبية في الكائن الحي وهو يتميز بقدرته على استكشاف الورشات الدماغية في الجسم الحي.

البحث الحالي تم على 24 مريضاً في مختلف المراحل العمرية ويعانون من خلل الثوبر وتم إجراء هذه الدراسة في الفترة من أغسطس 2014 وحتى فبراير 2015.

تم عمل رنين مغناطيسي على المخ متبوءاً بفحص الرنين المغناطيسي باستخدام الانتشار الجزيئي للمسارات العصبية لجميع الحالات.

وقد أوضح الدراسة الرنين المغناطيسي باستخدام الانتشار الجزيئي للمسارات العصبية أكثر حساسية من الرنين المغناطيسي العادي في الكشف عن وجود اضطرابات في المخ وعن طريق رسم المسارات العصبية تستطيع تحديد مسار العصب المتأثر بالمرض.

في حالات خلل الثوبر لم يكن الرين المغناطيسي العادي يسمح بتشخيصها وقد أوضح الرين المغناطيسي باستخدام الانتشار الجزيئي للمسارات العصبية دوره الكمي في تشخيص وتفاوت خلل الثوبر محل الدراسة.

أخيراً: فهو المأمون القول بأن التصوير المغناطيسي باستخدام الانتشار الجزيئي للمسارات العصبية قد هو لذا الفرصة لتحديد التغيرات في الآليات العصبية والتواترة عن خلل الثوبر.

وفي الختام، فإن الرنين المغناطيسي باستخدام الانتشار الجزيئي للمسارات العصبية آداة قوية وحديثة لدراسة وتشخيص خلل الثوبر.

وي ينبغي النظر أن هذه التقنية الجديدة خطوة هامة إلى الأمام في التشخيص الإشعاعي العصبي الحديث.