Does motor deficit in children with cerebral palsy correlate with diffusion tensor metrics abnormalities in thalamocortical pathways?

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Abstract

Background: Cerebral palsy (CP) is a group of motor-impairment signs secondary to many disorders that interfere with early brain development and are usually related to white matter injury in children. Most studies are focused on the study of motor tracts, mainly the corticospinal tract (CST). Diffusion tensor imaging (DTI) is a reliable imaging modality providing an appropriate method of detection of white matter microstructure abnormalities. The purpose of this study is to investigate the relationship between DTI observed motor CST injury, sensory pathways (thalamic radiations) injury, and motor functions.

Results: This study shows significant involvement (reduction in DTI fiber count) of the superior thalamic radiation (in severe cases) with atrophy of the anterior thalamic radiations (ATR) or posterior thalamic radiations (PTR) in most cases with a significant reduction in fractional anisotropy (FA) and elevation in mean diffusivity (MD) values. In addition, the degree of motor affection shows a significant negative correlation with FA and a significant positive correlation with MD values. Diffusion tensor imaging shows a significant reduction in FA within the examined tracts between CP and control at the Rt CST, Lt CST, Rt corticothalamic radiation (CTR), and Lt CTR with significant cutoff values of ≤ 0.449, ≤ 0.472, ≤ 0.432, and ≤ 0.44, respectively.

Conclusions: This study demonstrates disruption of thalamocortical and corticospinal tracts in CP patients, which reflects that both sensory and motor tract affection have a valuable role in the pathophysiology of motor dysfunction in CP patients.

Keywords: Cerebral palsy, Diffusion tensor imaging, Diffusion tensor tractography, Gross motor function, Motor pathway, Sensory pathway

Background

Population-based studies revealed that the incidence of CP range from 1.5 to 5 per 1000 children of a defined age range [1]. The overall birth incidence of CP is about 2 per 1000 live births, and it is considered the commonest etiology of disability in children [2].

The term CP describes a variable group of conditions comprising irreversible non-progressive central motor dysfunction, which lead to impairment in muscle tone, movement, and posture. Multiple other signs are frequently associated with the primary motor abnormalities, such as altered sensation, communication, behavioral difficulties, intellectual disability, seizures, and musculoskeletal problems [3].

Periventricular leukomalacia (PVL) is supposed to be the most common neuropathological condition in premature infants and the primary etiology of CP development [4].

From whole white matter tracts, the pyramidal tract and thalamic radiations undergo early maturation. Throughout the process of brain maturation, these two

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essential white matter pathways are susceptible to injuries that lead to neurologic affections, with subsequent development of the typical manifestations of bilateral (either diplegia or quadriplegia) spastic CP in children born preterm [5].

Brain imaging researches via conventional magnetic resonance imaging (MRI) have demonstrated that 80% of affected children have abnormal brain structures [6].

Despite conventional magnetic resonance imaging has a role in recognition of WM affection, it does not give data about the extent of specific WM tracts injury. Diffusion tensor imaging (DTI) detects restrictions in the random water molecules movement by different tissue barriers as myelin and can be used to reconstruct affected WM tracts [7].

DTI estimation of fractional anisotropy (FA) values in different brain areas can provide quantitative as well as qualitative information about the white matter tracts, and could evaluate abnormalities in white matter, and also can provide useful data in terms of white matter repair. Nowadays, DTI is considered a helpful tool in evaluating white matter injury, providing precise data about the disease severity and prognosis [8].

In this study, we assess the average values of fractional anisotropy (FA) and mean diffusivity (MD), as well as fiber count in CST and thalamic radiations in children diagnosed as CP with age/sex-matched controls, aiming to determine if both motor and sensory tract injury would show correlation with clinical motor grades assessed by Gross Motor Function Classification System (GMFCS).

Methods

Informed consent was obtained from the parents according to our Institutional Review Board.

Patients

This prospective case–control study was done between 2017 and 2020 on 96 children; of them, 70 were diagnosed clinically as CP patients, and 26 were the control group. A total of 70 patients with CP, 46 males (65.7%) and 24 females (34.3%), were recruited; their ages ranged from 2 to 15 years. Enrollment criteria were as follows: children aged more than 2 years; they are diagnosed clinically as CP patients; they required brain MRI either for diagnosis or follow-up. Exclusion criteria were as follows: children with myelodysplasias and neuromuscular disorders; children with cochlear implants or cardiac pacemaker. The control group included ten girls (38.5%) and 16 boys (61.5%); their ages ranged from 2 to 15 years.

Assessments

Clinical assessment was done with the detailed perinatal history of preterm labor, caesarian section delivery, low birth weight, birth hypoxia, and neonatal intensive care unit (NICU) admission; motor neurological examination by a pediatric neurologist was also recorded and involved CP type (either diplegia, quadriplegia or hemiplegia), and best motor skill achieved by patients using GMFCS.

MRI acquisition protocol

MRI study with standard sequences (axial T1/T2 & FLAIR) precede the DTI protocol, done on a 1.5-T whole-body scanner (Ingenia; Philips Healthcare Medical Systems, Best, Netherlands) using head-neck coil with the head maintained in a supine position.

All patients were sedated using 10% Chloral hydrate. It was given in a dose of 0.25–0.50 ml/kg orally or by nasal feeding; then, patients were subjected to a scan after sleeping soundly. No patient was in need of general anesthesia.

(A) Conventional MRI sequences

All imaging was performed in the axial plane with the following parameters: 5 mm slice thickness, 0.5 cm interslice gap, FOV 250×170 mm^2, and matrix 80×80. Routine sequences with the following parameters were used: T1-weighted sequences (TR 450 ms, TE 15 ms); T2-weighted sequences (TR 3960 ms, TE 110 ms); FLAIR (TR 6000 ms and TE 120 ms and TI 1800 ms).

(B) Diffusion tensor imaging (DTI)

It was acquired after the routine sequences using single-shot EPI sequence with the sensitivity-encoding, or SENSE, parallel-imaging scheme (reduction factor, 2) (repetition time: 7300 ms; echo time: 75 ms), with a diffusion-encoding gradient in 15 independent orientations, imaging matrix 128×128, FOV of 230 mm, b value of 1000 mm^2/s, and number of acquisitions = two. Transverse sections of 2.75 mm thickness were obtained parallel to the anterior commissure–posterior commissure line. Fifteen sections enclosed the whole hemisphere and brainstem with no gaps. The total imaging time range from 10 to 25 min according to the sequences added to the routine MR imaging examinations.

(III) Diffusion tensor tractography (DTT)

Reconstruction of specific WM tracts was conducted by streamline tractography by utilizing fiber assignment

continuous tracking algorithm (FACT). It is mainly reliant on anisotropy direction and proceeds from an initially determined point in the direction of the principal eigenvector from voxel to voxel. Multiple ROIs were manually defined by freehand drawing and assigned to the specific tract anatomical course. The termination criteria used for fiber tracking comprised an FA threshold of < 0.2 and an angle change between the ellipsoids of > 45°, at which points the fiber path is terminated.

Multiple ROIs were utilized for a tract of interest, with two ROI types; inclusion (and) ROI and exclusion (not) ROI, the choice of which depended on the distinctive trajectory of each tract. WM fibers that penetrate the manually defined inclusion ROIs with dissection of those penetrating the exclusion ROIs were assigned to the specific tracts. Fibers outside the tracts of interests were discarded by utilizing the "NOT" operation.

MRI data processing and analyses

DTI imaging data was transferred to an offline workstation (extended workspace "EWS") (Release 2.5.3.0; Dell, Round Rock, Tex); Pride software (Philips Medical Systems). The following maps were obtained: FA maps, directionally encoded color FA maps, 3D fiber tractography maps.

(A) Qualitative analyses

(1) 2D analyses

Anisotropy values are calculated for each voxel, and FA uncolored and colored maps are created, where color scheme (red–green–blue colors) reflects tract direction (i.e., the red color representing fibers with right-left orientation; green representing antero-posterior direction; and blue color for cranio-caudal orientation) and color brightness/hue represents diffusion anisotropy (FA) value.

(2) 3D analyses ⇨ Diffusion tensor tractography (DTT)

The 3D track reconstruction was carried out by utilizing the FACT approach.

Reconstruction of tracts

Thalamic radiations

To reconstruct the thalamic radiations, *anterior thalamic radiation*: the first ROI was placed in the axial slice (thalamus), and the second ROI was placed in the coronal slice (frontal lobe); *superior thalamic radiation*: the first ROI was placed in the axial slice (thalamus), while the second ROI was placed over (frontal and parietal lobes) in the axial slice; *posterior thalamic*

radiation: the first ROI was positioned in the axial slice (thalamus), and the second ROI was positioned in the coronal slice (occipital lobe).

Corticospinal tract (CST)

The CST arises from the precentral motor cortex and descends via the corona radiata and posterior 1/3 of the PLIC to the pons and caudally the medulla and spinal cord. The first ROI is positioned on the color map over the anterior pons. The second ROI is positioned ipsilateral over the motor cortex.

(B) Quantitative analyses (estimation of DTI metrics)

DTI metrics including FA, MD (ADC values) for CST, and CTRs were automatically computed for the entire reconstructed tract, and the average values for each tract were calculated. After that, the number of fibers was measured in all depicted tracts individually. Such measurements are considered as a type of DTT parameter, which means a quantitative measure of connectivity between anatomical locations as detected by the ROIs.

For this study, the analysis was focused on thalamo-cortical pathways and corticospinal tracts. We suppose that the corticothalamic radiations (transmitting sensory impulses) and the corticospinal tracts (transmitting motor orders) are responsible for the clinical picture of CP patients.

Statistical analysis

Statistical analysis was carried out by utilizing IBM SPSS (Statistical Package for Social Science) Corp. Released 2013. IBM SPSS Statistics for Windows, Version 20. Armonk, NY: IBM Corp. Qualitative data were defined by utilizing number and percent, while quantitative ones were defined by utilizing median (minimum and maximum) for non-parametric data and mean, and the standard deviation for parametric data following testing normality using Kolmogorov-Smirnov test. Analysis of ranked variables was performed using Spearman's rank correlation test. A significance level of 0.05 was utilized for all the previously utilized tests.

Results

Descriptive results and clinical features

In this study, 96 children were scanned (Table 1): 70 of them were diagnosed clinically as CP, they included 46 males (65.7%) and 24 females (34.3%) with an average age of 3 years (range 2–15 years). The other 26 children constitute the control group (including ten girls (38.5%) and 16 boys (61.5%) with a mean age of 5 years (range

Table 1 Demographic characters of the studied cases

Variables	CP group (n = 70)		Control group (n = 26)		Test of significance
	No	%	No	%	
Sex					²= 0.145
Male	46	65.7%	16	61.5%	p = 0.704
Female	24	34.2%	10	38.4%	
Age/years					z = 1.79
Mean	3		5		p = 0.073
Range	2–15		2–12		

2–12 years). The difference in age and sex among both groups was not significant ($p > 0.05$).

The CP group included 46 (65.7 %) preterm children and 24 (34.3%) term children. The mean gestational weight was 2812.86 ± 503.52 (range, 1600–3800 g). The gestational age in infants with CP was less than those in controls. The birth weight of children with CP (2812.86 ± 503.52) was significantly lower than birth weight among the control group (3161.54 ± 181.28) ($p = 0.001$). In total, 26 (37.1%) of children were suffering from perinatal hypoxia in the CP group, whereas 36 (51.4%) were admitted to the intensive care infant unit following delivery.

In terms of gross motor functions, minimal or moderate affection (classes I, II, and III at GMFCS) was reported in 30 cases (42.85%), whereas severe affection (classes IV and V at GMFCS) was reported in 40 (57.14 %).

The pattern of damage at conventional MR imaging

In the CP group, abnormalities were observed in 54 children (77.1%) on conventional imaging. In 16 children (22.9 %) of the CP group, conventional MRI imaging could not find abnormalities compatible with motor affection.

Most of the studied patients had periventricular white matter injury (57.1 %), followed by grey matter damage (8.6%), malformations (5.7%), and miscellaneous disorders (2.9 %). In terms of MRI results, 22.9% of the studied CP patients and all control groups showed normal conventional MRI studies.

DTI metrics analysis

Group comparison of FA values among CP cases and controls revealed lower FA values within CST and CTRs in the patient group.

Tables 2 shows mean FA and MD measurements in each tract compared among two groups. There is an overall tendency of decreased FA in the CP groups compared to FA in the control group with statistically significant p values ($p < 0.001$).

Correlation among DTI metrics and clinical motor grade

A significant negative association among clinical motor grade assessed by GMFCS and FA values was noticed in both right* and left** CST (*$r = -0.749$, $p < 0.001$; **$r = -0.651$, $p < 0.001$) and CTR (*$r = -0.653$, $p < 0.001$; **$r = -0.642$, $p < 0.001$) tracts. Significant positive correlation with MD was noticed in right CST ($r = 0.216$, $p = 0.034$) and right* and left** CTR (*$r = 0.408$, $p = 0.005$;

Table 2 Mean FA, MD values, fiber counts, and standard deviations measured in both CST and thalamic radiations in CP group and control group

	Right			Left		
	Case	Control	Test of significance	Case	Control	Test of significance
CST						
FA	0.395 ± 0.045	0.520 ± 0.058	**t = 11.15 p < 0.001***	0.379 ± 0.09	0.516 ± 0.05	**t = 7.55 p < 0.001***
MD	0.997 ± 0.165	0.930 ± 0.149	t = 1.79 p = 0.08	0.962 ± 0.234	0.913 ± 0.119	t = 1.01 p = 0.313
Fiber count	204.65 ± 154.68	1520.08 ± 126.0	**t = 38.80 p < 0.001***	182.83 ± 141.59	1480.38 ± 160.06	**t = 38.50 p < 0.001***
CTR						
FA	0.371 ± 0.02	0.469 ± 0.09	**t = 6.15 p < 0.001***	0.359 ± 0.08	0.458 ± 0.03	**t = 4.33 p < 0.001***
MD	1.042 ± 0.01	0.923 ± 0.02	**t = 27.44 p < 0.001***	1.066 ± 0.08	0.925 ± 0.05	**t = 5.92 p < 0.001***
Fiber count	773.84 ± 250	2022.11 ± 310	**t = 14.39 p = 0.001***	765 ± 102	1969 ± 120.5	**t = 34.60 p = 0.001***

RT, right; *LT*, left; *CST*, corticospinal tract; *CTR*, corticothalamic radiations; *MD*, mean diffusivity

A two-sample *t*-test analysis was performed to compare the results of ROI-based data between the CP and control groups. $p < 0.001$ was applied to correct for multiple comparisons

*Bold text denotes significant between group differences following multiple comparisons correction with a level of significance determined at $p \leq 0.001$. Units for MD is 10^{-3} mm²/s whereas FA is dimensionless

Table 3 Correlations between clinical motor grade and diffusion tensor imaging metrics (fractional anisotropy, mean diffusivity, and fiber count) of motor corticospinal and sensory corticothalamic tracts in cerebral palsy children (no = 70)

		Right CST	Left CST	Right CTR	Left CTR
FA versus GMFCS	r	− 0.749**	− 0.651**	− 0.653**	− 0.642**
	p	< 0.001	< 0.001	< 0.001	< 0.001
MD versus GMFCS	r	0.216*	0.040	0.408**	0.422**
	p	0.034	0.701	0.005	< 0.001
Fibers count versus GMFCS	r	− 0.834**	− 0.815**	− 0.708**	− 0.728**
	p	< 0.001	< 0.001	< 0.001	< 0.001

r Spearman correlation coefficient
**Statistically significant
Range of correlation coefficient values r: − 1.00 to − 0.80 very strong negative; − 0.79 to − 0.60 strong negative; − 0.59 to − 0.40 moderate negative; − 0.39 to − 0.20 weak negative; − 0.19 to − 0.01 very weak negative; r: 0.80 to 1.00 very strong positive; 0.60 to 0.79 strong positive; 0.40 to 0.59 moderate positive; 0.20 to − 0.39 weak positive; 0.00 to 0.19 very weak positive

$**r = 0.422$, $p < 0.001$). Also, significant negative correlation among fiber count was noticed in both right* and left** CST (*$r = − 0.834$, $p < 0.001$; **$r = − 0.815$, $p < 0.001$) and right* and left** CTR (*$r = − 0.708$, $p < 0.001$; **$r = − 0.728$, $p < 0.001$) (Table 3).

ROC curve analysis

ROC curve analysis (Figs. 1 and 2) was carried out to assess the significance of cutoff values of FA distinguishing CP and the control group (Table 4), demonstrating right CST FA cutoff value was 0.449 with sensitivity 88.6%, specificity 92.3%, PPV 75%, NPV 96.9%, and accuracy 89.6%, whereas left CST cutoff value was 0.472 with sensitivity 91.4%, specificity 84.6%, PPV 78.6%, NPV 94.1%, and accuracy 89.6%.

For right CTRs, FA cutoff value was 0.432 with sensitivity 94.3%, specificity 92.3%, PPV 97.1%, NPV 85.7%, and accuracy 93.8%, whereas for left CTRs cutoff value was 0.44 with sensitivity 97.1%, specificity 76.9%, PPV 91.9%, NPV 90.9%, and accuracy 91.7%.

Also, there were significant differences among both studied groups in the measurement of MD values in different tracts (Table 5). For right CST, MD cutoff value was 0.903 with sensitivity 71.4%, specificity 69.2%, AUC = 0.638, PPV 86.2%, NPV 74.4%, and accuracy 70.83%; whereas for left CST cutoff value was 0.885 with sensitivity 91.4%, specificity 53.8%, AUC = 0.622, PPV 80.6%, NPV 41.2%, and accuracy 66.7%.

For right CTRs, MD cutoff value was 0.905 with sensitivity 70.1%, specificity 68.6%, PPV 45%, NPV 85.7%, and accuracy 69%, whereas for left CTRs cutoff value was 0.909 with sensitivity 75.7%, specificity 76.9%, PPV 89.7%, NPV 52.6%, and accuracy 77%.

Discussion

DTI has been essential to understanding the complexity and variability in brain injuries among CP children [9].

In this study, we assessed abnormalities on diffusion magnetic resonance imaging associated with CP. CP group included 46 (65.7 %) preterm children and 24 (34.3%) term children. The mean gestational weight was 2812.86 ± 503.52 (range, 1600–3800 g). The gestational age in infants with CP was less than those in controls. The birth weight of children with CP (2812.86 ± 503.52) was significantly lower than birth weight among the control group (3161.54 ± 181.28) ($p = 0.001$).

Such findings followed those of Schieve et al. [10], who reported that low birth weight-preterm and average birth weight-preterm were associated with CP. Also, coping with the study done by McIntyre et al. [11], it described that the smaller the infant for gestational age and the lower the birthweight, the higher CP risk.

In this study, we found that 26 (37.1%) of children suffer from perinatal hypoxia, whereas 36 (51.4%) were admitted to the intensive care infant unit following delivery. These findings are in coping with a study done by Mcintyre et al. [11], which conclude that birth asphyxia was the powerful and the most reliable predisposing factor for CP and also with a study done by Ahlin et al. [12], which conclude that a neonatal

Table 4 The overall sensitivity, specificity, PPV, NPV, and AUC of FA values in CP and control group in CST and CTR

Test result variable(s)	AUC	p	Cutoff point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
RT CST	0.951	< 0.001*	0.4490	88.6	92.3	75.0	96.9	89.6
LT CST	0.956	< 0.001*	0.4725	91.4	84.6	78.6	94.1	89.6
RT CTR	0.965	< 0.001*	0.432	94.3	92.3	97.1	85.7	93.8
LT CTR	0.965	< 0.001*	0.440	97.1	76.9	91.9	90.9	91.7

*means that the values are Statistically significant

Table 5 The overall sensitivity, specificity, PPV, NPV, and AUC of MD values in CP and control group in CST and CTR

Test result variable(s)	Area	p	Cutoff point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
RT CST	0.638	0.038*	0.9035	71.4	69.2	86.2	47.4	70.83
LT CST	0.622	0.067	0.8855	71.4	53.8	80.6	41.2	66.7
RT CTR	0.758	0.001*	0.905	70.1	68.6	45.0	85.7	69.0
LT CTR	0.762	0.001*	0.909	75.7	76.9	89.7	52.6	77.0

*means that the values are Statistically significant

encephalopathy and NICU admission are among the most substantial risk factors for CP.

This study revealed that the most common brain lesions on conventional MRI were white matter lesions (60%), followed by grey matter lesions (8.6%), brain malformations (5.7%), and lastly, postnatal events (2.9 %). Finally, 22.9% of studied patients had normal conventional MRI findings.

These findings were in agreement with those of Bax et al. [13], who observed that conventional MRI scans demonstrated that white matter injuries, such as PVL, were the most typical feature (42.5%), followed by basal ganglia affection (12.8%), cortical/subcortical lesions (9.4%), malformations (9.1%), focal infarcts (7.4%), and miscellaneous disorders (7.1%). Only 11.7% of children showed normal MRI study.

Also, our results are coping with a study done by Franki et al. [14], which observed that most of the recorded lesions in CP cases are composed of white matter lesions (66.9% of entire lesions) then grey matter affection (18.6%) and brain malformations (4.3%). Of note, postnatal lesions developed in 16 children (1%) and the miscellaneous group (1%), while they (8.2%) show no insult on conventional MRI.

In contrast to conventional MRI, this study demonstrated a significant decrease in fractional anisotropy and fiber count and the CST on the affected side compared with control subjects. Also, there has been an increase in MD observed in this tract.

Such findings are consistent with those of Scheck et al. [15], who reported decreased FA and increased MD within the corticospinal pathway. These findings propose a reduction in CST integrity in comparison with typically developing children. Diffusion MRI and tractography research revealed additional proof of injury or perturbed initial development of this pathway.

Our results are also in the same line with those of Cho et al. [16] study who displayed that many DTI and DTT researches had demonstrated evidence of deficits in the CST of CP cases. The most expected recorded findings were the reduction in the number of fibers [17], reduction in FA, and increase in MD values [18].

These findings were in disagreement with those of Rha et al. [17], who reported that the numbers of fibers, but not FA or MD values, are lower in the CSTs in children with low gross motor function. This difference is due to the small sample size in a study done by Rha et al. [17], and the standard deviations were large, which was associated with more possible false-negative results. Besides, narrow age ranges of cases in which DTT was performed (between 7 months and 2.9 years) may be considered another explanation.

This study showed significant involvement (decrease in DTI fiber count) of the superior thalamic radiation (in severe cases) with atrophy of the ATR or posterior thalamic radiations (PTR) in most cases with a significant reduction in FA and increase in MD values.

These findings are coping with a study done by Trivedi et al. [7] in which a significant decrease in FA values was noted in both corticothalamic tracts moving from controls to GMFCS level V. Also, all the studied groups showed higher MD values in tract than the control group.

Also, our results agree with the study done by Arrigoni et al. [19], which discover that FA was significantly reduced in the thalamic radiations; therefore, such findings revealed the significance of sensory integration in the determinism of the multilevel damage in CP.

This result was different from that of Thomas et al. [20], whose research demonstrated significant involvement (decrease in DTI fiber count) of the superior thalamic radiation without a change in the ATR or PTR. Such difference between our results may be due to a small number of subjects included in Thomas et al. [20] with different age distribution.

This study also found a strong negative correlation of FA with a clinical motor grade in the corticothalamic and a corticospinal tract, which proposes that damaged corticothalamic tracts along with CST affection might have an essential role in the pathophysiology of motor dysfunction in CP cases.

Such findings are in the same line with a study done by Weinstein et al. [21], who described correlations between diffusion measures in motor and sensory tracts and motor functions.

This result was not coped with Lee et al. [22], who reported that FA mostly within CST demonstrated a more significant correlation with motor dysfunction in

Fig. 1 ROC curve application for determination of sensitivity and specificity of FA values in (CST and CTR) in CP diagnosis
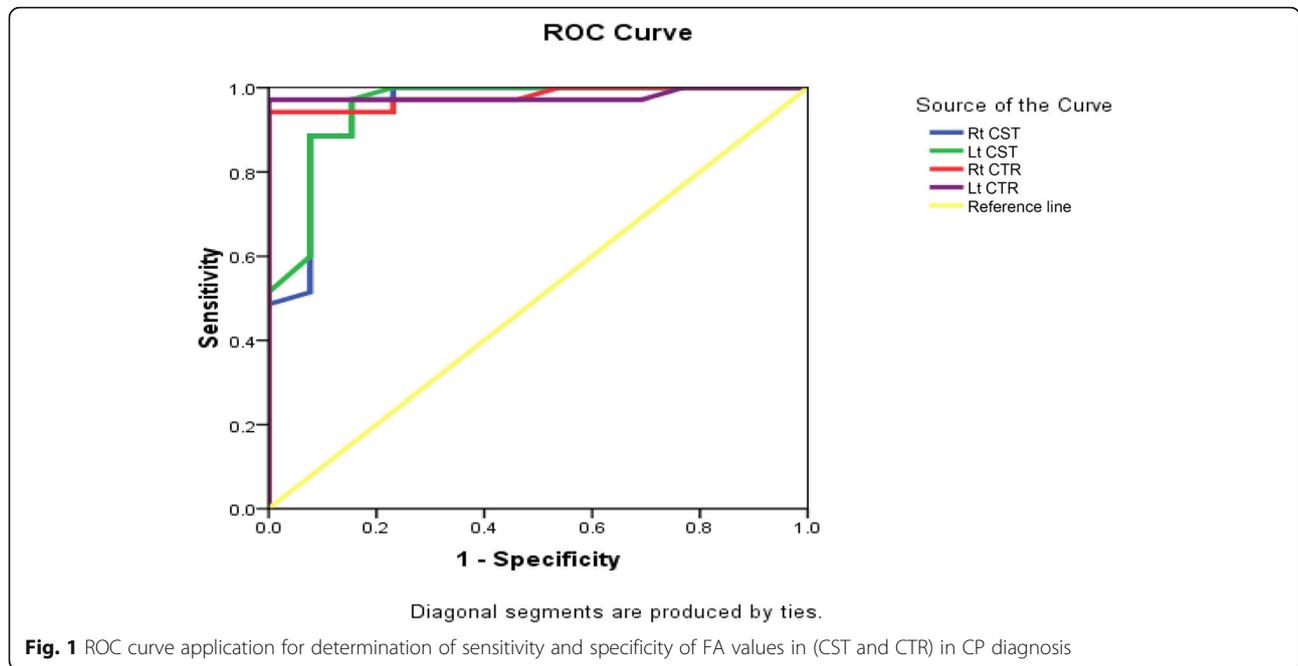
comparison with thalamocortical pathways. The difference in these results may be due to different CP (diplegic) types included in this study.

This study also revealed a significant negative correlation between fibers count and different levels of GMFCS with corresponding differences detectable on DTT in corticospinal tracts and corticothalamic radiation (Fig. 3). This agrees with that of Yoshida et al. [23], who observed that in CP cases with different GMF levels, there were difference in fiber count in CST and thalamic radiations.

The higher MD values in motor and sensory tracts of the CP cases compared with the control group may be

Fig. 2 ROC curve application for determination of sensitivity and specificity of MD values in (CST and CTR) in CP diagnosis

secondary to increased extracellular water contents due to marked gliosis and microscopic/macroscopic cystic changes that occurred in affected areas [24]. In this study, the MD values in CP cases were higher in both sensory corticothalamic and motor corticospinal tracts compared to controls, with a significant positive correlation noticed among GMFCS grade and MD values in sensory and motor pathways, which reflects an increase in extracellular water content and gliosis with higher GMFCS levels.

These findings are coping with those of Trivedi et al. [7], who observed the significant correlation between MD values noted in sensory corticothalamic and motor corticospinal tracts with clinical motor grades assessed by GMFCS.

This study revealed high sensitivity and specificity of DTI quantitative and qualitative measures in evaluating the WM tracts injury underlying CP disorders. The current results confirmed that FA values had high diagnostic values. Significant variations in FA values were observed among CP patients, and controls with detectable cutoff values of FA within CST were 0.472 (left) and 0.449 (right) tracts, and within CTR were 0.44 (left) and 0.432 (right) tracts. The significant predictive power of FA within the CTR had the highest value of accuracy (AUC 0.965), showing 97.1% sensitivity, 76.9% specificity, 90.9% negative, and 91.9% positive predictive values on the left side and 94.3% sensitivity, 92.3% specificity, 85.7% negative, and 97.1% positive predictive values on the right side.

Previous research done in 2008 by Murakami et al. [25] demonstrated that an FA threshold of 0.5 within the CST was efficient in distinguishing CP and non-CP groups, and a study done by Jiang et al. [26] also
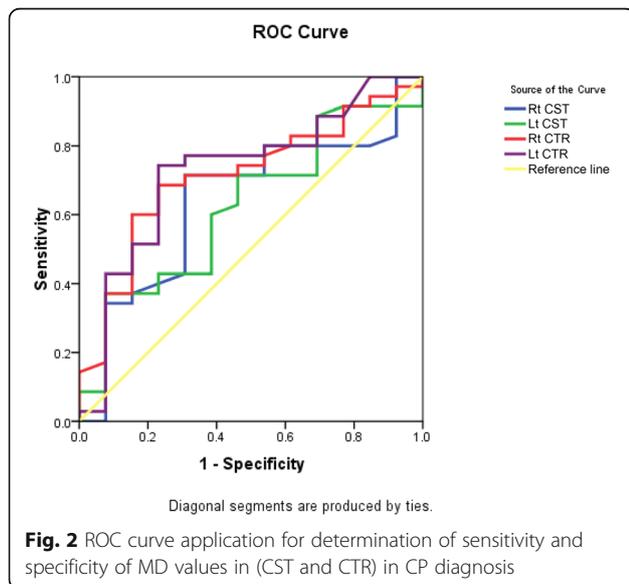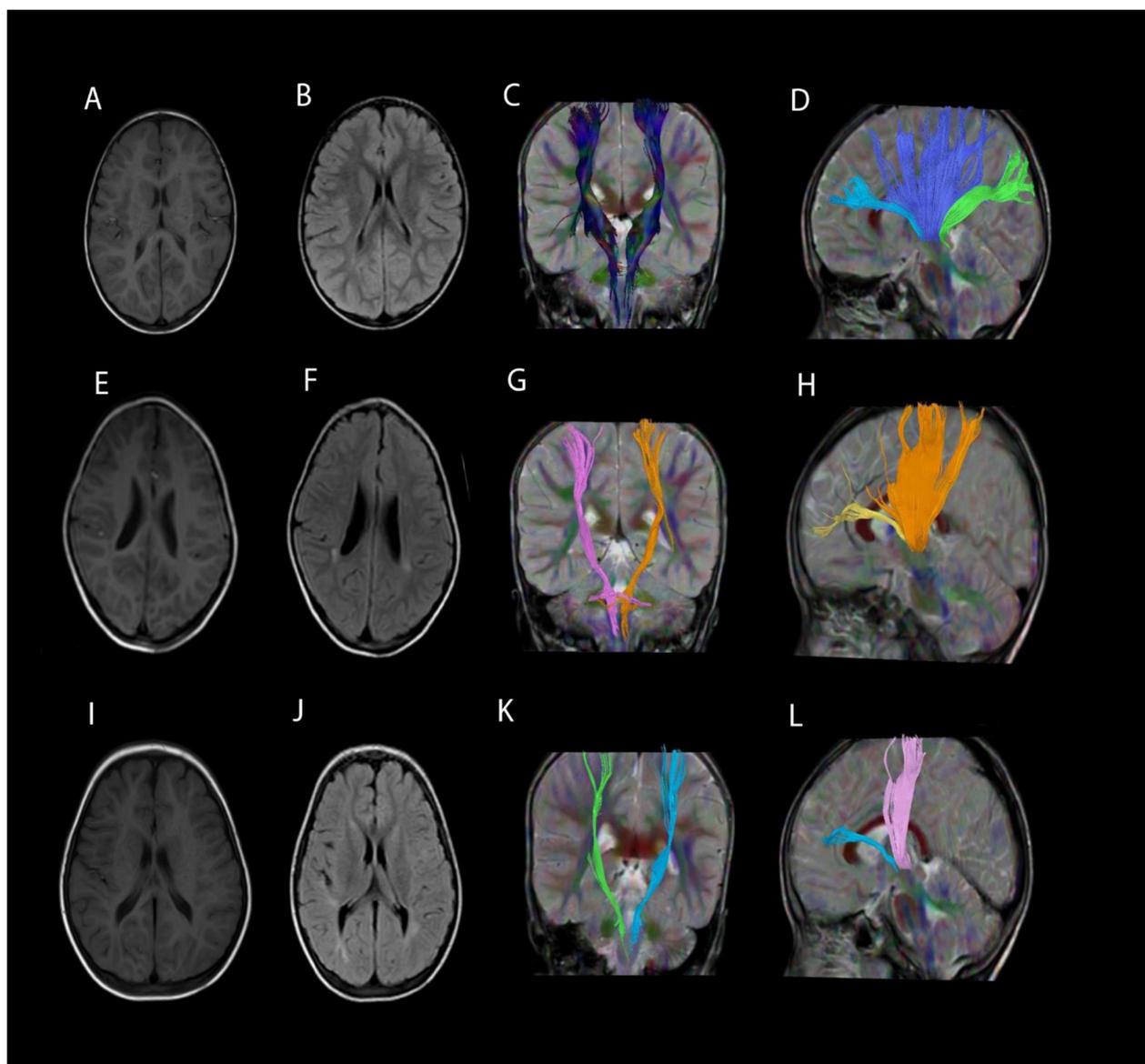
Fig. 3 Comparison between control, lower grades, and higher grades of GMFCS; control case 1st row (**a**, **b**) T1 WI and FLAIR images show normal study; **c** normal CST and **d** normal ATR (light blue colored), STR (blue colored), and PTR (green colored). Second row represents a case with mild motor affection (GMFCS II) with **e**, **f** T1 WI and FLAIR images revealed mild PVL; **g** mild thinning of CST, **h** mild thinning of STR (orange colored) and ATR (yellow colored) and absent PTR. Third row represents the case with severe motor affection with (GMFCS IV); **i**, **j** T1 WI and FLAIR images revealed mild PVL; **k** mild thinning of CST (more on right side) with **l** moderate tinning of STR (pink colored) and ATR (light blue colored) and absent PTR

revealed that FA threshold in CST for diagnosis of CP was 0.48 (left) and 0.49 (right).

This study suggests that sensory and motor tracts are affected in different degrees in CP cases, which lead to various clinical presentations in CP cases. These findings came following previous studies, which were carried out by Glenn et al. [27] and Thomas et al. [20], who suggest that both motor and sensory pathways are involved in CP patient with PVWI and a complex interplay of relative involvement of such pathways may define the

terminal outcomes of such cases and not the degeneration of either of them alone.

Our results are in agreement with those of Scheck et al. [15], who demonstrated that marked impairment to descending motor and ascending sensorimotor tracts plays a role in the neuro-pathogenesis of CP and emphasize the significance of preservation of ascending sensorimotor networks in motor functions and also offer novel insights for the design of neurorehabilitation therapy.

Also, they consist of Jiang et al. [26] and Mailleux et al. [28], who demonstrated clear associations among upper limb function and white matter integrity of the descending CST and ascending thalamocortical tracts in unilateral CP cases.

The current study has some limitations. First, the parenchymal damage in CP cases, with loss of WM volume and ventricular enlargement, might interfere with creating a standard DTI template among cases and control and affect DTI outcomes. However, the current study displayed moderate to marked ventricular enlargement in 8.5% of CP cases. The second limitation is the lack of dyskinetic and ataxic types of CP.

Conclusion

This study revealed a significant correlation between DTI measures and tractography in motor and sensory tracts with clinical motor grading. This recommends that WM tracts from the somatosensory and the motor cortex display an essential role in terms of pathophysiology of motor disability in CP cases.

Abbreviations

ATR: Anterior thalamic radiation; CTR: Corticothalamic radiation; DTI: Diffusion tensor imaging; DTT: Diffusion tensor tractography; FA: Fractional anisotropy; GMFCS: Gross Motor Function Classification System; MD: Mean diffusivity; NICU: Neonatal intensive care unit; PTR: Posterior thalamic radiation; PWI: Periventricular white matter injury; ROI: Region of interest; STR: Superior thalamic radiation

Authors' contributions
NE and AM designed the research. AM performed the research and wrote the manuscript. NE and GA analyzed the collected data. AE, AM, GA, and KM revised data and manuscript. All authors read and approved the final manuscript.

Availability of data and materials
Available on request with the corresponding author.

Declarations

Ethics approval and consent to participate
This study was approved by the research ethics committee of the Radiology Department of the Faculty of Medicine Mansoura University on 13/7/2017, Reference number of approval: MS/17.07.10. All patients included in this study gave a written informed consent to participate in the research.

Consent for publication
All patients included in this study gave a written informed consent to publish the data contained in this study.

Competing interests
The authors declare that they have no competing interests.

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