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Clinical Features Post–Anterior Cruciate Ligament Reconstruction Associated With Structural Alterations in the Corticospinal Tract

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Context: Structural evidence for corticospinal tract (CST) abnormality in patients with anterior cruciate ligament reconstruction (ACLR) compared with healthy controls and the relationships between CST structure and clinical features of the patients (eg, objective sensorimotor outcomes and postoperative duration) are lacking.

Objective: To investigate whether the structural features of the CST differ between patients with ACLR and healthy controls and are associated with clinical features in patients after ACLR.

Design: Cross-sectional study.

Setting: Sports medicine laboratory.

Patients or Other Participants: A total of 26 patients who had undergone ACLR (age = 36.35 ± 6.39 years, height = 173.88 ± 5.97 cm, mass = 74.80 ± 10.61 kg) and 26 healthy controls (age = 32.85 ± 9.20 years, height = 173.35 ± 7.19 cm, mass = 72.88 ± 11.06 kg) participated.

Main Outcome Measure(s): Using the CST as the region of interest, we performed diffusion tensor imaging to measure the microstructure of white matter tracts. Between-groups comparisons and correlation analyses with clinical features in patients with ACLR were performed.

Results: Patients with ACLR had moderately lower fractional anisotropy (Cohen d = −0.666; 95% CI = −1.221, −0.104; $P = .01$), lower axial diffusivity (Cohen d = −0.526; 95% CI = −1.077, 0.030; $P = .03$), higher radial diffusivity (RD; Cohen $d = 0.514$; 95% CI = −0.042, 1.064; $P = .04$), and smaller Y-Balance Test anterior-reach distance (Cohen d = −0.743; 95% CI = −1.302, −0.177; $P = .005$) compared with healthy controls. The RD values were correlated with the postoperative duration ($r = 0.623$, $P < .001$) after controlling for age, sex, and body mass index in patients with ACLR.

Conclusions: Patients with ACLR had impaired integrity (lower fractional anisotropy values and higher RD values) in the CST contralateral to the ACLR injured limb in comparison with healthy controls. Decreased integrity (higher RD) of the CST in patients was associated with longer postoperative duration, which hinted that impaired structural integrity of the CST may be a maladaptive process of neuroplasticity in ACLR.

Key Words: diffusion tensor imaging, sensorimotor deficit, postoperative duration, neuroplasticity

Key Points

- Patients with anterior cruciate ligament reconstruction demonstrated impaired integrity (lower fractional anisotropy values and higher radial diffusivity values) in the corticospinal tract (CST) contralateral to the anterior cruciate ligament reconstruction injured limb and smaller Y-Balance Test anterior-reach distances (sensorimotor deficits) compared with those of the healthy controls.
- Decreased integrity (lower fractional anisotropy and higher radial diffusivity) of the CST in patients was associated with longer postoperative duration.
- Novel interventions that target the corticospinal pathway might provide more effective treatments for the sensorimotor deficits and maladaptive neuroplasticity of the CST.

Anterior cruciate ligament (ACL) rupture is a common knee injury in daily life and sports, with an estimated occurrence of 8000 to more than 250 000 cases annually in the United States.[1] Individuals with ACL rupture generally undergo ACL reconstruction (ACLR) to restore the mechanical stability of the knee joint and to

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reestablish knee function,[2] followed by therapeutic rehabilitation to increase the strength of the muscles surrounding the injured knee joint.[3] However, neuromuscular deficits in cortical and spinal neural pathways,[4,5] muscle strength,[5–7] voluntary activation,[5,8] balance,[3] or a combination often persist in patients after surgery and rehabilitation. Thus, potential physiological mechanisms should be identified to develop more effective treatments targeting these neuromuscular deficits.

The corticospinal tract (CST) is essential for somatosensory and motor function.[9] Therefore, identifying existing abnormalities in the CST microstructure is imperative for clarifying the sensorimotor deficits after ACLR. Needle et al proposed that ongoing inhibition and disuse of uninjured musculature surrounding an injured joint after ligamentous injury, such as ACL rupture, might lead to maladaptive changes in both the microstructure and function of the central nervous system (CNS).[10] Based on the above hypothesis, authors of recent electrophysiological studies have shown neural excitability alterations after ACLR. For example, Lepley et al[11] observed that increased corticospinal excitability relates to increased quadriceps strength in patients after ACLR, and Pietrosimone et al[8] indicated that lower corticomotor excitability of the vastus medialis was present after surgery. However, CST structural abnormalities after ACLR are rarely explored. Given that the neural structure is the basis of function, investigating CST structural abnormalities after ACLR would provide further explanation of the aforementioned dysfunctions as well as the underlying pathological mechanisms.[10,12]

Recently, diffusion-weighted imaging (DWI) has been applied in ACLR studies to determine white matter fiber tracts via volume and the direction of water diffusion.[10] Lepley et al initially attempted to study the CST using DWI via diffusion tensor imaging (DTI) analysis; they reported differences in structural white matter anisotropy and diffusivity outcomes (ie, fractional anisotropy [FA] and mean diffusivity [MD]) between the CSTs of bilateral hemispheres after ACLR.[13] The FA is the most widely used measure of anisotropy, corresponding to the degree of anisotropic diffusion, and ranges from 0 (*isotropic diffusion*) to 1 (*anisotropic diffusion*), with higher FA representing better neural integrity in white matter fiber tracts. The MD is calculated as the mean water diffusion in 3 axes, with higher MD reflecting greater diffusion of water molecules in white matter fiber tracts. However, in previous studies, researchers have shown bilateral sensorimotor deficits after unilateral ACLR[12]; thus, the results of Lepley et al[13] may require validation with an uninjured healthy control group. In addition, the correlation between the CST microstructure and the clinical measures of sensorimotor deficits (eg, dynamic balance) and chronicity of ACLR (ie, postoperative duration) have not been fully explored in patients with ACLR. Hence, we suggest that the DTI outcomes of patients with ACLR and healthy controls and their association with clinical features could deepen our understanding of the neurologic origins of neural alterations and persistent functional deficits in patients with ACLR.

Therefore, the purposes of our study were to (1) evaluate the differences in the CST microstructure (measured by FA and MD) according to DTI between patients with ACLR and healthy controls and (2) explore the possible correlations between the structural features of the CST in patients with ACLR and sensorimotor deficits or postoperative duration. Based on a previous study,[13] we hypothesized that patients with ACLR would have lower FA and higher MD in the CST compared with healthy controls, and the DTI outcomes would be correlated with the severity of sensorimotor deficits or the postoperative duration in the patients with ACLR (eg, worse dynamic balance or longer chronicity of ACLR and worse CST microstructure).

METHODS

Study Design

This cross-sectional descriptive laboratory study was performed at Zhangjiang International Brain Imaging Center of Fudan University. The study was approved by the Institutional Research Ethics Committee of Huashan Hospital Affiliated with Fudan University (approval number 2022M-001). The report of this investigation followed the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology statement.

Sample Size Calculation

The mean and SD of the active motor threshold of the corticospinal pathway reported in a previous study of patients with ACLR compared with healthy controls were used to calculate the sample size (effect size = 0.92).[14] Active motor thresholds are one of the variables that reflect the excitability of the corticospinal pathway. Given that we were the first to compare the difference in the CST between patients with ACLR and healthy controls, we could not use those variables to calculate the power of this study, so we used active motor thresholds to indirectly calculate the power. Using G*Power Version 3.1, we determined that 40 participants (20 per group) were required to achieve a power of 0.8 at an α level of .05.[15] Considering up to a 20% withdrawal rate, we planned to recruit a minimum of 48 individuals (24 per group).

Recruitment of Participants

In total, 52 participants were included: 26 participants with a history of primary unilateral ACLR and 26 healthy individuals serving as controls were recruited from Huashan Hospital, volunteered to participate, and were enrolled in this study between September 2022 and March 2023.

Participants in the ACLR group were at least 6 months post-ACLR. No restrictions were placed on length of time since ACLR or age. Exclusion criteria for participants in the ACLR group were a history of knee surgery other than any type of concurrent meniscal procedures at the time of ACLR surgery, multiple ligament ruptures, or other lower extremity musculoskeletal injury sustained in the 6 months before the study. Individuals were included in the healthy control group if they had not experienced lower extremity musculoskeletal injury and had no history of lower extremity orthopaedic surgery.

Further exclusion criteria for all participants included a history of head injury or concussion in the 6 months before the study, stroke, cranial surgery, cancer in the brain, migraines, a diagnosed neurological or psychiatric disorder, use of medications that altered neural activity, and embedded intracranial metallic clips.

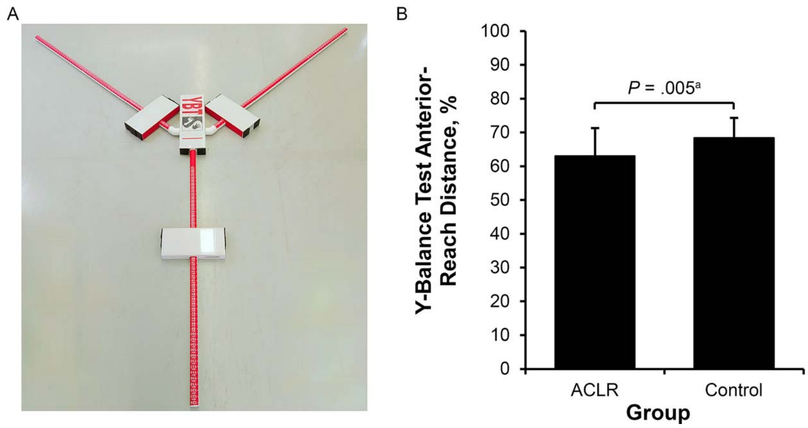

Figure 1. A, The Y-Balance Test Kit, and B, Y-Balance Test anterior-reach distance outcomes between the 2 groups. Abbreviation: ACLR, anterior cruciate ligament reconstruction. [a] Indicates difference ($P < .05$).

Data Acquisition

Demographic and Clinical Features. A single orthopaedic surgeon conducted the participant interviews and obtained the demographic and clinical data in the same session on the same day, including age, sex, height, mass, body mass index (BMI), injured limb, visual analog scale (VAS) scores of knee pain, Lysholm knee scoring scale assessment of self-reported knee function, Tegner activity scale score, postoperative duration, and an objective sensorimotor evaluation of the Y-Balance Test (YBT).

Pain in the knee joint was assessed using a 10-point VAS. We drew a 10-cm vertical line, with 0 representing *no pain* and 10 representing the *worst imaginable pain*. Pain was assessed in 2 states over the past 24 hours: walking and vigorous exercise. Postoperative duration was calculated as the time between ACLR surgery, according to the hospital inpatient records, and our test.

The YBT, which has demonstrated good to excellent intrarater and interrater reliability, is used to assess deficits in dynamic balance and involves standing on a single limb and reaching in 3 directions.[16] Clagg et al reported a difference in only the anterior reach direction (not in the posteromedial or posterolateral direction) between the ACLR injured limb and control groups at 6 months post-ACLR.[17] Therefore, we chose the YBT anterior-reach (YBT-A) direction distance to measure dynamic balance. All participants completed the YBT-A via the YBT Kit (Move2Perform, Evansville, IL, Figure 1A). In brief, participants were asked to maintain a single-limb stance with no weight-bearing on the reaching limb for recorded trials and perform 3 maximum trials in the anterior direction on both limbs with bare feet. Participants completed the warm-up protocol, including 2 practice trials on both limbs in the anterior direction, to familiarize themselves with the movements before performing recorded trials. The maximum distance of each trial was measured by reading the tape measure at the edge of the reach indicator, at the point reached by the most distal part of the foot. We chose the greatest distance among the 3 trials of the ACLR limb as the reach distance of patients with ACLR and that of the involved limb as the reach distance of the healthy controls. The reach distances were normalized to anatomic lower limb length and expressed as a percentage (reach distance/limb length $\times$ 100).

Magnetic Resonance Imaging Data Acquisition and Analysis. All participants completed a magnetic resonance imaging (MRI) session consisting of a structural T1-weighted image and DWI sequence. The MRI data were quality controlled by an experienced technologist (Z.Y.) blinded to the group assignment and acquired by one 3.0-T Prisma scanner (Siemens) with a 32-channel head coil. We immobilized and cushioned participants' heads with foam pads to reduce head movement. Two appropriately sized earplugs were applied to reduce noise, and if participants had discomfort, the participant or researcher could terminate the scanning using a handheld alarm.

The preprocess and analysis of the T1-weighted image and DWI data followed a series of steps using the functional MRI of the brain software library (FSL version 5.0.9; University of Oxford) based on previously validated protocols.[18] We calculated the individual maps of the DTI outcomes, including FA, MD, axial diffusivity (AD), and radial diffusivity (RD), based on the results of between-limbs comparisons in a previous study.[13] Mean values of the bilateral, left, and right sides of the CSTs were extracted from the voxels within the individual masks registered from previously published tracts.[19] The averaged bilateral values were recorded for the healthy controls to limit bias due to limb dominance, and the values of the ACLR injured-limb hemisphere (ie, the left hemisphere of the right ACLR injured limb) were selected for further analysis. We also compared the CST structure of ACLR uninjured limbs and healthy controls and quantified hemispheric differences in structural properties of the CST in patients with a history of ACLR. Detailed image acquisition variables and image processing steps are provided in the Supplemental Material.

Statistical Analysis

Descriptive variables were calculated as the mean $\pm$ SD or median (interquartile range). Height, body mass, and BMI were compared between patients with ACLR and healthy controls using the independent-samples t test, and sex was compared using the χ^2 test. The use of parametric or nonparametric tests for the numerical variables followed normality and homogeneity of variance using the Kolmogorov-Smirnov Z test and homogeneity tests of variance. The YBT-A distance and DTI

Table. Participant Demographic and Clinical Characteristics

Characteristic	ACLR Group (n = 26)	Control Group (n = 26)	Effect Size	P Value
	No.		χ^2 Value	
Sex, female/male	3/23	4/22	0	>.99
Injured limb, left/right	12/14	NA	NA	NA
	Mean ± SD		t Value	
Age, y	36.35 ± 6.39	32.85 ± 9.20	1.593	.12
Height, cm	173.88 ± 5.97	173.35 ± 7.19	0.294	.77
Mass, kg	74.80 ± 10.61	72.88 ± 11.06	0.638	.53
Body mass index	24.67 ± 2.75	24.16 ± 2.61	0.682	.50
	Median [Interquartile Range] (Minimum, Maximum)		z Value	
Visual analog scale – walking	0 [0–0] (0, 3)	0 [0–0] (0, 0)	−3.835	.02[a]
Visual analog scale – exercising	1.00 [0–3.00] (0, 6)	0 [0–0] (0, 3)	−2.326	<.001[a]
Lysholm	91.00 [80.75–95.25] (60, 100)	100.00 [90.00–100.00] (81, 100)	−3.354	<.001[a]
Tegner	4.00 [4.00–6.00] (2, 7)	4.00 [4.00–6.00] (3, 7)	−0.203	.84
	Median [Interquartile Range]			
Postoperative duration, mo	15 [12–19.5]	NA	NA	NA

Abbreviations: ACLR, anterior cruciate ligament reconstruction; NA, not applicable.
[a] Indicates difference ($P < .05$).

outcomes were normally distributed and had homogeneous variances between the ACLR group and the control group, whereas clinical features, including postoperative duration, the VAS, Lysholm knee-function scores, and Tegner activity scores, were nonnormally distributed. Therefore, the Mann-Whitney *U* test was used to assess the difference in clinical features between patients with ACLR and the healthy controls. The YBT-A distance and DTI outcomes were compared between groups using independent 2-sample *t* tests. Cohen d effect sizes with 95% CIs were also calculated for the magnitude of differences in the normally distributed YBT-A distance and DTI outcomes between groups. The strength of effect sizes with the absolute values of *d* was classified as *weak* (d = 0.2–0.5), *moderate* (d = 0.5–0.8), or *strong* (d > 0.80).[20] The simple Pearson correlation and partial Pearson correlation (with age, sex, and BMI as covariates) were performed for DTI outcomes with between-groups differences and normalized YBT-A outcomes in patients with ACLR, whereas both simple and partial (with age, sex, and BMI as covariates) Spearman correlation coefficients were estimated to explore the relationships between DTI outcomes with between-groups differences and postoperative duration in patients with ACLR. The absolute values of correlation coefficients were classified as *weak* (r = 0–0.4), *moderate* (r = 0.4–0.7), or *strong* (r = 0.7–1.0).[20] Given our robust hypothesis of maladaptive neuroplasticity (eg, worse dynamic balance or longer chronicity of ACLR and worse CST microstructure) in patients with ACLR, we performed 1-tailed analyses for between-groups comparisons of YBT-A distance, DTI outcomes, and correlation tests. We also performed 2 sensitivity analyses in this study: (1) using 2-tailed analyses with the 95% CIs as the sensitivity analysis and (2) removing women in both groups to conduct the between-groups comparison and correlation analysis as the sensitivity analysis given the small number of women in the groups. All statistical analyses were performed using SPSS software (version 27.0; IBM). The α level was set at .05.

RESULTS

Demographic and Clinical Features

Based on the inclusion criteria, 26 participants with unilateral ACLR (3 women, 23 men; age = 36.35 ± 6.39 years, height = 173.88 ± 5.97 cm, mass = 74.80 ± 10.61 kg) and 26 healthy controls (4 women, 22 men; age = 32.85 ± 9.20 years, height = 173.35 ± 7.19 cm, mass = 72.88 ± 11.06 kg) from the local community were enrolled in this study and included in the analyses. The left and right limbs were injured in 12 and 14 of the 26 patients with ACLR, respectively. The median postoperative duration in patients with ACLR was 15.0 months (interquartile range = 12.0–19.5 months) in this study. We observed no differences in age, sex, height, mass, BMI, or Tegner activity level scores between groups ($P > .05$). The post-ACLR group showed higher VAS-walking and VAS-exercising scores and lower Lysholm knee scores compared with the control group, indicating that the ACLR group had knee-joint deficits with pain and self-reported function ($P < .05$). The ACLR group achieved a moderately smaller YBT-A distance compared with the control group (Cohen d = −0.743; 95% CI = −1.302, −0.177), indicating a dynamic balance deficit in the ACLR group (Figure 1B). The demographic and clinical features data of all participants are displayed in the Table.

DTI Outcomes of the CST

The means and SDs of the CST structural measures are reported in Figure 2. The CST of the ACLR group demonstrated lower FA than that of the averaged bilateral CST of the healthy group (Cohen d = −0.666; 95% CI = −1.221, −0.104; $P = .01$), indicating altered white matter with loss of coherence in the CST direction.[21] Regarding outcomes of AD (Cohen d = −0.526; 95% CI = −1.077, 0.030; $P = .03$) and RD (Cohen d = 0.514; 95% CI = −0.042, 1.064; $P = .04$), moderate differences were also observed between

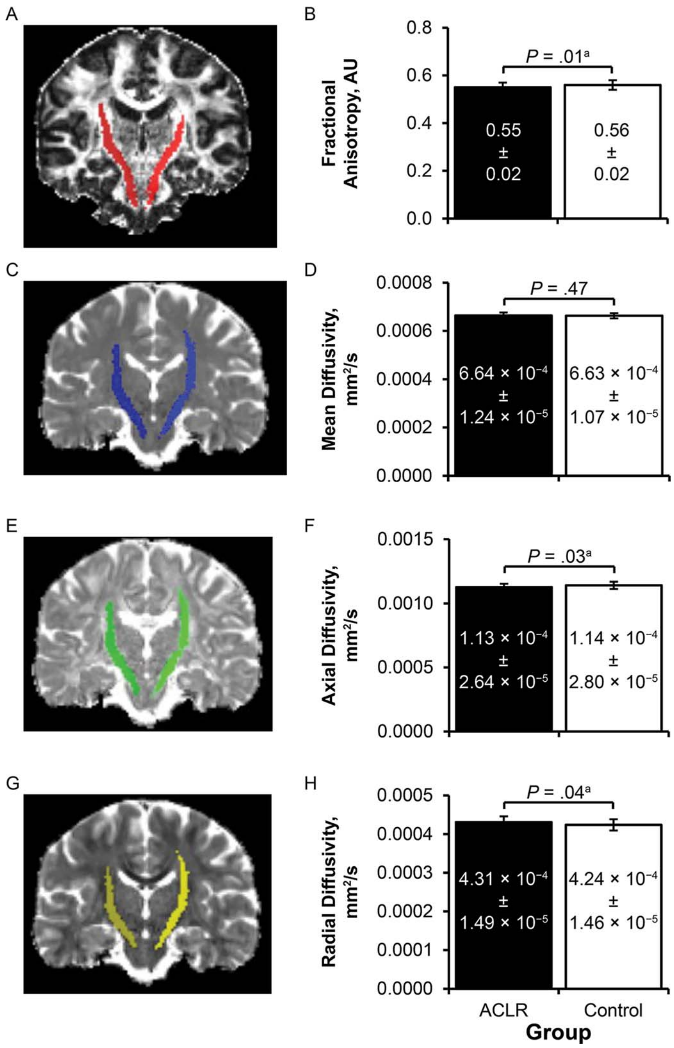

Figure 2. Masks of corticospinal tracts (in red, blue, green, and yellow) on the images of diffusion tensor imaging outcomes and the between-groups comparisons of the extracted values of diffusion tensor imaging outcomes, with the numeric data presented as mean ± SD. A and B, Fractional anisotropy. C and D, Mean diffusivity. E and F, Axial diffusivity. G and H, Radial diffusivity. Abbreviation: ACLR, anterior cruciate ligament reconstruction. [a] Indicates difference ($P < .05$).

groups ($P < .05$) (Figure 2). However, we did not observe a difference in MD between groups (Cohen d = 0.025; 95% CI = −0.519, 0.568; $P = .47$). We found differences in FA and AD values between the CSTs of the uninjured limb of the ACLR group and the control group ($P < .05$) but no hemispheric differences in structural properties of the CST in the ACLR group ($P > .05$) (Supplemental Tables 1 and 2). Using 2-tailed tests and 95% CIs as the sensitivity analysis, we found a difference only in FA values of the CST structure between groups (Supplemental Table 3). After removing women in the groups for the sensitivity analysis, we found a difference only in FA values of the CST structure between groups (Supplemental Tables 4 and 5).

Relationships Between DTI Outcomes and Both YBT-A Distance and Postoperative Duration

Among the exploratory correlation analyses, no correlations were observed between DTI outcomes with between-groups differences and YBT-A distance or postoperative duration before controlling for age, sex, and BMI (P range, .10–.46) (Supplemental Figure). After controlling for age, sex, and BMI, we observed no correlation of the FA values within the CST structure of the ACLR group and YBT-A distance ($r = 0.138$, $P = .25$) or postoperative duration ($r = -0.306$, $P = .06$) (Figure 3A and B). No correlations were found between AD values and YBT-A distance ($r = -0.034$, $P = .43$) or postoperative duration ($r = 0.045$, $P = .41$) or between RD values and YBT-A distance ($r = -0.173$, $P = .20$) (Figure 3C–E), but a moderate correlation was found between postoperative duration and RD values within the CST structure of the ACLR group ($r = 0.623$, $P < .001$) (Figure 3F).

After removing women in the ACLR group for the sensitivity analysis, no correlations were observed between the DTI outcomes with between-groups differences (FA values) and YBT-A distance or postoperative duration after controlling for age and BMI (Supplemental Table 6).

DISCUSSION

To the best of our knowledge, we are the first to assess whether the contralateral CST microstructure of the injured limb in patients with ACLR differs from that of healthy controls and the first to attempt to establish the relationship between the CST microstructure and both sensorimotor deficits and postoperative duration. We found that the integrity of the ACLR-related CST was impaired (lower FA and higher RD) and that the impairments were moderately correlated with postoperative duration (longer postoperative time and higher RD).

Maladaptive Alteration in the CST

Researchers have hypothesized that deficits of sensory input after ligament injury would lead to maladaptive neuroplasticity of the CNS associated with motor output and would affect the muscles surrounding the injured joint.[10,22] In our study, DTI was used to quantify the overall white matter microstructure of the CST. According to the primary DTI outcomes, and in line with the results of a previous DTI study in which the CST structure between hemispheres was compared in patients with ACLR,[13] we observed reduced FA in the CST of the ACLR group compared with the control group. The FA was the DTI outcome of the CST microstructure that was different between groups in this study, with higher FA representing better integrity of white matter fiber tracts, which has been widely applied as an index of neural integrity in various clinical events, including lateral ankle sprain.[18] On the other hand, the MD is determined by the mean water diffusion in all axes, representing fiber atrophy. Lepley et al recently reported higher MD values for the CST of the ACLR injured limb hemisphere than the uninjured limb hemisphere; however, we found no difference in the MD values between groups in this study.[13] Two variables may account for this discrepancy in results: (1) Lepley et al[13] did not include a healthy control group to detect differences in affected CNS structure compared with patients with ACLR, and (2) the older age of our participants (about 10 years) might lead to different neuroplasticity in the MD, which is more reflective of age-related tissue breakdown, atrophy, and increased water content.[13,23] Meanwhile, we suggest that CST structural alteration

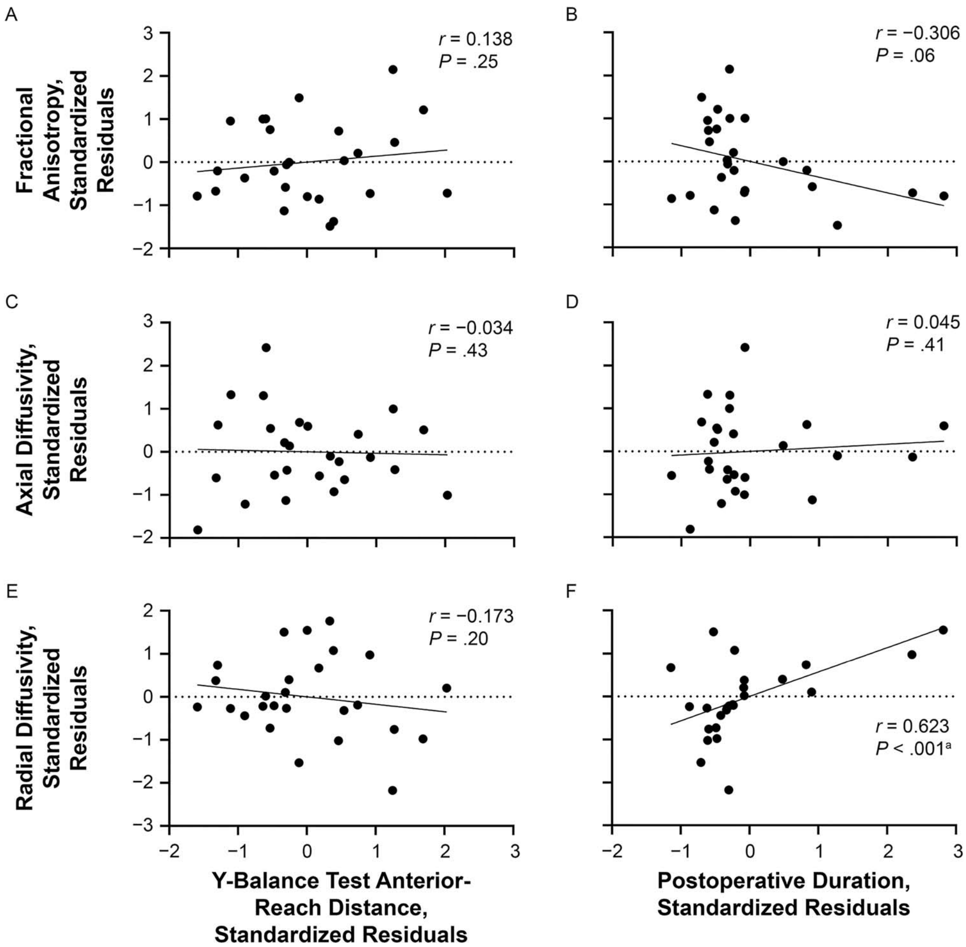

Figure 3. Scatterplots of the relationship between diffusion tensor imaging outcomes with between-groups differences and A, C, and E, Y-Balance Test anterior-reach distance, or B, D, and F, postoperative duration after controlling for age, sex, and body mass index in patients with anterior cruciate ligament reconstruction. [a] Indicates difference ($P < .05$).

may not occur in fiber atrophy, and there might be other reasons for the impaired CST microstructure.

Regarding the DTI outcomes of AD and RD values, AD is calculated using the axial diffusion, representing axonal degeneration; RD is calculated through the diffusion perpendicular to the longitudinal axis, reflecting myelin alteration.[24] Given that we found differences in AD and RD between the groups, which were different from the results reported by Lepley et al,[13] we suggest that the reason might be that they included only a small sample size and had no healthy controls to confirm their results due to the bilateral sensorimotor deficits after ACLR.[12] Meanwhile, we speculate that axonal degeneration or demyelination may contribute to the CST structural alteration seen post-ACLR, and there may be factors contributing to impaired CST integrity. However, our study is a cross-sectional study, and the causal relationship between ACLR and CST impairments requires further exploration through future longitudinal studies.

However, using the 2-tailed analyses with the 95% CIs or removing women in the 2 groups for the sensitivity analyses, we found differences only in FA values of the CST structure between the ACLR and control groups, which hinted that the results need to be considered with caution and require more studies to investigate the maladaptive changes of the CST structure in patients with ACLR.

Neural Correlates of Sensorimotor Deficits and Postoperative Duration in ACLR

Our YBT-A distance results indicated that patients with ACLR had worse dynamic balance compared with healthy controls. Another study also demonstrated that individuals with ACLR had lower anterior reach distance on the injured limb compared with a control group.[17] The alterations in dynamic balance related to ACL rupture or ACLR have been attributed to altered sensorimotor association within the CNS.[25] The CST plays multiple roles in sensory and motor performance and is related to quadriceps strength, which is associated with dynamic balance performance.[9,11] Researchers have reported that lower dynamic skill levels are highly associated with a lower FA value in the CST microstructure of patients after traumatic brain injury.[26] Thus, we hypothesized that the worse CST microstructure might also be associated with functional deficits in patients with ACLR. We replicated the previous results in an independent cohort with ACLR but found no evidence that decreased CST integrity (lower FA) was correlated with poorer dynamic balance (smaller YBT-A distance), which was not consistent with our hypothesis that maladaptive neuroplasticity was associated with persistent sensorimotor deficits. We speculated that the reason might be the complexity of the YBT (integrating strength, balance, and flexibility) that reduces its accuracy in reflecting the sensorimotor alteration in ACLR.[16] More studies are needed to further explore the functional meanings of the structural impairments in the CST that we observed in the ACLR group.

On the other hand, our results are in agreement with the excitability literature in which researchers observed no difference in the corticospinal excitability in the initial stage of ACL injuries and ACLR, and corticospinal deficits appeared to progress over time.[5,10] We found that postoperative duration was positively correlated with RD values within the CST structure of the ACLR group. Researchers have reported that increased RD is associated with the demyelinating condition.[27] We suggest that the demyelinating condition of the CST microstructure might also be a process of maladaptive neuroplasticity alterations along with the chronicity of ACLR. Unfortunately, given the cross-sectional nature of our study, we cannot determine causality or when these changes occur during the recovery process. Therefore, the causal relationship between the CST and postoperative duration or sensorimotor deficits needs further investigation through prospective controlled trials with repeated measurements.

However, after removing women in the ACLR group in the sensitivity analysis, we found no correlations between the DTI outcomes with between-groups differences (FA values) and YBT-A distance or postoperative duration after controlling for age and BMI, which suggested that the results of the correlation analysis were unstable and further longitudinal studies to validate the results of our study are needed.

Implications

The results of this study have the potential to advance studies on the central mechanisms of dynamic balance deficits after ACLR and rehabilitation. First, the results suggest that CST microstructure abnormalities may evolve after ACLR and lead to sensorimotor deficits; novel interventions that target the corticospinal pathway might provide more effective treatments for these deficits. For example, transcranial direct-current stimulation, which can safely restore muscle strength and activation across short-term treatment paradigms,[28] and neuromuscular electrical stimulation, which can activate the corticospinal pathway, can be used to improve dynamic balance deficits.[29] Second, the results of our study could facilitate the clinical identification and management of patients with ACLR if the classic integrity index (FA value) is used as a biomarker to assess the severity and treatment of neurological outcomes after ACLR. However, MRI is expensive, and its popularity for diagnosing and treating people with ACLR needs to be improved. Finally, our results could encourage future longitudinal investigations of the CST microstructure to identify the causal relationship between ACLR or ACL injuries and sensorimotor deficits (ie, dynamic balance, muscle strength, and voluntary activation).

Limitations

Our study had several limitations. First, although we detected differences in the CST structure and sensorimotor deficits between the ACLR and control groups and identified a relationship between postoperative duration and the CST structure in the ACLR group, the lack of correlation between the CST microstructure and dynamic balance limited the implications of our study. More research is needed to understand what is causing the changes in the CST structure to better understand interventions that would help. In addition, the causal relationship between the abnormal CNS features and the development of sensorimotor deficits post-ACLR requires further longitudinal investigation. Second, given the difficulty of integrating objective sensorimotor measurements with MRI scanning, we only used the YBT to assess the sensorimotor deficits; thus, we need more sensitive measurements to evaluate the functional association of the structural deficits of the CST after ACLR in the future. Third, the region-of-interest analysis focused on the entire CST analysis, which may have reduced the sensitivity in detecting differences because the tract with the knee is only part of the CST. In addition, more methods of assessing the human brain with higher microstructure sensitivity and physiological importance, such as neurite orientation dispersion and density imaging, should be applied based on our DTI outcomes in further studies.[30] Fourth, our study had confounding factors, including graft type, presence of associated injuries, and inconsistent postoperative durations, which may have caused biases in the research findings. In future studies, researchers should control for these factors. Fifth, we used Cohen d effect sizes, which might not be suited for the field of sports medicine for between-groups comparisons, rather than standardized effect sizes. However, no better method of calculating effect sizes is available for use in sports medicine. We hope that future researchers will request our raw data and calculate effect sizes using a method better suited to the field of sports medicine. Sixth, we performed 1-tailed tests with 95% CIs based on our hypothesis that patients with ACLR would have lower FA and higher MD in the CST compared with healthy controls and found that the patients with ACLR showed moderately lower FA, lower AD, and higher RD compared with healthy controls, with the RD values correlated with postoperative duration after controlling for age, sex, and BMI in patients with ACLR. However, in our sensitivity analysis using 2-tailed tests with 95% CIs or removing women in the 2 groups, we found differences for FA values in the CST structure between groups and no associations between DTI outcomes with significant between-groups differences (FA values in the CST structure) and YBT-A outcomes or postoperative duration in patients with ACLR after controlling age and BMI. Therefore, readers should interpret the statistically significant results with caution. Finally, we analyzed only the structural aspects of the CST, without assessing its function (CST excitability) in patients after ACLR. Therefore, further research should be done to integrate both the structural and functional analyses of the CST with dynamic balance in individuals with ACLR to provide a comprehensive understanding of the underlying physiological mechanisms.

CONCLUSIONS

This study revealed that participants with ACLR demonstrate impaired integrity (lower FA values and higher RD values) in the CST contralateral to the ACLR injured limb and decreased YBT-A distances (sensorimotor deficits) compared with healthy controls. Decreased integrity (higher RD) of the CST in patients was associated with longer postoperative duration, which hinted that impaired structural integrity of the CST might be a structural maladaptive process of neuroplasticity in ACLR. Further longitudinal studies are needed to identify novel assessment and therapeutic techniques that can recognize and correct potential maladaptation of the CST structure after ACLR.

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DATA STATEMENT

The original imaging data used to support the findings of this study have not been made available because of data security; the CST features are available upon reasonable request to the senior authors (R.W., wangru@sus.edu.cn; H.W., hewang@fudan.edu.cn; and Y.H., hua_cosm@aliyun.com).

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SUPPLEMENTAL MATERIAL

Supplemental Figure 1. Scatterplots of the relationship between diffusion tensor imaging outcomes with between-groups differences and A, C, and E, Y-Balance Test anterior-reach distance, or B, D, and F, postoperative duration before controlling for age, sex, and body mass index in patients with anterior cruciate ligament reconstruction. [a] Indicates difference.

Supplemental Table 1. Diffusion tensor imaging outcomes between the corticospinal tract of anterior cruciate ligament reconstruction uninjured limbs and controls.

Supplemental Table 2. Diffusion tensor imaging outcomes between the corticospinal tract of anterior cruciate ligament reconstruction injured and uninjured limbs.

Supplemental Table 3. Sensitivity analysis of corticospinal tract structure between groups using 2-tailed analysis.

Supplemental Table 4. Between-groups comparisons of diffusion tensor imaging outcomes.

Supplemental Table 5. Relationships between diffusion tensor imaging outcomes and Y-Balance Test anterior-reach outcomes or postoperative duration.

Supplemental Table 6. Relationships between age or body mass index and diffusion tensor imaging outcomes, Y-Balance Test anterior-reach outcomes, and postoperative duration in patients with anterior cruciate ligament reconstruction.

Supplemental Material. Image acquisition variables and image processing steps.

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