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Review Article

An overview of fractional anisotropy as a reliable quantitative measurement for the corticospinal tract (CST) integrity in correlation with a Fugl-Meyer assessment in stroke rehabilitation

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Abstract. [Purpose] Understanding the essential mechanisms in post-stroke recovery not only provides important basic insights into brain function and plasticity but can also guide the development of new therapeutic approaches for stroke patients. This review aims to give an overview of how various variables of Magnetic Resonance-Diffusion Tensor Imaging (MR-DTI) metrics of fractional anisotropy (FA) can be used as a reliable quantitative measurement and indicator of corticospinal tract (CST) changes, particularly in relation to functional motor outcome correlation with a Fugl-Meyer assessment in stroke rehabilitation. [Methods] PubMed electronic database was searched for the relevant literature, using key words of diffusion tensor imaging (dti), corticospinal tract, and stroke. [Results] We reviewed the role of FA in monitoring CST remodeling and its role of predicting motor recovery after stroke. We also discussed the mechanism of CST remodeling and its modulation from the value of FA and FMA-UE. [Conclusion] Heterogeneity of post-stroke brain disorganization and motor impairment is a recognized challenge in the development of accurate indicators of CST integrity. DTI-based FA measurements offer a reliable and evidence-based indicator for CST integrity that would aid in predicting motor recovery within the context of stroke rehabilitation.

Key words: Fractional anisotropy, Corticospinal tract, Stroke

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INTRODUCTION

Stroke is a very severe public health issue, resulting in substantial morbidity and mortality for developed and developing countries. Stroke has been ranked as the second most common cause of death worldwide and the third most common cause of disability-adjusted life years in the Global Burden of Diseases, Injuries and Risk Factors Study (GBD) of 2017[1)]. Ischemic stroke is a common global health-care problem that continues to affect quality of life[2)], and around 55–75% of stroke survivors still have functional disabilities and reduced quality of life months after the stroke onset[3)].

Neurorehabilitation is the clinical subspecialty devoted to repairing and optimizing functions that have been damaged because of nervous system impairments caused by injury or disease[4)]. Neurorehabilitation is crucial for improvement of motor recovery of post-stroke patients. A strategic rehabilitation plan, however, is vital for post-stroke patients to recover,

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and knowledge of post-stroke brain reorganization is essential for us to identify components of the brain that are associated with post-stroke motor recovery. Currently, elucidation of corticospinal tract (CST) integrity is possible using magnetic resonance imaging (MRI) modalities, specifically diffusion tensor imaging (DTI) metrics such as fractional anisotropy (FA) that has been identified as a reliable tool of structural integrity identification of CST after stroke[5, 6]. This review aims to give an overview of how FA can be a reliable quantitative measurement and indicator of CST integrity and how it correlates with the functional motor outcome of Fugl-Meyer Assessment (FMA) in chronic stroke patients.

METHODS

PubMed database (www.ncbi.nlm.nih.gov/pubmed) was utilized for the literature search. We used keywords of dti, corticospinal tract, and stroke. In addition, references in retrieved articles were also searched for cross references. We studied relevant articles which were published in the last 20 years and the articles was limited to English only. These included randomized clinical trials, systematic reviews, and cohort studies. One hundred and twenty-two results were found, and 27 papers were used for this review. Excluded papers and/or studies were the ones with a different focus topic from this review (n=57); the FMA score was not assessed (n=12); included patients who were <one month of stroke onset (n=11); specific site/side of stroke lesion was not stated (n=6); the FA value from entire CST or region of interest (ROI) within the CST pathway was not included (n=5); and the correlation between CST-FA with FMA was not made (n=4).

RESULTS

From the total of 27 papers, FMA scores showed a significant relationship with ipsilesional CST-FA only in thirteen studies (n=13, 48.1%), contralesional CST-FA only in five studies (n=5, 18.5%), both ipsilesional and contralesional CST-FA in five studies (n=5, 18.5%), and ratio FA (rFA) or asymmetric FA (aFA) in four studies (n=4, 14.8%) (see the summary in Table 1).

Table 1. FA variables with their respective processes in early stroke and during rehabilitation

FA variable	Utility
Ipsilesional CST-FA [46, 47, 50, 53, 60–65, 68–73, 78, 79]	Early stroke • Loss of axonal integrity, resulting in Wallerian degeneration or loss of structural tissue integrity. Wallerian degeneration then causes breakdown of the myelin sheath and disintegration of axonal microfilaments. • In a longstanding cerebral infarction, it is assumed that cell lysis and the loss of normal tissue architecture will cause the extracellular space to expand. During rehabilitation • Biophysical changes and improvements in synaptic efficacy in the CST; axonal sprouting, the development of new synapses and increased myelinating operation by oligodendrocytes. • Associated with increased angiogenesis and local cerebral blood flow.
Contralesional CST- FA [38, 46, 60, 64, 74–79]	Early stroke • Similar loss in the integrity of the axolemma and/or the myelin sheath to that in the case of ipsilesional CST. During rehabilitation • Similar biophysical changes and improvements in synaptic efficacy to that in the case of ipsilesional CST. • Sprout and form new associations with the ipsilesional motor nuclei in the brainstem and spinal cord.
Ratio FA (rFA) and asymmetric FA (aFA) [6, 55, 80, 81]	Early stroke • Physiological balance of activity between two brain hemispheres can be disturbed after stroke. • Extensive remote changes in the coordination of the motor areas in and between the two brain hemispheres. During rehabilitation • These changes are stable over time and improve gradually, in parallel to the functional recovery. • Comparing the two sides with calculated aFA and rFA values gives useful and reliable knowledge about CST structural improvements in patients with stroke.

DISCUSSION

In this section, we discuss the role of physical therapy in stroke rehabilitation, the mechanism of CST remodeling in brain neuroplasticity during rehabilitation and how it modulates the value of FA and FMA-UE. We also discuss the role of FA in monitoring CST's structural integrity changes and how it can be used to predict the motor recovery after stroke.

1. Physical therapy in stroke rehabilitation: At any time after stroke onset, a continuous, skilled motor retraining is essential for continued gains of motor recovery. A favorable outcome from this physical retraining should also take into account the potential engagement it may yield with the attention, motivation, and learning networks in the brain where neural connectivity may well correspond to the components of a physical therapy. It was recommended that maximal functional gains are made by 3 months after the stroke onset. However, other changes that can occur with regular practices should be accounted such as improved walking speed and distance or greater coordination in the use of an affected hand[7]. Therefore, in early physical rehabilitation, therapists and physicians ought to instill in their stroke patients a regime of daily repetitive skills practice that can be performed within the outpatient setting and at the comfort of patients' own home environments. There are many interventions for physical mobility such as fitness and muscle strength workout, over-ground walking and balance training, body weight-supported treadmill training, and robotic gait assist devices[8]. Besides physical therapies, the adult central nervous system is also adaptive, or plastic, that bears a certain capacity to re-organize itself to recover any disrupted cognitive and motor functions following a stroke. In stroke patients, modulation of brain activation can be appreciated by MRI and other non-invasive imaging techniques which reflect regional plasticity that represent motor activity and motivation. Such plasticity is time-dependent and related to learning and practice behavioral compensation for the diminished pre-stroke neural control. Thus, the brain networks of stroke patients, like healthy persons, can be expected to continually undergo anatomic and/or physiologic changes that could be induced by motor learning from the targeted physical therapy employed in stroke rehabilitation.

2. Role of neuroplasticity in rehabilitation: Neuroplasticity is the capability of the nervous system to react to intrinsic or extrinsic stimuli by rearranging their structures, features, and interactions. It may occur at multiple levels, from molecular to cellular to behavioral systems, and during development, in response to stimuli, learning, disease or treatment[9]. Several factors are likely to affect neural functional changes and by knowing how they affect the brain can benefit the stroke recovery. These may include stroke type and severity, time of post-stroke onset, motivation, mood, stress level, surroundings, learning and participation skills, and plasticity capacity of the brain's viable networks[10]. Other factors, such as structural[11] and functional[12] integrity of white matter tracts in motor recovery, may contribute. It was also found that the knowledge of structural integrity of functionally connected networks is more critical than knowledge of localized site of infarction area alone, with greater white matter structural integrity (measured in FA) that can elucidate greater functional outcomes[13]. This is in accordance with the theory that neuroplasticity changes rely on the stability of particular pathways and networks that occur during stroke recovery and rehabilitation.

3. CST's structural integrity in the context of stroke rehabilitation: The motor controls delivered to the spinal cord through CST from the primary motor and sensory cortices are served by direct (lateral and medial CST) and indirect pathways. The extent of post-stroke injury is recognized as a key factor in determining the severity of motor damage following stroke episodes[14]. For optimal brain rehabilitation, understanding the detailed neurological symptoms associated with nerve damage, the prognosis and estimation of stroke recovery, the assessment of potential recovery mechanisms and the preparation of successful strategies to promote recovery mechanisms for the best outcome are important. The neurological symptoms of patients are important consideration because they can predict patients' recovery courses and prognoses[15]. Such knowledge is helpful in helping clinicians to implement and adapt more precise recovery methods for patients with strokes. For example, several studies have demonstrated that when a patient has retained lateral CST in the affected hemisphere, the rehabilitation strategy can focus on the fine motor activity and strength of the affected hand recovery[16–21]. Although the role of the lateral CST has been studied fairly well, not much is known about other CSTs that could overtake the position of an injured CST[22]. For instance, it has been studied that the anterior CST, along with the cortico-reticulospinal tract, functions as a motor recovery pathway of the ipsilateral motor pathway from the unaffected motor cortex to the affected extremities when there is an injury of the lateral CST[23–27]. However, this could not be confirmed because detailed visualization and identification of the anterior CST in the live human brain could not be attained. Nonetheless, anterior CST studies are now possible using MRI modalities, specifically the DTI technique that is documented as a reliable tool for in vivo identification of the anterior CST[5, 6]. In addition to the lateral CST, more research into the CSTs is required in terms of their normal functions and roles in motor recovery.

4. DTI as surrogate neuronal biomarker of brain reorganization after stroke: Understanding the essential mechanisms in post-stroke recovery not only offers important fundamental insights into brain function and plasticity but may also guide the development of new therapeutic approaches to treat stroke patients. Imaging modalities, such as MRI, can contribute significantly to stroke recovery research by allowing serial in vivo whole-brain measurements of both functional and anatomical changes in the affected brain[28]. Well-known MRI approaches such as T2-, diffusion-, and perfusion-weighted MRI are widely used in both clinical diagnosis and pre-clinical research for the evaluation of acute stroke[29–31]. Furthermore, MRI can also be used to describe long-term improvements in brain structure and post-stroke activity[32–36]. In previous studies,

structural improvements in both gray and white matter areas after clinical and experimental stroke have been successfully measured and analyzed using diffusion tensor imaging (DTI)[37–39]. Brain reorganization or neuroplasticity is often closely associated with structural modification of neuronal elements in the brain. DTI offers an MRI-based means for the assessment of neuroanatomical white matter tract changes related with brain injury and repair. DTI gives information on the three-dimensional displacement of tissue water, mathematically characterized by an effective diffusion tensor comprising of nine matrix elements, which can be exploited to assess the microstructure of the entire white matter tract[40, 41].

White matter tracts consist of an arrangement of highly directed fibers. This results in a relatively high anisotropy of diffusing tissue water restriction; thus, DTI is very suitable for measuring the structural on the integrity of the white matter tract. Because the diffusion of tissue water is restricted by the presence and orientation of biological barriers such as cell membranes and myelinated fibers, structural changes induced by strokes can significantly alter the characteristics of tissue water diffusion[42]. Most widely used DTI metrics include FA, mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD). FA measures the degree of directionality of diffusion of water molecules in the white matter tract; a higher FA value reflects higher white matter tract integrity, and a lower FA value reflects lower white matter tract integrity. It can rank from 0 (isotropic) to 1 (anisotropic). In strongly directed fibers, the anisotropy value is high. This suggests that the greater value should be in the middle of the tracts. MD represents the magnitude of diffusion, and the greatest value should be found in the ventricles. It reflects tissue directionality and sensitivity for white matter integrity and ultrastructural damage. Contrarily to FA, higher MD reflects lower white matter tract integrity, and lower MD reflects higher white matter tract integrity. RD determines the average diffusivity perpendicular to the first eigenvector, and AD is the first eigenvalue that represents the diffusivity along the dominant diffusion path. Most work primarily concentrated on FA. Appropriate definition of FA also requires knowledge of the effects of the three other DTI metrics[43]. Changes in anisotropy can replicate many biological structures, such as axonal packing density, axonal diameter, myelination, neurite density and distribution of orientation[44]. This changes may involve multiple processes at different post-stroke levels, ranging from acute cell swelling and the subacute cell lysis stage (causing FA decrease) to chronic axonal regeneration or remyelination and gliosis (causing FA increase)[42, 45–47].

Studies that investigated the reduced FA in ipsilesional white matter at the subacute stroke stage in humans and animals have demonstrated reduced FA correlated with demyelination or axonal impairment at this point[31, 39, 48, 49]. A few serial DTI studies in experimental stroke models have demonstrated that this initial decrease in FA may be followed chronically by normalization or elevation in the ischemic lesion border zone[50]. In another study, part of the ipsilesional internal capsule with elevated FA for post-stroke rat brains also reported significant manganese enhancement of T1-weighted MRI following injection of the paramagnetic neuronal tracer into the perilesional sensorimotor cortex[50]. This means that rearranging white matter at the ischemic boundary is accompanied by preserving or restoring neuronal structural connectivity and, hence, improves functional outcomes. In accordance with these findings in animal stroke models, chronic stroke models have reported increased FA in CST, associated with improved motor function[32, 51, 52]. The corticospinal pathway's structural integrity is an important imaging marker that should be correlated with the effect of sensorimotor performance after stroke (Fig. 1).

5. FA variables as a CST integrity indicator in correlation with Fugl-Meyer Assessment-Upper Extremities (FMA-UE): Ipsilesional, contralesional, ratio and asymmetry indices of FA between ipsi- and contra-lesional CSTs were the most common variables of the CST integrity indicator in DTI studies among many DTI-derived variables (Table 1). Many previous studies demonstrated that these variables were strongly correlated with the functional motor outcome, especially Fugl-Meyer Assessment-Upper Extremities (FMA-UE)[6, 32, 46, 47, 53–55]. FMA-UE are the fourth most commonly used clinical outcome after the Rankin Scale (RS) or modified RS, the National Institute of Health Stroke Scale (NIHSS) or modified NIHSS motor portion, and the Barthel Index (BI)[56]. Although RS, NIH and BI clinical outcome measures have been proven to be highly reliable and valid[57], they lack specificity for motor impairment or performance in individuals post stroke[58]. Besides, these low-level categorical scales lack sensitivity and resolution for detecting motor recovery[57], unlike FMA-UE which is proven to be reliable, valid and more specific for post-stroke functional motor outcome[55, 59]. In the following section, we discuss in further detail each of the FA variables; ipsilesional, contralesional, ratio and asymmetry indices of FA between ipsi- and contra-lesional CSTs; that have been widely used as reliable CST integrity indicators in correlation with FMA-UE in chronic

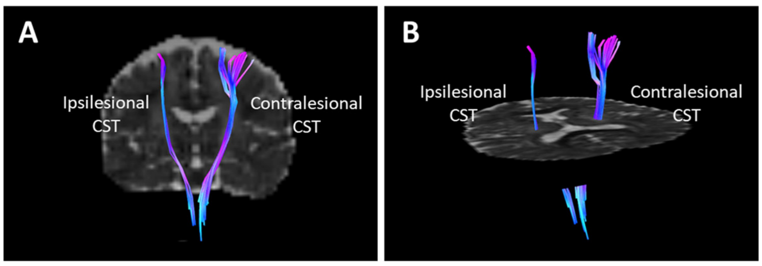

Fig. 1. Visualization of the corticospinal tract (CST) after DTI tractography processing. A) coronal view B) axial view.

post-stroke patients.

Ipsilesional FA: Ischemic stroke injury results in functional and structural reorganization of ipsilesional sensorimotor regions, i.e., transcallosal and corticospinal connections. Studies have found the essential role of FA as a marker of structural integrity of the white matter tract in motor recovery after stroke. Chronic stroke patients with higher motor skill levels, as measured by the Purdue Pegboard test and the maximum index finger tapping rate, had higher FA in the ipsilesional CST[60]. Several DTI-based studies have measured the FA values along the ipsilesional CST and found a reduced FA in the ipsilesional CST of stroke patients, which was further related to subsequent recovery after stroke[60–62]. In a group study of chronic stroke patients, FA was reduced with an increase in RD in the ipsilesional CST and transcallosal M1–M1 tract compared to healthy controls[53], and this may suggest that a decline in FA may be related to reduced myelin sheath integrity[63]. Moreover, the decreased FA in the ipsilesional CST after stroke was also suggested to occur because of loss of axonal integrity, resulting in Wallerian degeneration or loss of structural tissue integrity[64]. Wallerian degeneration then causes breakdown of the myelin sheath and disintegration of axonal microfilaments. In addition, in a longstanding cerebral infarction, it is assumed that cell lysis and the loss of normal tissue architecture will cause the extracellular space to expand. These changes would account for decreased anisotropy shown in chronic stroke patients[65]. The alterations in CST typically cause significant motor neuron symptoms and basic motor function deficits, e.g., irregular reflex behavior and muscle tone and decreased motor speed and accuracy[66], that could be measured directly using the FMA-UE, a performance-based impairment index[67]. Several longitudinal studies examined that changes in FA in the ipsilesional CST were increased over time and that this increase was associated with greater improvements in FMA-UE in both interventions and conventional rehabilitation after stroke[46, 47, 68]. Interventions such as repeated Transcranial Magnetic Stimulation (rTMS) have been shown to have obvious effects in enhancing motor control by inhibiting contralesional motor cortex and activating the ipsilesional cortex[69]. In a similar study, the pre-to-post differences in FA values along the ipsilesional CST were also found to have increased in participants who underwent intensive bilateral arm training, demonstrated morphological plasticity and altered synaptic efficacy in the ipsilesional CST after recovery training[46, 70]. Furthermore, the changes in FA values along the CST have been reported to increase because of biophysical changes and improvements in synaptic efficacy in the CST that occurred during rehabilitation training[70, 71]. Liu and others observed substantial recovery of CST on the ipsilesional side of the spinal cord in a rodent model of stroke, 32 days after occlusion of the middle cerebral artery, and a good correlation between axonal density and functional motor outcome[72]. In addition to histological evidence of white matter reorganization, the improvement in FA in ipsilesional white matter was found to be associated with increased angiogenesis and local cerebral blood flow[73]. An improved neural contact with the perilesional sensorimotor cortex was also found on manganese-enhanced MRI research[50]. These results indicate that structural remodeling of the ipsilesional CST is important for restoring motor function after stroke rehabilitation.

Contralesional FA: After stroke episodes, both ipsilesional and contralesional CSTs developed changes. It has been demonstrated that the integrity of contralesional tracts can be measured reliably and reduced after stroke. Aside from the ipsilesional tract, changes in structural connectivity for the contralesional corticospinal pathways have also been identified. It has been demonstrated that decreased integrity of contralesional white matter in chronic stroke has been associated with poorer motor skill recovery. For instance, decreased FA values were detected bilaterally in severely disabled chronic stroke patients, whereas increased values were found in patients with better motor outcomes[60]. In addition, a previous analysis found that there was a gradual loss of FA in contralesional white matter post stroke[74], similar to the decrease of ipsilesional CST FA. Schaechter et al. found that in individuals with chronic stroke, lower contralesional posterior limb of internal capsule (PLIC) integrity was associated with decreased hand dexterity[60]. Similarly, another study found that degenerative changes in contralesional PLIC were correlated with increased physical disability rates and lower hemiparetic upper extremity strength, grip strength and hand dexterity in chronic stroke[75]. This indicates that the contralesional descending motor outputs play an important role in mediating post-stroke motor recovery. Contralesional CST regions of reduced FA are suggested to inflict a similar loss in the integrity of the axolemma and/or the myelin sheath to that in the case of ipsilesional CST[64]. Previous research has demonstrated that increased FA rates over a longer period of time since stroke and contralesional tract integrity may be associated with improved motor recovery[60]. Findings from animal stroke recovery models suggest that improvements in the microstructure of white matter in the contralesional hemisphere are associated with axonal sprouting, the development of new synapses and increased myelinating operation. They are potentiated by therapies that also boost the regeneration of motor recovery[76]. The CST axons have been demonstrated to sprout and form new associations spontaneously following experimental stroke with the ipsilesional motor nuclei in the brainstem and spinal cord. This form of axonal remodeling is enhanced in conjunction with improved motor recovery by certain post-stroke treatments[76, 77]. Moreover, previous immunohistochemical studies have suggested that oligodendrocyte myelinating activity in ipsilesional and contralesional white matter is increased after experimental stroke[78, 79]. This is supported by several studies that demonstrate that chronic stroke patients undergoing rehabilitation have both increased contralesional CST in FA and improved FMA-UE with a strong relationship between them[38, 46, 75]. This suggests that the integrity of the motor output tract may be a vital biomarker of the motor recovery level during the chronic stroke phase and may provide insights into future research aimed at tailoring rehabilitation strategies. Although many studies found that ipsilesional and contralesional FA values had significant FMA-UE relationships, some studies reported on the contrary[38, 53, 75]. Such difference may be due to the fact that only the entire non-lesioned CST tract was examined in patients with a range of abilities, and only voxels that were part of the "skeleton", which are voxels that form the middle of the CST tract, were examined[53]. In addition, this also may be the result of the very small number of recruited stroke patients and relatively low levels of motor dysfunction observed in those chronic stroke patients[38]. Studies also reported relatively homogeneously in terms of location of the lesion, recovery rates and, to a lesser degree, the period since the onset of the stroke[75].

rFA and aFA: Apart from ipsilesional and contralesional FA, recent studies have used ratio FA (rFA) and asymmetric FA (aFA) as a variable indicator for CST integrity changes in chronic stroke patients[6, 55, 80, 81]. The rFA was determined using a definition of the ratio between ipsilesional FA and contralesional FA (FAipsilesional/FAcontralesional), and the asymmetry of the CST was determined using the CST's mean FA: (FAcontralesional − FAipsilesional) / (FAcontralesional + FAipsilesional). It was found that changes are developed in both ipsilesional and contralesional CSTs and that physiological balance of activity between them can be disturbed after stroke[82]. Previous research indicated a decreased integrity of contra- and ipsi-lesional PLICs in individuals with chronic stroke that correlated with a variety of specific functional measures[33, 83]. Such interhemispheric imbalances were linked to poorer recovery, and several studies found that approaches of rehabilitation aimed at restoring this balance reported beneficial results[82]. Following a focal lesion such as that in stroke, it has been demonstrated that there are extensive remote changes in the coordination of the motor areas in and between the two brain hemispheres[84], including both ipsilesional and contralesional CSTs. Such remote connectivity shifts can be explained by a condition called a connectional diaschisis. To date, studies have demonstrated how focal lesions affect the connectivity in various functional and structural networks. This was demonstrated on the basis of the functional and structural connectivity measured by fMRI and DTT, respectively, referring to the temporal and structural correlations between neural or hemodynamic signals from separate brain regions across brain hemispheres. Changes in the motor network were most studied, using resting state[85] and seed-based functional methods in humans[86] and rats[87], where a reduction of interhemispheric functional connectivity between homotopic cortical motor network areas after strokes has been reported. These changes are stable over time and improve gradually, in parallel to the functional recovery. These effective connectivity studies reported consistent results when interhemispheric connectivity in the motor network was investigated. The findings indicate that ipsilesional and contralesional CSTs are connected to each other structurally and functionally through directly and/or indirectly connections, thus playing an important role in mediating post-stroke motor recovery as an indicator of CST integrity. Comparing the two sides with calculated aFA and rFA values gives us useful and reliable knowledge about CST structural improvements in patients with stroke. Moreover, the significant relationship of aFA and rFA with FMA-UE is not always consistent between studies. In studies where the selected region of interest (ROI) was PLIC, it was found that both aFA and rFA had a significant relationship with the FMA-UE[6, 17, 55, 81], but this was not the case if the selected ROI was pontine CST[75, 80, 88]. Nonetheless, there are other factors to be considered that include the small sample sizes in the reported studies, and relatively low levels of motor dysfunction of chronic stroke patients[38] would give a different result even when the ROI selected was PLIC.

6. FA variables as novel neuroimaging biomarkers in predicting motor recovery after stroke: Using the advantages of the FA/FMA-UE relationship, many recent studies have identified the potential of DTI-FA as an essential clinical biomarker to be used to predict post-stroke motor recovery[35, 39, 52]. Ipsilesional FA-CST DTI metrics can predict the response of chronic stroke patients to rehabilitation; the more their diffusivity profiles resemble those of healthy subjects, the greater their functional recovery potential[71]. These findings are consistent with evidence from fMRI, where good recovery is associated with reactivation of motor cortex in the affected hemisphere[89], suggesting that recovery requires concerted activation of all premotor cortices and reactivation or enhanced stimulation of motor cortex in the affected hemisphere[90]. Even though contralesional tract-specific FA values correlated with motor impairment in chronic stroke patients, the contralesional tract did not predict functional potential for motor recovery[60]. This suggests that even when remodeling of a contralesional motor tractoccurs after stroke[91], it might not necessarily provide the structural basis for further functional gains in the chronic phase. In a review comparing different clinical biomarkers to predict motor recovery, the ratio and asymmetry index of FA between ipsi- and contralesional CSTs were the most popular predictor variables in DTI studies among many DTI-derived variables[56]. However, some studies employ multiple neurological biomarkers, such as a combination of DTI and conventional MRI biomarkers and TMS biomarkers[56]. It is not surprising that predictive models using neurological biomarkers along with clinical measures (e.g., Fugl-Meyer score, age, and chronicity) would be more meaningful than models using neurological biomarkers alone.

Heterogeneity of post-stroke brain disorganization and motor impairment is a recognized challenge in the development of accurate indicators of CST integrity. Accurate indicators and prediction models of recovery are critical for defining the best neurorehabilitation protocol that will promote motor recovery and maximize functional outcomes for the stroke survivors. This narrative review proposed that DTI-based FA measurements offer a reliable and evidence-based indicator for CST integrity that would aid in predicting motor recovery within the context of stroke rehabilitation.

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Conflicts of interest

There are no conflicts of interest.

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