

# Diffusion tensor imaging of pyramidal tract reorganization after pediatric stroke

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## Abstract

**Background** Plasticity of the developing motor tracts is a contributor to recovery of motor function after pediatric stroke. The mechanism of these plastic changes may be functional and/or structural in nature. The corticospinal tract (CST) represents the major pathway responsible for voluntary movement. Stroke-induced damage to the CST as well as to other motor tracts leads to motor deficits which may show favorable functional recovery particularly in the pediatric population.

**Methods** We report the case of a 3-year-old girl demonstrating reorganization of the pyramidal tracts after an extensive left MCA territory stroke secondary to head trauma. Reorganization is characterized using serial diffusion tensor imaging (DTI) of the pyramidal tracts which contain the CST.

**Results** Imaging shows decreased ipsi-lesional fractional anisotropy (FA) suggestive of Wallerian degeneration and increased contralesional FA.

**Conclusions** These results point to plastic reorganization of the pyramidal tract post-stroke and the utility of DTI in recognizing these changes.

**Keywords** Neuroplasticity · DTI · Corticospinal tract · CNS reorganization · Pediatric stroke

## Introduction

Neural plasticity contributes variably to recovery after stroke, but is thought to be particularly important after insults to the

developing brain. Pediatric patients often exhibit better post-stroke functional outcome than adults, especially regarding motor function and mobility [1, 2]. The majority of this functional recovery, both in adult and pediatric populations, occurs within a 2–3 month period after the initial insult with smaller gains made in the subsequent months [3]. Plasticity of cerebral connectivity includes functional changes such as alterations in synaptic efficiency or recruitment of existing otherwise “silent” pathways as well as structural changes such as synaptogenesis and enhanced dendritic arborization [4, 5].

The corticospinal tract (CST), as the major facilitator of voluntary movement, is particularly important for the recovery of motor functioning following stroke. The majority of CST fibers crosses in the pyramidal decussation at the level of the cervicomedullary junction and descend to form the lateral corticospinal tract while a minority remains ipsilateral forming the anterior corticospinal tract. Limb movement is mediated by the lateral CST resulting in contralesional motor deficits when disrupted. The anterior CST, however, innervates axial and girdle muscles bilaterally, often preserving these movements post-stroke dependent upon the site of the lesion. Several hypotheses exist regarding the mechanisms underlying motor recovery. The possibilities include the advent of new connections from the ipsilateral (anterior) CST, recruitment of other pathways such as the reticulospinal tract, enlistment of unaffected cortical areas, or sprouting from intraspinal CST collaterals which recross to the ipsi-lesional side after decussation [6, 7]. Mirror movements which can often be demonstrated in stroke patients [8] suggest novel branching of pathways originating from the undamaged hemisphere.

The CST can be beautifully visualized utilizing diffusion tensor imaging (DTI), a specific application of magnetic resonance imaging (MRI) to enhance structural analyses. DTI takes advantage of the anisotropic movement of water molecules within biological structures such as the axon. Unrestricted, water molecules undergo isotropic motion; however, when constrained within the linear space within or along

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an axon, the molecules move preferentially in the direction of the axonal process and pathways. Anisotropy may additionally be modulated by the degree of axon myelination which causes further restriction of perpendicular diffusion due to the lipid-dense myelin sheath surrounding most axons. By detecting the degree of anisotropy, the orientation of fiber tracts can be calculated and illustrated. Fractional anisotropy (FA) quantifies the degree of anisotropic motion of the water molecules. As motion becomes more coherent and aligned, FA values approach 1.0. Clinical applications of measuring disease-induced variations in DTI have primarily focused on the normal development of white matter and traumatic brain injury; however, other clinical applications have emerged including identifying structural derangements in the integrity of white matter due to multiple sclerosis, epilepsy, and brain tumors.

We describe a pediatric patient who suffered an extensive middle cerebral artery (MCA) territory infarct which resulted in profound hemiparesis who subsequently recovered the majority of her motor function. DTI imaging attained 7 months and 3.5 years post-stroke indicates significant change in CST anatomy, presumably the structural basis for her functional improvement.

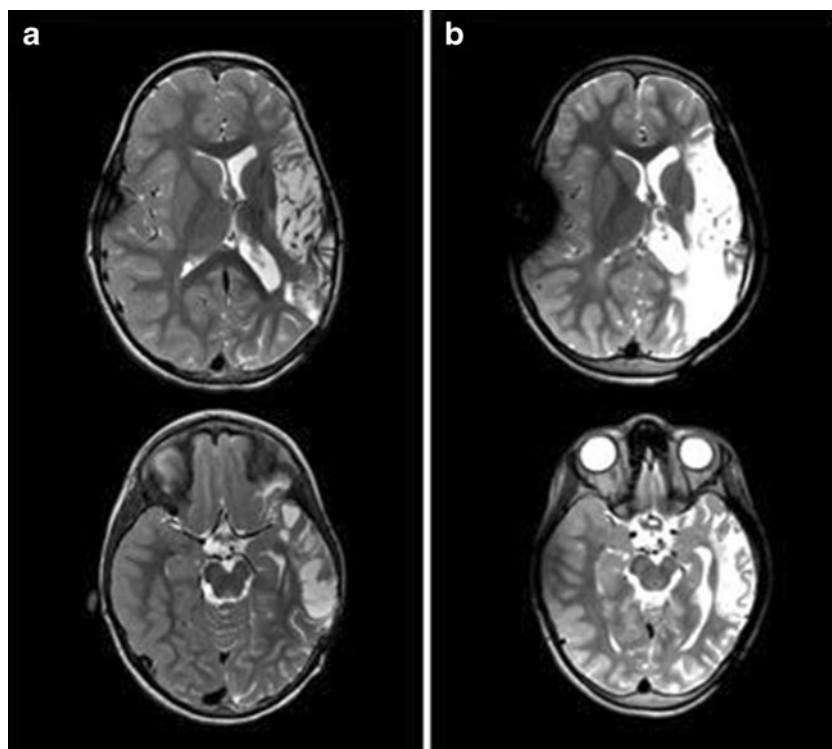
### Case report

A 3-year and 6-month-old female presented to the emergency room after being struck by a motor vehicle as a pedestrian.

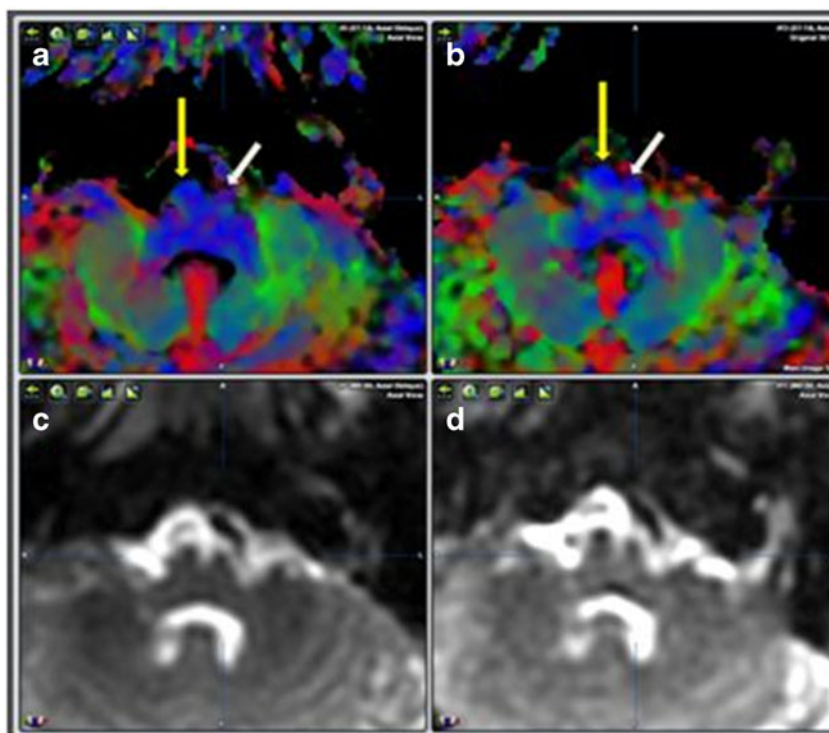
Initial head computed tomography (HCT) revealed a closed, displaced left occipital bone fracture, a non-displaced right temporal bone fracture with underlying subarachnoid hemorrhage, and a left temporal bone fracture through the foramen magnum and the posterior margin of the left jugular foramen extending into the base of the left sphenoid bone and pterygoid plate. There was no initial evidence of intraparenchymal, subdural, or epidural hemorrhage. A magnetic resonance venogram demonstrated thrombosis of the left transverse and sigmoid sinuses involving the left jugular vein. Occlusion of the left internal carotid artery (ICA) resulting from the skull base fracture was noted on the MRI. Flow within the left anterior cerebral artery and MCA was reestablished distally. The patient was placed on antiplatelet therapy with aspirin.

Approximately 40 h after admission, she became combative and aphasic with an acute right hemiparesis. At this point, HCT demonstrated extensive cerebrovascular compromise of the left MCA territory. Angiogram confirmed dissection of the left ICA and occlusion of the distal M1 segment of the left MCA. At this point, an emergent hemicraniectomy was performed. After extubation on postoperative day 11, the patient was successfully following commands on the left; however, she demonstrated only minimal movement on the right side accompanied by right-sided spasticity. At 4 weeks postoperatively, the right lower extremity had progressed to 3/5 strength while the right upper extremity continued to show only minimal movement. By 3 months, both the upper and lower right extremities had improved to 4/5 strength with a stable right-sided facial weakness. At 5 months, the patient was able to stand unassisted. By

**Fig. 1** T2-weighted axial images obtained in 2010 (**a**) and 2013 (**b**) reveal chronic infarction with progressive cystic encephalomalacia and Wallerian degeneration seen as asymmetric atrophy of the left cerebral peduncle



**Fig. 2** Colored FA map(a, b): the thickness and FA values of the R medullary pyramid have increased, but the left medullary pyramid remains small due to Wallerian degeneration on the 2013 exam (b, d) as compared to the 2010 exam (a, c). The medullary pyramids are indicated by arrows, c and d are T2 W (B0) images



1 year post-stroke, she demonstrated a stable right hemiparesis with symmetric reflexes and decreased strength on the right side. With the assistance of a right lower extremity orthosis, the patient was independently ambulatory and had returned to preschool. At this time, she began experiencing seizures of varying frequency and intensity with origins in both the right and left hemispheres.

Serial DTI imaging was performed 7 months (2010) and 42 months (2013) post-stroke. MRI shows chronic infarction of the left M1 territory (Fig. 1). The initial DTI imaging of the medullary pyramids (Fig. 2a) revealed the right pyramidal tract (PT) with a greater FA value (0.9) than the left (0.6) and greater cross-sectional area (Table 1). Imaging at the same level 3 years later (Fig. 2b) showed a more pronounced difference in the PTs. Both sides increased in cross-sectional area (Table 1); however, the right side remained substantially larger than the left. Tractography at the two time points (Figs. 3 and 4) clearly illustrates the disparity between the

tracts. In the right PT, the FA value increased to maximum (1.0) and decreased substantially on the left (0.3). The contralesional to ipsi-lesional FA ratio increases from 1.5 to 3.3 between the two DTI images.

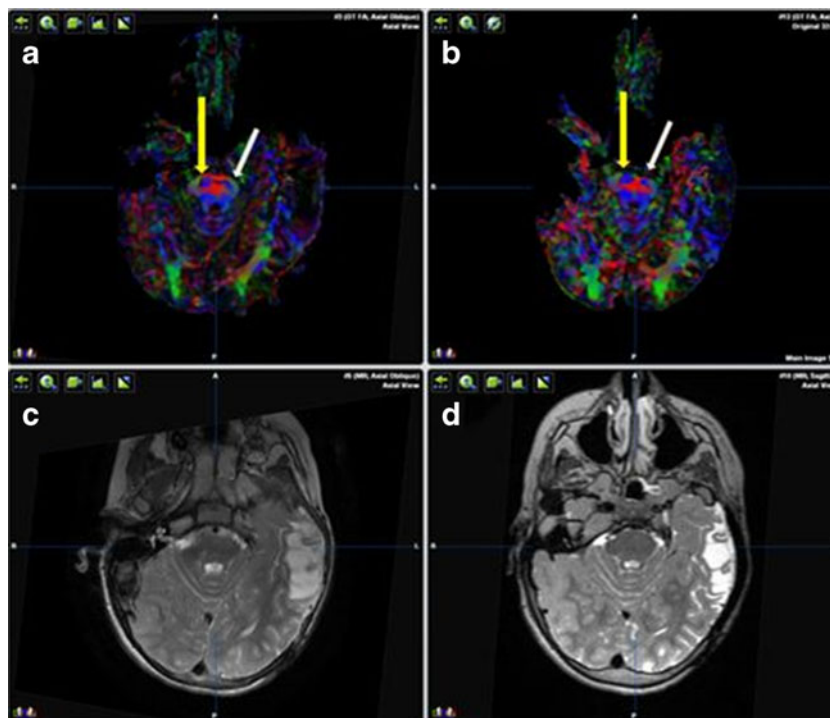
**Discussion**

Reorganization of the CST is an important substrate for the recovery of motor function after stroke, especially in the pediatric population. Visualizing white matter tracts like the CST and the plastic changes that occur within the brain during post-stroke recovery is accomplished particularly well with DTI. The response to injury like stroke in both the central and peripheral nervous system involves Wallerian degeneration (WD). Occurring distal to the site of injury, WD is the disintegration of axonal structures followed by eventual degradation of myelin and atrophy of affected fiber tracts. In the case presented here, the reduction in FA values of the left medullary pyramid between the two DTI images is most likely due to WD of the left-sided PT [9, 10]. As myelin and axonal microfilaments disintegrate, water molecules are less constrained to move anisotropically. WD measured by FA and the FA ratio has been shown to correlate with concurrent motor deficits and to be predictive of motor deficits 1 month post-injury [11–13]. While the ipsi-lesional tract demonstrated a decrease in FA values, the contralesional tracts show a compensatory increase which may suggest a more anatomically robust tract including greater axonal diameter and increased myelination of fibers [14].

**Table 1** Measurements of the medullary pyramids

	2010		2013	
	Right pyramid	Left pyramid	Right pyramid	Left pyramid
FA values	0.9	0.6	1.0	0.3
Anterior/posterior diameter (mm)	4.2	2.1	4.4	2.6
Right-left diameter (mm)	6.0	3.1	6.5	4.1

**Fig. 3** FA colored maps of DTI (a 2010, b 2013) show a progressive asymmetry between the R and L corticospinal tracts indicated with *arrows* (L smaller than R side) which is more prominent on the 2013 exam (b, d). c and d are axial T2-weighted images



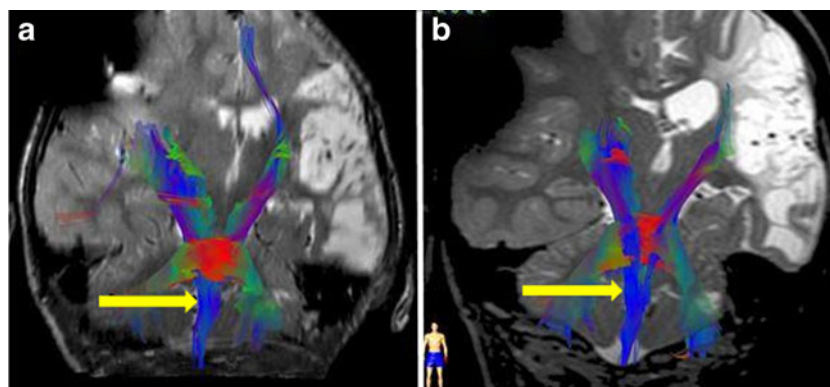
This imaging clearly indicates changes in the PTs as a whole; however, it is not apparent which component(s) of the PT may be responsible for return of motor function. The PT contains not only the CST which is itself comprised of the lateral and anterior CSTs but also the reticulospinal tract. Thus, there are three distinct possibilities to explain the growth and increased FA of the contralesional pyramid. Evidence drawn from studies of stroke recovery as well as motor reorganization in cerebral palsy suggests that all three of these pathways may demonstrate compensatory reorganization following CST compromise.

First, there is evidence suggesting that the reticulospinal tract is an important route of ipsilateral motor control after CST damage [15, 16]. Although in healthy subjects the crossed lateral CST facilitates the vast majority of limb movement, there are indications that ipsilateral innervation of the distal limbs (at least the upper extremities) does exist and is

potentially mediated through corticoreticulospinal projections [17, 18]. A second explanation involves persistent ipsilateral CST projections. Ipsilateral CST projections are more abundant in childhood after which they are pruned in favor of contralateral ones [19, 20]. Early childhood insult, therefore, may result in improved recovery due to the presence and preservation of these fibers which have yet to be eliminated. A third possibility involves the abnormal branching of corticospinal axons descending from the contralesional cortex. In this case, homologous left and right motor neuron pools share a common descending axon with presynaptic branching at the segmental level not seen in healthy anatomy. This scenario can be accompanied by mirror movements as a result of the shared input [18, 21].

Although this imaging study is focused only at the medullary pyramids, any of these three proposed explanations of reorganization could be accompanied by atypical connections

**Fig. 4** Comparison of the CST fiber tractography from 2010 (a) and 2013 (b) created by using the same imaging parameters and FA threshold values: reduced corticospinal tracts in the left cerebral peduncle and brainstem while the thickness on the right side is increased



between the hemispheres as a further attempt to compensate [22]. This potential increase in connectivity could theoretically lead to aberrant propagation of electrical activity and manifest as the focally originating seizures displayed by the patient. Furthermore, these explanations do not take into account afferent sensory pathways that can also be contributing to functional deficits if they continue to project to the lesioned hemisphere.

DTI can be utilized post-stroke as a useful detector of early Wallerian degeneration, a predictor of future motor deficits and an indicator of patterns of reorganization. Coupled with clinical observations, motor mapping, and other forms of imaging, DTI can help to elucidate neural organization and contribute to the planning of rehabilitation and, when indicated, surgical intervention.

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**Conflict of interest** The authors declare that they have no conflicts of interest.

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