Role of Diffusion Tensor Tractography in Diagnosis of Limb-Kinetic Apraxia in Stroke Patients: A Mini-Narrative Review

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Financial support: This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean Government (MSIP) (No. 2021R1A2B5B01001386)
Conflict of interest: None declared

Limb-kinetic apraxia (LKA) is an execution disorder of movements caused by an injury to the secondary motor area (the supplementary motor area and premotor cortex) with preservation of an intact corticospinal tract (CST). A precise diagnosis of LKA is often limited because it is made based on the clinical observation of movement characteristics with confirmation of the CST state, and no specific clinical assessment tools for LKA have been developed. Diffusion tensor tractography (DTT) enables a three-dimensional estimation of the neural tracts related to LKA, such as the CST and corticofugal tract from the secondary motor area. This article reviewed 5 DTT-based studies on LKA-related neural tracts in stroke patients. These studies suggest that DTT could be a useful diagnostic tool for LKA along with previous diagnostic tools, such as brain magnetic resonance imaging and transcranial magnetic stimulation. In particular, DTT for the affected corticofugal tract can provide useful evidence for diagnosing LKA when clinicians cannot observe the movement characteristics because of severe weakness after a severe injury to the affected CST. Furthermore, a reviewed study suggested that LKA might be related to the unaffected neural tracts for motor function when the affected neural tracts were severely injured. This review summarizes the role of DTT in the diagnosis of LKA in stroke patients.

Keywords: Apraxias • Cerebral Infarction • Diffusion Tensor Imaging • Hemorrhagic Stroke • Stroke

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/936417
Background

Motor weakness is a serious disabling sequela of stroke; more than 50% of stroke patients experience a residual motor deficit [1,2]. Motor weakness is a typical clinical feature of an injury to neural tracts for motor function, but apraxia can also accompany motor weakness-like clinical features [2]. Apraxia is the inability to execute learned, skilled movements despite the preservation of power, sensation, coordination, and comprehension for the execution of movements [3-7]. Limb apraxia is an impairment of the performance of skilled, purposive limb movements and is classified into 3 subtypes: ideational apraxia, ideomotor apraxia, and limb-kinetic apraxia (LKA) [4,5,7-9]. LKA is the execution disorder of movements caused by an injury to the secondary motor area (the supplementary motor area and premotor cortex) with preservation of an intact corticospinal tract (CST) [7-11]. However, LKA has been a controversial subtype of apraxia that has been largely neglected [10].

A diagnosis of LKA is clinically important because the treatment strategy differs according to whether the motor weakness is ascribed to a CST injury or LKA. In particular, recent studies reported that dopaminergic agonists are effective for improving LKA [2,12-19]. On the other hand, a precise diagnosis of LKA is often limited because it is made based on clinical observation of the movement characteristics with a confirmation of the CST state, and no specific clinical assessment tools for LKA have been developed [2]. According to previous studies, the movement characteristics of LKA can be summarized as follow: 1) impaired, clumsy, coarse, and mutilated execution of simple movements contralateral to the lesion (patients are asked to open and close the affected fingers at a comfortable pace); 2) lack of voluntary-automatic dissociation; and 3) normal conceptual knowledge of motor performance [2-4,7,8,10,11,20].

The CST state in patients with LKA has been estimated using conventional brain computed tomography or magnetic resonance imaging (MRI), nuclear medicine imaging, and transcranial magnetic stimulation (TMS) [7,20-22]. Classically, LKA is considered based on the condition of intactness of the affected CST. However, recent studies reported that the patients who had injury of the CST presented with LKA [15,16,19,23]. Therefore, a precise diagnosis of LKA can be limited in patients who cannot execute movements due to severe weakness caused by the partial injury of the CST combined with LKA [15,16,19,23]. Nevertheless, a few recent studies reported that the corticofugal tract (CFT) from the secondary motor area is strongly overlapped with the CST at the subcortical level [24-26]. These results suggest that LKA can accompany a CST injury at the subcortical level due to the CFT injury, but this topic has generally been neglected.

Diffusion tensor imaging (DTI) allows an estimation of the microstructural characteristics of the white matter by the water diffusion characteristics [27]. Diffusion tensor tractography (DTT) reconstructed using the DTI data enables a three-dimensional estimation of the neural tracts [28-30]. The unique advantage of DTT compared to DTI is that a neural tract can be estimated three-dimensionally through the configuration and various parameters, such as fractional anisotropy, mean diffusivity, and tract volume (fiber number) [15,23,30,31]. Several neural tracts related to motor function, including the CST, CFT, and corticoreticulospinal tract, could be reconstructed using a DTT reconstruction method [15,18,28-30]. As a result, many DTT-based studies have reported that LKA is related to injuries of the above neural tracts in various brain pathologies [2,7,15-19,23,32-34].

This review presents the findings from recent studies on the role of DTT in the diagnosis of LKA in stroke patients (Table 1) [2,7,15,16,23].

| Authors          | Publication year | Number of patients | Pathology of brain injury | Analyzed neural tracts | DTT analysis method | Combined study |
|------------------|------------------|--------------------|---------------------------|------------------------|---------------------|----------------|
| Hong et al       | 2012             | 1                  | Cerebral infarct          | CST, CFT               | Configuration       | TMS            |
| Jang SH          | 2013             | 1                  | ICH                       | CST, CFT               | Configuration       | TMS            |
| Jang et al       | 2016             | 1                  | Cerebral infarct          | CST, CFT               | Configuration       | TMS            |
| Jang and Seo     | 2016             | 20                 | Cerebral infarct          | CST, CFT               | DTT Parameters      | TMS            |
|                  |                  |                    |                           |                        | (fractional anisotropy, tract volume) |                |
| Jang and Byun    | 2022             | 1                  | ICH                       | CST, CFT               | Configuration       | TMS            |

DTT – diffusion tensor tractography; CST – corticospinal tract; CFT – corticofugal tract; TMS – transcranial magnetic stimulation; ICH – intracerebral hemorrhage; CRT – corticoreticulospinal tract.
Studies That Demonstrated the Role of Diffusion Tensor Tractography in the Diagnosis of Limb-Kinetic Apraxia in Stroke Patients

In 2012, Hong et al reported a patient who presented with LKA and ideomotor apraxia following a cerebral infarct that was demonstrated by movement characteristics, the clinical assessment tool, TMS, and DTT [7]. A 67-year-old man was diagnosed with a cerebral infarct in the left middle cerebral artery territory. At the time of the evaluation (5 months after onset), he showed right moderate hemiparesis except for the finger extensors, which was severe weakness. An abnormality of the ideational plan for motor performance and cognition was not observed, but his movements corresponded to typical movement characteristics of LKA during the affected hand grasp-release movements. By contrast, the abnormality was detected on the ideomotor apraxia test as 20 points (cut-off score <32 points) [35]. The affected (left) CST presented normal findings on DTT in terms of the configuration and motor evoked potential, which was obtained at a hand muscle in terms of latency (the fastest velocity of the CST) and amplitude (the number of neural fibers of the CST) [36]. However, the affected CFTs from the supplementary motor area and premotor cortex and superior longitudinal fasciculus revealed partial injuries compared with the right side. As a result, the authors demonstrated LKA based on the movement characteristics, brain MRI, motor evoked potentials of TMS, and DTTs for the CST and CFT. The authors also found concurrent ideomotor apraxia based on findings of the clinical assessment tool (the ideomotor apraxia test) and DTT for the superior longitudinal fasciculus [37]. The advantage of this study was that LKA was demonstrated using DTT for the CST and CFT and the evoked motor potential of TMS. The limitation of this study was that the neural tracts were analyzed only by the configurational data without DTT parameter data.

Jang (2013) reported on a chronic stroke patient who showed delayed rapid motor recovery by improving LKA through 1 month of rehabilitation, which was started at 30 months after onset [2]. A 50-year-old man was diagnosed with a right thalamic hemorrhage. At 30 months after onset, he was assessed for rehabilitation: his cognition and the ideomotor apraxia test results were within the normal range [35,38]. He revealed moderate weakness of his left arm and leg. Furthermore, he exhibited the typical movement characteristics of LKA while performing open and close movements of his affected fingers. He underwent rehabilitation, including the dopaminergic agonists (ropinirole, 3 mg; bromocriptine, 10 mg; levodopa, 375 mg) for 1 month [2,12-19]. He gained 22% motor recovery after 1 month between 30 and 31 months after onset, his movement characteristics of LKA almost disappeared. The authors found that the affected CST was intact in terms of the configuration on DTT and motor evoked potential obtained at an affected hand muscle (latency and amplitude) on TMS [36]. Despite the significant motor recovery, follow-up motor evoked potentials obtained at 30 and 31 months after onset did not reveal a significant change. As a result, the authors attributed the motor recovery during 1 month of rehabilitation at the chronic stage in this patient to the improvement of LKA. This study had the following advantages. First, the authors demonstrated the intactness of the affected CST using DTT for the CST and motor evoked potential obtained at an affected hand muscle. Another advantage of this study was that the authors demonstrated that the patient’s motor recovery was attributed to an improvement of LKA, not neural recovery of the affected CST, based on evidence of no significant change of the affected CST and the motor evoked potentials. These results show that even a patient who passed the motor recovery phase of stroke (6 months after onset) can recover to some extent when the patient had LKA through rehabilitation, including the dopaminergic agonists [2,12-19]. However, this study was limited because only the CST was analyzed by configuration without DTT parameters and the CFT findings [35,38].

In 2016, Jang et al reported a patient who presented with motor weakness caused by a CST injury concurrent with LKA due to a CFT injury after a cerebral infarct [15]. A 52-year-old man showed left hemiplegia caused by a middle cerebral artery territory infarct. When he started rehabilitation 2 weeks after onset, he presented with severe left hemiparesis with complete weakness of the finger muscles. The patient’s cognition and the ideomotor apraxia test were within the normal range [35,38]. Brain MRI showed a large lesion including the primary motor cortex and secondary motor area (the supplementary motor area and premotor cortex) (Figure 1A). The patient underwent rehabilitation, including the dopaminergic agonists (ropinirole, 3 mg; amantadine, 300 mg; levodopa, 500 mg) [2,12-19]. After 2 weeks of rehabilitation, the patient showed significant motor recovery in his left extremities to a nearly normal state. On 2-week DTT, although the integrities of the affected (right) CST and CFTs from the secondary motor area were preserved, the affected neural tracts showed findings of partial injuries compared to those of the unaffected side (Figure 1B). As a result, the authors concluded that the motor recovery during the 2 weeks after onset in this patient was attributed to the improvement of LKA, the recovery of the injured CST, and resolution of local factors such as perilesional hematoma and edema [39,40]. The authors showed that, in a patient who cannot show typical movement characteristics due to severe weakness of the affected finger muscles, some motor weakness could be attributed to LKA due to the affected CFT injury. Although the classical concept of LKA resulted from injury of the secondary motor area on the condition of intact preservation of the CST in the affected hemisphere, this study suggested that LKA could accompany the affected CFT injury with the affected CST injury [7,8,10].
During the same year, Jang and Seo (2016) reported injuries of the CST and CFTs from the secondary motor area in patients with cerebral infarct [23]. Twenty consecutive patients with a corona radiata infarct who exhibited definite hand weakness by partial injury to the affected CST demonstrated by DTT and abnormal amplitude of the motor evoked potential at the ear-ly stage (1-4 weeks after onset) of the cerebral infarct [23]. The affected CST and CFTs revealed low FA values and tract volumes compared to those of the unaffected side, indicating injuries of these neural tracts. As a result, the authors concluded that differential diagnosis of the weakness-like clinical features due to LKA from actual motor weakness resulting from an injury of the affected CST is difficult. However, weakness-like clinical features due to LKA can be demonstrated using DTT for the CFT. The advantage of this study was that it suggested that LKA due to the CFT injury could be accompanied by pure weakness or by an injury of the CST in stroke patients with subcortical lesions. This study agreed with the results of previous studies in that the CFTs from the secondary motor area are overlapped with the CST fibers at the subcortical white matter [24-26]. However, this study did not provide data on the movement characteristics of LKA in the patient group.

Recently, Jang and Byun (2022) reported a chronic stroke patient who showed delayed gait recovery and improved LKA through 24 days of rehabilitation that started 19 months after onset [16]. A 49-year-old man was diagnosed with a spontaneous intracerebral hemorrhage in the left basal ganglia. Beginning at 3 weeks after onset, he underwent rehabilitation, including the dopaminergic drugs (pramipexole 1 mg, ropinirole 1 mg, amantadine 100 mg, carbidopa/levodopa 25 mg/250 mg, and bromocriptine 3.75 mg) at a local rehabilitation hospital until 19 months after onset [2,12-19], but he could not walk independently. Hence, he re-started rehabilitation at another university hospital 19 months after onset. He could not even stand or walk, due mainly to the severe motor weakness of the affected (right) leg (manual muscle test [MMT]: hip flexor, trace; knee extensor, trace; ankle dorsiflexor,
zero). He underwent a rehabilitation program similar to the previous rehabilitation hospital with increased doses of the dopaminergic agonists (pramipexole 1 to >1.5 mg, ropinirole 1 to >1.5 mg, amantadine 100 to >150 mg, carbidopa/levodopa 25 mg/250 mg to >50 mg/500 mg) [2,12-19]. After 24 days in the second hospital, he could walk independently concurrent with the motor recovery of the affected leg (MMT: hip extensor, poor [range: 20°]; knee extensor, fair; ankle dorsiflexor, zero). At 19-month DTT, the affected (left) CST and corticoreticulospinal tract showed discontinuities at the brainstem and subcortical white matter, respectively, whereas the unaffected CST and corticoreticulospinal tract revealed intact integrities. The authors suggested that the improvement of LKA of the affected leg was the main reason for the delayed gait recovery in this patient because he had rapid motor recovery of the affected leg by increasing the dopaminergic agonists from 19 months after onset (knee extensor: trace [admission] > poor [10 days after admission] > fair [24 days after admission]). This study suggested that the unaffected CST or corticoreticulospinal tract might be related to LKA in the case of the severe injuries of the affected CST and CRT like this patient, even though the majority of studies of LKA have reported LKA related to the affected CST [2,7,15-17,19,23,34]. However, other studies showed that the unaffected CST or corticoreticulospinal tract is responsible for the motor recovery of the affected leg in the case of complete injuries of the affected CST and corticoreticulospinal tract, like this patient [30,41]. As a result, the LKA of the affected leg in this patient might be related to the unaffected CST or corticoreticulospinal tract. Furthermore, this study suggested that the appropriate dose of dopaminergic agonists for improving LKA might be necessary. Nevertheless, this study was limited in that the authors did not show a change of the affected and unaffected CST and corticoreticulospinal tract by follow-up DTTs.

Conclusions

This article reviewed 5 DTT-based studies on LKA-related neural tracts in stroke patients [2,7,15,16,23]. These reviewed studies suggest that DTT could be a useful diagnostic tool for LKA along with previous diagnostic tools, such as brain MRI and TMS. In particular, DTT for the affected CFT can provide useful evidence for a diagnosis of LKA in patients who do not show movement characteristics because of severe weakness after a severe injury of the affected CST [15,22,23]. Furthermore, a reviewed study suggested that LKA might be related to the unaffected CST or corticoreticulospinal tract when the affected CST and corticoreticulospinal tract showed severe injuries [16]. Most of the reviewed studies presented the effect of the dopaminergic agonists on the improvement of LKA [2,7,15,16]. These coincide with previous studies that demonstrated the therapeutic effect of the dopaminergic agonists for apraxia [12-14,17-19]. In particular, a reviewed study suggested the importance of optimal doses of the dopaminergic agonists to improve LKA [16]. A few reviewed studies also suggested that rapid and significant recovery at a chronic stage that passed the motor recovery phase of stroke should indicate a concurrent LKA with pure motor weakness caused by an injury to the neural tracts for motor function [2,16]. These reviewed studies could facilitate the neurorehabilitation of patients with LKA because DTT can provide information on the proper application of neuromodulation considering the state of neural tracts related to LKA [42]. For example, non-invasive neuro-stimulation techniques could be applied to the neural correlates for LKA with an individual patient’s specific method based on DTT findings [42]. In this study, however, only 5 studies were reviewed, and 4 out of 5 were case reports. Therefore, further prospective studies recruiting a large number of patients will be needed.

This review presented the findings from 5 identified studies on the role of DTT in the diagnosis of LKA in stroke patients. The role of DTT shows promise for the diagnosis of LKA in stroke patients. Further studies are needed to evaluate the role of DTT in the diagnosis of LKA in other brain pathologies, such as Parkinson disease and hypoxic brain injury.

Declaration of Figures’ Authenticity

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