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Imaging and Diseases of the Ascending and Descending Pathways

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The corticospinal tract and other ascending and descending fibers are important in executing cerebral function. Conventional magnetic resonance and advanced neuroimaging findings of diseases involved in ascending and descending pathways are reviewed, including amyotrophic lateral sclerosis, secondary degeneration diseases, and intracranial tumors.
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Introduction

The cerebral ascending and descending fibers are critical components in functional pathways. The corticospinal tract (CST) is the largest descending white matter tract extending from the prefrontal gyri to the spinal cord. The CST is the major neuronal pathway for motor function in the human brain. Detailed knowledge of the CST somatotopy is important in terms of rehabilitative management and invasive procedures for patients with brain injury, particularly with regard to fine motor activity of the hands. The hand and leg somatotopies of the CST are arranged as anteroposterior orientation in the posterior limb of the internal capsule (PLIC),[1] mediolaterally in the mid-to-lateral portion of the cerebral peduncle, ventromedial-dorsolaterally in the pontine basis, and mediolaterally in the medullary pyramid.[2] The corticopontocerebellar (CPC) tract is the largest afferent pathway derived from cerebral cortex, projects to the ipsilateral pontine nuclei located ventral to medial lemniscus via the cerebral peduncle. Pontine nuclei send axons to the contralateral cerebellar cortex, transversing the anterior pons as transverse pontine fibers. Transverse pontine fibers connect to the contralateral cerebellar hemisphere mainly via the middle cerebellar peduncle with a small number of fibers passing via the inferior cerebellar peduncle.[3] Almost all CPC fibers cross into the contralateral cerebellum via the basis pontis[4] (Fig. 1).

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Many diseases may involve cerebral ascending and descending pathways. Advanced neuroimaging techniques, including magnetic resonance (MR) perfusion-weighted imaging (PWI), diffusion tensor imaging (DTI), MR spectroscopy (MRS), and positron emission tomography (PET), have provided additional functional information of metabolic, hemodynamic, and microstructural changes in the past decade. However, there are few dedicated neuroanatomical reviews of imaging in this area. In this article, we focus on imaging findings in amyotrophic lateral sclerosis (ALS), secondary degenerative disease, intracranial tumors, and inflammatory diseases.

Amyotrophic Lateral Sclerosis

ALS, also known as Lou Gehrig disease, is a fatal motor neuron disease affecting primary motor neurons in the motor cortex as well as second- and third-order motor neurons in the brainstem and spinal cord, whereas primary lateral sclerosis (PLS) is defined by pure first-order neuron involvement. The annual incidence and prevalence of ALS are about 2 per 100,000 and 8 per 100,000, respectively. There are 2 known types of ALS: sporadic and familial. The sporadic type is the most common one and accounts for 90% of ALS cases. Familial ALS is hereditary, which is passed on by a dominant gene and makes up the remaining 10% of cases. The cause of ALS and PLS is unknown. Approximately 2% of cases are due to mutations in the superoxide dismutase (SOD1) gene.[5,6]

The classical neuropathologic features of ALS include progressive loss and degeneration of the large motor neurons in the gray matter of the spinal cord, brainstem, and cortex, as well as degeneration of the CST. Histologic studies demonstrate loss of

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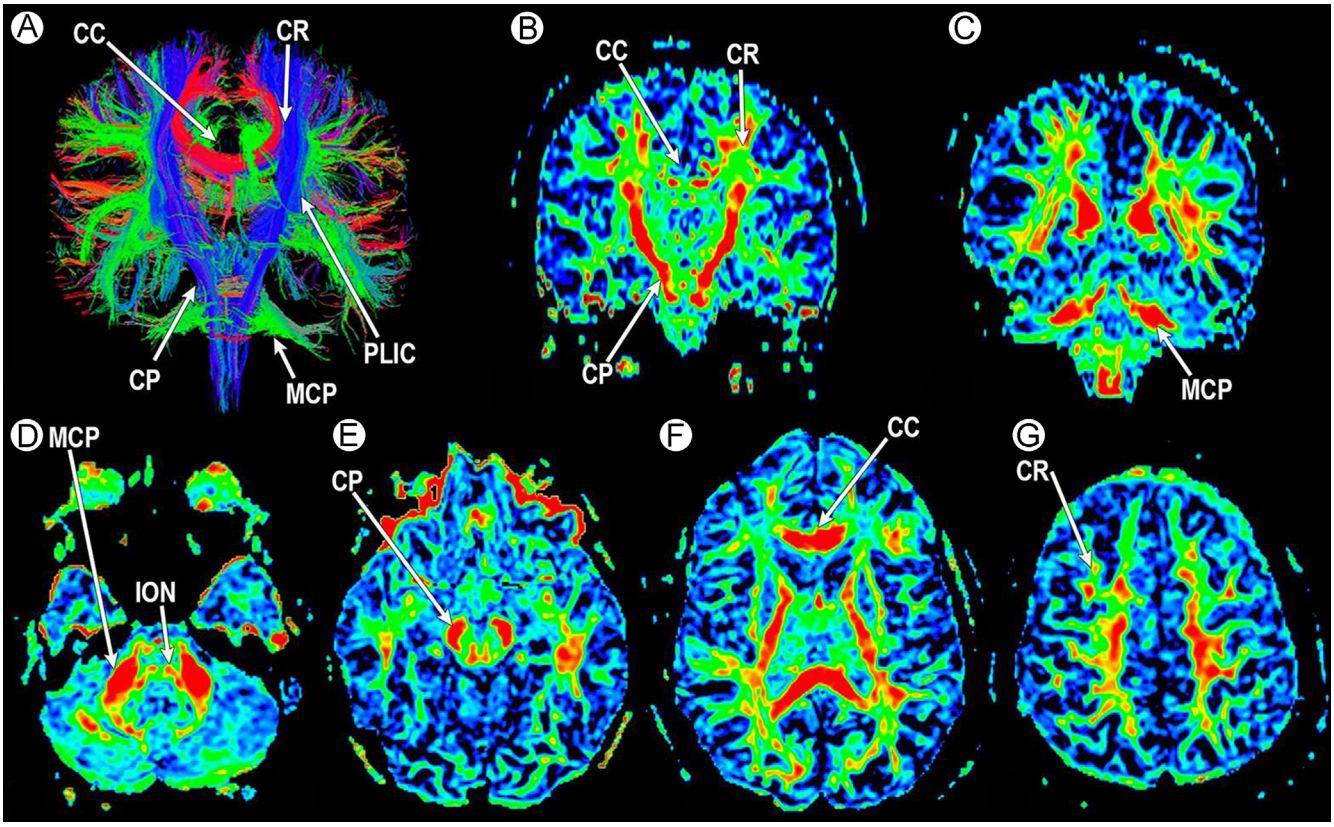

Figure 1 Normal anatomy of the white matter tracts. (A) Color-coded whole-brain tractography. (B and C) Coronal and (D-F) axial color directionless FA maps. CC, corpus callosum; CR, corona radiate; CP, cerebral peduncle; MCP, middle cerebellar peduncle.

the giant pyramidal Betz cells, accompanied by reactive gliosis in the motor cortex. Myelin pallor is the most conspicuous change secondary to degeneration in the CST. Therefore, major cerebral imaging findings of ALS and PLS include 2 categories, abnormalities in the cortex resulting from primary neuropathology of motor neurons and secondary CST degeneration.[5,6]

In previous studies on conventional MR imaging (MRI), hypointensity in the motor cortex on T2-weighted images and atrophy of the precentral gyri, as well as hyperintensity along the CST on T2-weighted images (Fig. 2) have been considered as diagnostic clues of ALS or PLS. The mechanism of hypointensity in the motor cortex on T2-weighted images may be related to the T2 shortening effect from excessive iron deposition, fibrillary gliosis, and macrophage infiltration. The atrophy of the precentral gyri is subsequent to the volume loss of motor neurons. A recent study reported that the cortical thickness is reduced in ALS not only in motor areas but also in widespread nonmotor cortical areas. Cortical thickness was related to clinical severity.[7] The T2 hyperintensity along the CST is proposed to be due to secondary axonal degeneration in the CST, also termed Wallerian degeneration (WD), which is discussed in more detail in the following section. However, it should be noted that these 3 signs are nonspecific and cannot confirm the diagnosis of ALS or PLS, as they could be observed in the normal aging brain or due to other etiologies.[5,6]

Application of DTI, MRS, MR PWI, and magnetization transfer (MT) imaging provides further functional information of the pathophysiological process of ALS and PLS.

Most studies of ^{1}H MRS in ALS or PLS have reported reduced N-acetyl aspartate (NAA) in the motor cortex (Fig. 3) using either quantitative NAA concentration or ratios of NAA-creatine, NAA-choline (Cho), and NAA-(creatine + Cho).[8-13] As NAA is found predominantly within neurons, reduced NAA level is proposed as a metabolic marker indicating loss or dysfunction of motor neurons in ALS or PLS.[5,6,8-12] Increased myo-inositol (mI) has also been found in the motor cortex in patients with ALS. In addition, increased Cho level has been reported in the PLIC.[13] These findings are nonspecific, being commonly encountered in gliosis of any origin.

Most of DTI studies in ALS and PLS have focused on secondary degeneration in the CST. Reduced fractional anisotropy (FA) value and increased apparent diffusion coefficient value can be demonstrated at nearly all levels of the CST; the most significant differences in myelin loss between patients and healthy volunteers have been found at the level of the PLIC, indicating this is the optimum site for quantitative evaluation. DTI tractograms reveal a decreased number of CST fibers in patients with ALS and patients with PLS (Fig. 3).[5,6,8] In addition, Prell et al[14] found that there are different DTI patterns owing to bulbar or limb onset. Recently, new and more advanced analytical