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THE USE OF ADVANCED MRI TECHNIQUES FOR THE EVALUATION OF SPINAL CORD AND PERIPHERAL NERVE DISORDERS

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Abstract

Extensive use of magnetic resonance imaging (MRI) has been made to identify pathological alterations in the central nervous system. MRI is, therefore, still largely underapplied in the assessment of the peripheral nervous system (PNS). The two perceived limitations of MRI that are typically to blame for this underutilization are: (1) the requirement for extremely high resolution in order to image the small structures within the peripheral nerves in order to visualize morphological changes; and (2) the absence of normative data in PNS MRI, which makes it challenging to interpret the data in a reliable manner. The most recent advancements in in vivo magnetic resonance imaging of human peripheral nerves are reviewed in this article. Its goal is to pinpoint the areas that have advanced and those that still need work. This study specifically discusses how MRI can be utilized to give objective, non-invasive biomarkers for the assessment of peripheral neuropathies, especially with a plethora of novel medications on the horizon. Despite the fact that there are numerous methods for identifying and monitoring PNS disorders, most of them focus on the distal peripheral nerves, which may be totally deteriorated when a patient attends their initial clinic appointment. Furthermore, the proximal nerves that are deeply entrenched in the tissue could not be accessible using these methods. An way to get around these issues would be peripheral nerve MRI. This analysis concludes with a clinical protocol at 3T that will enable high-resolution, high-contrast, quantitative MRI of the proximal peripheral nerves in order to answer the urgent clinical needs.

Keywords: Charcot-Marie-Tooth disease, peripheral neuropathy, sciatic nerve, peripheral nervous system, and peripheral nerves.

1. Introduction

Humans require the peripheral nervous system (PNS) to act as a communication channel between the brain and their "external devices," such as muscles or sensory organs, in order for the brain to carry out directives from the central nervous system (CNS), which is made up of the brain and spinal cord. Therefore, the purpose of these peripheral nerves is to transfer information

from the brain to the spinal cord and, ultimately, to organs situated outside the cranial area or spinal canal 1.

The well-organized tubular structures known as peripheral nerves extend from the brain and spinal cord to the cranial tissues and the limbs. This review will ignore the cranial nerves for simplicity's sake. Nerve fibers from the spinal cord's dorsal column, known as dorsal roots (mostly sensory nerve fibers), and ventral column, known as ventral roots (mainly motor nerve fibers), are extended. At the neural foramen, the ventral and dorsal roots come together and are surrounded by epineurial tissues before leaving the spinal canal. These nerves from various neural foramen levels branched into peripheral nerves in the limbs, including the ulnar, median, radial, femoral, and sciatic nerves. These merged nerves formed the brachial plexus in the neck or the lumbosacral plexus in the lower back 1.

On a transverse section, the peripheral nerves' structure is easily identifiable, as Figure 1 illustrates. The topmost layer in this case is termed the epineurium, a fibrous connective tissue. Inside the epineurium, a second layer of fibrous connective tissue called the perineurium organizes individual nerve fibers into bundles known as fascicles. Human peripheral nerve fascicles vary widely in size and number; their diameter normally falls between 0.1 and 1 mm 2. Neural fibers can be classified as either myelinated or unmyelinated. The former wraps axons concentrically using segments known as internodes, which are composed of layers of Schwann cell membranes (myelin) 3.

Punctual gaps known as nodes of Ranvier, where the axon is devoid of myelin, divide the segments. Another layer of connective tissue known as the endoneurium divides myelinated nerve fibers from one another. It is a component of the blood-nerve barrier, which keeps chemicals from passing from the blood into the endoneurial fluid. Numerous C fibers, or non-myelinated nerve fibers, run parallel to the myelinated axons. Without developing myelin, a single layer of Schwann cell membrane encircles these axons. This collection of unmyelinated axons is referred to as a Remak bundle. Blood veins abound in the nerve epineurium and perineurium as well. There is a low-protein fluid known as endoneurial fluid between the nerve axon and the endoneurium. Between the central nervous system and distal organs, the myelinated nerve axon transmits electrical signals known as action potentials. Axons are insulated by the myelin, which also allows the conduction of action potentials at a faster rate than in axons that are not myelinated 1–5.

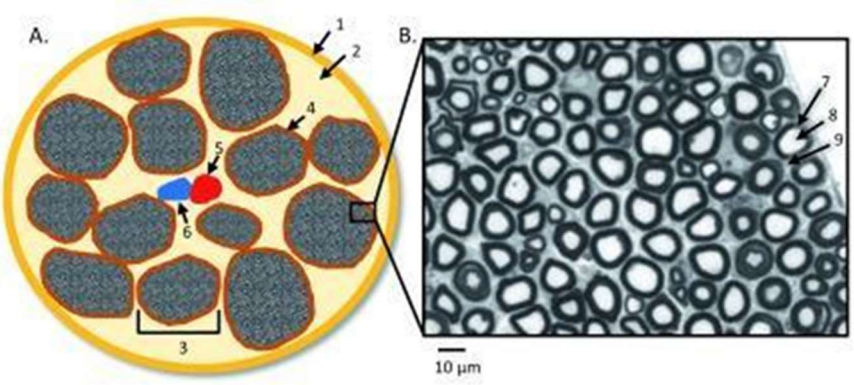

Figure 1. Structure of the peripheral nerve cross-section.

2. Peripheral neuropathy

Peripheral neuropathy refers to a group of diseases that damage peripheral nerves. These diseases can affect one or more nerves (mononeuropathy) or several nerves (polyneuropathy). Peripheral nerves in nearly symmetric portions of both limbs are affected by a group of illnesses called polyneuropathies. Clinically, it is characterized by scorching pain in the hands and feet, numbness, and muscle weakness. A length-dependent mechanism may cause the disease to spread to the proximal arms and legs, and on occasion, other body regions such the autonomic nerves. All all, these illnesses are extremely common and impact roughly 8% of those over the age of 55. Diabetic peripheral neuropathy (DPN), Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), HIV-associated neuropathy, alcoholic neuropathy, and paraproteinemic neuropathy are among the common forms of polyneuropathy.

The condition is referred to as Charcot-Marie-Tooth disease (CMT) when it is brought on by monogenic mutations. Similar to other forms of polyneuropathy, demyelination (or dysmyelination in cases where aberrant myelin formation occurs during development) and axonal degeneration are the primary pathogenic abnormalities affecting CMT. Type 1 (CMT1) anomalies in the myelin sheath, which are inherited autosomally dominantly, are the cause of a large variety of CMT illnesses. CMT1A is the most prevalent subtype of CMT1. Duplication of chromosome 17p12, a section of DNA that contains the gene 7 for peripheral myelin protein-22 (PMP-22), is the cause. Genetic alterations in the myelin protein zero (P0) gene 8 are the cause of CMT1B. Axonal degeneration is the main cause of symptoms in CMT2, the other primary kind of the condition. The most prevalent form of CMT2, known as CMT2A, is brought on by missense mutations in the Mitofusin-2 gene, which produces a protein that controls mitotic fusion 9. CMTX refers to all CMT patients with x-linked inheritance. CMT4 refers to all CMT patients with autosomal recessive inheritance.

About 3% of trauma patients have peripheral nerve injury, which is very common and is frequently brought on by auto accidents 10. According to Seddon 11 and Sunderland 12, there are three main categories of peripheral nerve injuries: neurapraxia, axonotmesis, and

neurotmesis. Primary demyelination in myelinated nerve fibers accompanied by a reversible conduction block is known as neuropraxia. Axonal degeneration is the result of axonotmesis. The axon can regenerate at a relatively modest rate (about 1 mm each day) since the neuronal cell body remains intact. When an axon splits off from the cell body, Wallerian degeneration occurs at its distal end. Axon loss and demyelination along with disruption of the endoneurium, perineurium, or epineurium characterize the neurotmesis. Axons may regenerate when endoneurium is injured, although poor development is anticipated in nerves that have perineurial injury. Usually, there is no regeneration when the epineurium is injured 5,13.

3. Present-day diagnostic instruments

Regardless of the origins or forms of polyneuropathies, axonal degeneration and de-/dysmyelination are the two main types of lesions that affect nerves. Determining the pathophysiology has been essential for polyneuropathy diagnosis and treatment. For example, immunomodulatory medications are generally beneficial in treating demyelinating polyneuropathies, whereas there is currently no treatment for axonal polyneuropathies. Furthermore, it is necessary to quantify axonal/myelin pathologies in order to precisely monitor the advancement of polyneuropathies, which is frequently essential for clinical trials. Traditionally, sural nerve biopsy—an invasive treatment that involves surgery to extract the nerve in the leg—has been required to examine these disorders. Longitudinal studies are not appropriate for nerve biopsy because the cost of repeat procedures is prohibitive. NCSs, or nerve conduction studies, are another method for evaluating peripheral nerves. NCSs with slowed conduction velocity, temporal dispersion, and conduction block 14 are suggestive of demyelinating polyneuropathy. Axonal polyneuropathy, on the other hand, results in lower amplitude of compound nerve action potentials but normal or slightly delayed conduction velocity 15. Despite the fact that NCS has been a highly useful technique, significant deterioration in the distal limbs of many individuals may lead the nerves to become non-responsive. The "floor" effect may make NCSs unable to offer insightful data.

Furthermore, NCSs typically cannot access nerves located in the deep tissues of the proximal limbs; as a result, diseases affecting the proximal nerves may go unnoticed. Numerous disorders of peripheral nerves, including plexopathies, nerve damage, and demyelination to the proximal regions, largely impact the proximal nerves. An other method for imaging the peripheral nerves is high-resolution ultrasonography. Real-time peripheral nerve imaging with a long-axis view and contralateral comparison is made possible by ultrasound. Intersubject reliability is impacted by the technician's experience, which is mostly responsible for the image quality. Similar to NCS, deep-tissue proximal nerves are typically not visible or amenable to ultrasonography 16, 17.

In patients with neuropathies, magnetic resonance imaging (MRI) has been demonstrated more recently to offer rich contrast, high resolution, and additional quantitative aspects that may serve as useful biomarkers for peripheral nerve damage. MRI has been used widely to identify

pathological alterations in the CNS, but it has not been used as much in vivo human PNS research. This is frequently caused by two main factors: first, inadequate normative data for MRI in the PNS makes a valid interpretation of the data difficult; second, high-resolution imaging is necessary to visualize morphological alterations due to the small structures in the nerves. However, a number of MRI tissue characteristics, including magnetization transfer (MT), longitudinal (T1) and transverse (T2) relaxations, susceptibilities, and proton density (PD), have been well studied for use in in vivo human brain imaging. The contrast between diseased and healthy tissues in MRI images has been enhanced by these quantitative assessments. Specifically, these MRI characteristics provide enhanced visualization of the processes during inflammation, infarction, demyelination, and axonal degeneration 18. However, the peripheral nerves have not yet been thoroughly examined for these quantitative imaging modalities.

4. Peripheral nerve imaging challenges

To name a few that are useful for imaging the PNS, MRI offers a broad range of contrasts derived from tissue characteristics, water mobility either macroscopically via blood flow or microscopically via diffusion, and magnetic susceptibility. Water content, or PD, T1, and T2 spin relaxation are examples of tissue characteristics. With these tissue properties, one can use either a gradient echo (GE)-based sequence or a spin echo (SE)-based sequence to alter the timing parameters, such as echo time (TE) and repetition time (TR), and generate proton density-weighted (PDW), T1-weighted (T1W), and T2-weighted (T2W) images. A second radiofrequency (RF) pulse added before the excitation can be used to nullify the signal at the imaging readout time in some tissues. These methods are called short-tau inversion recovery (STIR) for fatty tissues and fluid-attenuated inversion recovery (FLAIR) for bulk water. It should be noted that a GE acquisition causes the image contrast to change from PDW to T1W by altering the flip angle—from small to large angles—through which the spins are tipped. Although the techniques used here are qualitative, tissue characteristics can be measured by adjusting the imaging parameters and using the resulting set of images to create quantitative maps. However, the calibrations of RF transmit (B 1 +) and receiver (B 1 −) fields, as well as main field (B 0) inhomogeneity, must be incorporated in order to achieve genuinely quantitative maps of T1, T2, T2*, and PD.

In the human body, water mobility can be found in both macroscopic and microcosmic forms everywhere. Applications of the former kind of water motion are commonly found in MR angiography and venography, which image the human body's vasculature. Both the signal's phase information and signal magnitude can be used to quantify these hemodynamic properties. To minimize motion-related artifacts in images, these macro-water motions should be mostly avoided. However, techniques like diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI), and MT all play important roles in today's neurological and musculoskeletal imaging of the CNS and PNS when it comes to molecular-level water transport.

Due to the existence of susceptibility artifacts, which result in signal dephasing close to air/tissue interfaces and at the surfaces of metal implants, magnetic susceptibility—the other primary contrast mechanism—has drawn attention since the inception of magnetic resonance imaging. The intrinsic susceptibility variations amongst tissues exist independently of these bulk susceptibilities. This has been applied to both quantitative susceptibility mapping (QSM) and susceptibility-weighted imaging (SWI) to improve contrast between tissues and map the features of the magnetic source. In order to create an enhanced contrast image, conventional SWI uses a completely flow-compensated GE acquisition that takes use of the phase from local variations in susceptibility as well as the intrinsic T2* decay from various biological sources 29.

5. Conclusion

Peripheral neuropathies have been studied using a variety of MRI techniques. To access nerve diseases, direct examination of peripheral nerves is still necessary, despite the fact that muscle atrophy is frequently observed in peripheral neuropathy. One of the common changes in many peripheral neuropathies is nerve hypertrophy. Patients with DPN, CIDP, and CMT have been found to have decreased MTR and FA and increased T2W and ADC in their peripheral nerves. Although high-resolution fascicular quantifications show promise, more methodical research is required before they can be used as therapeutic tools. Proximal nerve probing techniques are crucial for researching how diseases progress and how well treatments work.

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