Magnetic Resonance Neurography Evaluation in Children

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Abstract
Magnetic Resonance Neurography has proven to be an excellent technique for the evaluation of peripheral neuropathies. However, its use in pediatric age has been less well described. In this article, the authors discuss the technical considerations, various common causes of peripheral neuropathies in children and the role of magnetic resonance neurography in their diagnosis and management.

Introduction
A wide spectrum of peripheral nerve pathologies are encountered in children, including hereditary neuropathy, traumatic birth injury and motor vehicle accident, neoplasm, infection and inflammation. Clinical features in these cases are often nonspecific and invasive electrodiagnostic tests, such as nerve conduction studies are usually uncomfortable and not feasible in the pediatric age group. Peripheral nerve imaging can therefore, be very useful in small children with strong clinical suspicion in whom the diagnosis cannot be firmly established. However, small sizes of the nerves and the relative lack of specific clinical features make imaging of the nerves challenging and requires high technical skill for performance and interpretation. There is a paucity of literature describing the diagnostic role of peripheral nerve imaging in children [1-3].

Magnetic Resonance Neurography (MRN) is a non-invasive imaging technique, which enables direct visualization of the anatomy and pathology of the peripheral nerves and regional muscles, thus helping in localizing the site of injury or tumor. It can not only help in confirming and localizing the neuropathy, but also in ruling out neuropathy by showing normal appearing nerves and regional muscles. The authors describe the MRN technique used in pediatric age group and discuss a spectrum of peripheral nerve pathologies that can be observed in children using relevant case examples.

MR Neurography technique
The currently available 3 Tesla scanners (MAGNETOM Skyra, Verio and Trio, Siemens Healthcare, Erlangen, Germany) are preferred over 1.5T systems because of the MRN technique (MRN Advant) due to higher signal-to-noise ratio (SNR) and short imaging times on the higher field scanners. Additionally 3D imaging with fat suppression is better obtained on 3T scanners. 2D imaging can be obtained similarly on both types of scanners, although it takes a little longer on 1.5 T scanners, especially when one tries to attain similar image quality on thin section (2–3 mm) scans. High resolution imaging with combined 2D and 3D isotropic spin echo type imaging is essential for optimal assessment of small peripheral nerves. The inability to stay still for infants and small children makes imaging more challenging, frequently requiring sedation or general anesthesia for adequate results and to avoid repeat acquisition [1].

One should use dedicated coils as far as possible. For MRN imaging around the joints, use joint specific coils, such as wrist, elbow, ankle etc. If a joint specific coil is not available, use the smallest possible flex coil to cover the expected anatomy. For contiguous imaging of the joint and extremity, e.g. wrist and forearm, use wrist coil and flex coil separately in the adolescent child to avoid excess blank (air) space around the extremity. In a child or infant, a single flex coil can suffice for such imaging due to the relatively small size of the extremity. During pulse imaging, use a combination of body array in the front and spine elements on the back to attain uniformity of magnetic signal in the field-of-view.

High resolution 2D (dimensional) axial T1-weighted (T1w) and T2 SPAIR (Spectral Adiabatic Inversion Recovery) sequences are useful for demonstrating regional anatomy of the nerve fascicles. Fascicular architecture of nerves is consistently seen with T2 SPAIR images in larger branches, such as femoral nerves and sciatic nerves, as well as in smaller nerves that are affected and enlarged due to neuropathy, such as lateral MAGNETOM Xeo and Genoufermoral nerves [4, 5]. Fluid sensitive sequences such as STIR (short tau inversion recovery) images have more uniform fat suppression and higher T2 contrast, especially in the presence of metal or in off-center areas [6]. However, STIR imaging is often marred by low SNR, pulsation artifacts and increased baseline nerve signal intensity. SPAIR produces higher SNR images and are less prone to blood flow artifactual images than STIR imaging, which could be disadvantageous as peripheral nerves travel in neurovascular bundles. Use a TR/TE/TF of ~ 3800–4500/65–65/15–25 for T2 SPAIR imaging. Sagittal STIR imaging is particularly useful in brachial plexus imaging to obtain uniform image with higher SNR and STIR suppression in a difficult neck area and to tease out asymmetrical or individual nerve signal intensity and localizing the neuropathy. Dixon type fat suppression is also useful in generating uniform fat suppression.

3D images complement information generated from 2D imaging by showing nerves in longitudinal planes. The imaging can be obtained using isotropic 3D SPACE (Sampling Perfection with Application optimized Contrasts using different flip angles) technique. A variety of contrasts are available on SPACE sequence, including T1, T2, PD, STIR and SPAIR. Non-fat suppressed T2 SPACE (TR/TE/TF ~ 1500–1700/110–120/42–50) is useful for spine imaging, which is necessary in plexus evaluation. One can routinely obtain 0.8–0.9 mm isotropic images through the cervical or lumbar spine. In cases of suspected nerve root avulsions, one should also obtain 3D CISS imaging focused at spine for high resolution (0.6–0.65 mm isotropic) evaluation of preganglionic nerve rootlets. For post ganglionic nerve assessment in plexus, fat suppressed 3D imaging using STIR SPACE (TR/TE/T/FLS ~ 2000–2200/70–80/50–60/1.3–1.5 mm isotropic) is most useful. There is virtually no pulsation artifact on the 3D imaging and once thick slab (8–15 mm) maximum intensity projections (MIPs) are created, the image looks smoothed and shows the high intensity nerves along their long axis or in any desired anatomic plane, e.g. oblique sagittal planes are useful to depict femoral and sciatic nerves along their long axes (Fig. 1). SPAIR SPACE (0.9–1.0 mm isotropic) is very useful in extremity imaging due to higher SNR and similar fat suppression. The nerve perpendicularly plane shows cross-sectional appearance of the fascicular anatomy of the nerve. The longitudinal plane along the long axis of the nerve shows focal or diffuse nerve enlargement and mass effect of regional peripheral lesion. [1, 3]. 3D imaging is helpful in localizing the lesions along the axis of the nerve, course deviations, focal neuroma, neurotmesis and for better preoperative planning. In extremities, another 3D imaging, i.e. 3D DW PSIF (diffusion-weighted reversed steady state in free uniform fat suppression) is very useful to create nerve specific isotropic images due to effective fat and vascular suppression (60–70/60–80 ms and 6.25 ms echo time). Additional coronal T1w, STIR/PAIR SPAIR images aid in detection of lesions along the long axis of the nerves as well as allow assessment of regional joints and musculoskeletal structures. These also serve as fall back sequences, in case the subject moves during the scan or if there is failure of 3D imaging for any reason. IV gadolinium contrast is not routinely used in infants, however, is useful for differentiating types of neural hyperintensity such as suspected neoplasms, infection, inflammation, diffuse polyneuropathy, neuromuscular syndromes, or post-operative complication [7, 8].

Normal and abnormal peripheral nerves
Normal peripheral nerves show isointense signal on T1w and T2w images. On T2 SPAIR images, minimal hyperintensity is normal, especially where the nerves curve around the joints. On 3D SPACE images, the nerves usually are uniformly hypointense in the plexus due to increased sensitivit y to the endoneural fluid. Most hyperintensity is seen at the dorsal nerve root ganglion level and the signal fades distally along the course of the nerves. Pathological nerves show one or a combination of findings, such as increasing hyperintensity approaching the signal of the regional vascular bundles and encompassing a long segment of the nerve; focal or diffuse caliber enlargement (more than adjac ent regional nerve or artery). Hyperintensity in the counterpart nerve or artery in the neurovascular bundle; intrinsic fascicular [9].

*MR scanning has not been established as safe for imaging fetuses and infants less than two years of age. The responsible physician must evaluate the benefits of the MR examination in comparison to those of other imaging procedures.
enlargement, effacement or atrophy; intra-epineural fat deposition; epineu- rial or perineurial thickening; perineurial fibrosis with or without nerve entanglement; nerve displacement due to mass lesion; heterogeneous nerve thickening suggesting a neuroma in continuity or end bulb neuroma from complete rupture or failure of nerve regeneration (Fig. 2); and finally, regional muscle denervation changes, which by definition are distal to the site of the entrapment [2, 4-6].

Indications

Hereditary neuropathy is the most common etiology in children. Acquired cases can be seen due to infection, inflammation, neoplastic and trauma causes. On the other hand, adults usually suffer from neuropathies secondary to entrapment, toxic insult or systemic disease, such as diabetes. It is thus important to understand the differing etiologies in adults and children in order to make a proper diagnostic plan for evaluation of peripheral neuropathies in pediatric age group. MR Neurography is indicated in children with suspected but unclear underlying hereditary or acquired pathology that may cause neuropathy, known neuropathy without any identifiable underlying cause, and to characterize neuropathy in cases of infection, inflammation or trauma.

Advantages of MRN

MRN is particularly useful in children due to frequent inability of electrophysiologic studies (EDS) to yield diagnostic information. Moreover, MRN is not operator dependent and can localize the exact site of nerve pathology. It provides useful data for preoperative planning and postoperative response to surgical treatment even before clinical and functional improvement is noticeable [1]. The EDS give vital physiologic information about the nerve pathology by evaluating nerve conduction velocity or muscle action potential and can depict subtle changes in signal intensity, as well as MRN in cases with mild neuropathy without fascicular enlargement. Deep nerves are difficult to interrogate using US and muscle denervation is usually not apparent till late stage. MRN can evaluate the nerves, their innervated muscles and regional soft tissue structures. With its combined 2D and 3D imaging capabilities, it can illustrate neuromuscular anatomy and pathology in multiple planes for better interpretation by the radiologist and localize the pathology for preoperative planning for the referring physician.

Spectrum of peripheral neuropathies in children

The causes of neuropathies differ between adults and children. More than 70% of neuropathies in children are related to inherited causes, while most cases of neuropathies in adults are acquired (60%). Adults with acquired neuropathy are mostly related to trauma, entrapment or chronic injury from sports or occupation. In children, acquired neuropathies are more likely secondary to infection and inflammation [11].Clinically, neuropathy results in numbness, pain, paresthesia and weakness of the innervated muscles. In small children these symptoms may be less noticeable, and thus reflex testing is of vital importance. Following is a discussion of various common causes of peripheral neuropathies.

Neuropathies

Inherited Neuropathies

Hereditary Neuropathies are a heterogeneous group of pathologies in which neuropathy is either the primary presentation of the disease (such as Charcot Marie Tooth disease, CMT) or a part of a more generalized or systemic disorder. The latter group encompasses a large group of rare disorders such as familial amyloid polyneuropathy (FAP), paroxysmal, ataxia telangiectasia and many other syndromes. The most common of hereditary neuropathies is CMT, which is classified into various types based on pathogenesis – demyelination or axonal degeneration. Clinical features include muscle denervation changes (weakness, atrophy), high plantar arches, impaired sensation and diminished deep tendon reflexes [12, 13]. The most common form of CMT is autosomal dominant demyelinating CMT (CMT type 1A), which is seen in 70% cases. MR imaging is a useful adjunct to clinical and electrodagnostic suspicion of the neuropathy. One would see diffuse enlargement of bilateral peripheral nerves with abnormally increased signal intensity and/or fascicular prominence in a symmetric fashion. Most enlargement is observed in CMT type 1A. No significant enhancement is seen on postcontrast imaging. Whole-body MR Neurography (WBMRN) is likely to be useful in future to assess the disease burden in these diffuse polyneuropathy cases [14]. Nerve biopsy is the most accurate test to diagnose CMT, however it is rarely necessary these days.

Neoplastic

The most common peripheral nerve sheath tumors (PNSTs) in children are neurofibromas (NF) and schwannomas [15]. These are benign tumors arising from the Schwann cells with additional non-neoplastic cells including neurons, perineurial cells and endothelial fibroblasts [16]. NFs may be described as localized, diffuse or plexiform. Most of NFs are localized variant seen as small (< 5 cm) fusi- form masses involving a superficial or major peripheral nerve. Plexiform NF, on the other hand, comprises pro- liferation of cells in the nerve sheath spreading along the length of the nerve and involving multiple nerve fascicles. They are more commonly associated with neurofibromatosis type 1 (NF-1; 90% cases) than localized variants and have a higher propensity to develop malignant PNSTs later in life. Schwannomas are commonly solitary slow-growing subcuta- neous lesions < 5 cm in size. They can occasionally be multiple and associated with several hereditary neurocutaneous syndromes, most well defined of these being neurofibromatosis type 2 (NF-2) and Schwannoma- tosis [17].

On MR imaging, the lesions appear isointense on T1w images and show homogenous to heterogeneous increased signal intensity on T2w images. PNSTs have classi- cally been described using several imaging signs on MRI. The ‘tail sign’ describes a tail forming at the superior and inferior margin of the nerve lesion. The ‘target sign’ is central hypointense tissue due to collagen- ous stroma with peripheral increased signal intensity on T2w images due to more myxomatous tissue. It is observed in NF more commonly than Schwannoma. The ‘split fat’ sign may give intraparenchymal fat in association with slowly growing lesion. The ‘fascicular sign’ depicts prominent fascicular neuromegaly appearance within the margin of the lesion. The ‘bag of worms’ sign is seen in superficial plexiform NFs [17, 18]. While NF may show multi- fascicular involvement of the nerves, schwannoma shows one or two fascicular continuity with the mass lesion. It is difficult to differentiate between benign and malignant PNSTs on conventional MRI. Diffusion tensor imaging provides the means to assess the apparent diffusion coefficient (ADC) value (< 1.1 × 10^-3 mm²/s) is useful to find most cellular areas for evaginating malignancy and can be directed for biopsy. In underlying neurofibroma- tosis, this is increased chance of malignancy and it may develop at an earlier age in life as compared to the isolated form of myxomatosi- nal nerve sheath tumors. New onset of severe pain, neurologic deficit, rapid increase in size, heterogeneous appearance and low ADC value can
serve as important signs of incipient malignancy (Fig. 3). Perineurioma is another classic benign tumor, seen in young children in their adolescence showing uniform fascicular thickening and nerve thickening over a long segment, usually in a sciatic distribution. Perineurioma is also seen in young adults, albeit the causes are different. Trauma

Traumatic peripheral nerve injuries are common in both children and adults, albeit the causes are different. About 80% peripheral nerve injuries in children occur in the upper extremity, and the most common causes include obstetric lesions (46.78 %) (Fig. 5) and iatrogenic (16.95 %), with predominant involvement of the brachial plexus and sciotic nerve [19]. Sunderland classified peripheral nerve injuries into five grades of increasing severity [20].
- Neurapraxia (Sunderland Grade I) is a mild form of neural insult leading to temporary impulse conduction block along the affected nerve segment. It is reversible and muscle denervation changes do not occur.
- Axonotmesis (Sunderland Grade II) is more severe than neurapraxia involving physical disruption of the axon with preservation of outer covering layers of endoneurium, perineurium and epineurium. Wallerian degeneration follows such an insult, which later results in regeneration of the axon along its original course as the nerve coverings are preserved. Although the duration and severity vary, it usually carries an excellent prognosis similar to neurapraxia.
- Neurotmesis (Sunderland Grade III) refers to complete disruption of the axon and supporting connective tissue structures. There is loss of continuity of the nerve fibers, and the regenerating nerve fibers are no longer confined to the endoneurium. This complicates the regeneration process and may lead to dysfunctional distal end of the nerve.
- Grade IV injury results in neroma-in-continuity (NIC), which encompasses perineural disruption and entangled disorganized mass of regenerating nerve fibers.
- Sunderland grade V injury leads to end bud neuroma, also called stump neuroma with underlying discontinuity with the nerve (Sunderland Grade V) [17, 21].

On MR imaging, NIC appears as a heterogeneous mass with ‘tail sign’ which does not show enhancement on contrast administration (differentiating it from neurogenic tumor, which shows enhancement). Stump neuromas are seen as fusiform masses with an irregular outline showing decreased signal intensity on T1w images and increased signal intensity on T2w images [21]. MRN can clearly show abnormal nerve hyperintensity and/or enlargement with otherwise underlying nerve continuity in Grade III injuries, which undergo medical management, except that one might release superimposed nerve entrapment. Grade IV and V injuries show a focal neuroma and these can also be distinguished based on the presence of nerve continuity or discontinuity.

Infection / Inflammation

Infectious neuropathy may result from direct nerve involvement or immunologic response of the body towards the infectious agent. The most common and important of these is the Guillain-Barré Syndrome (GBS), also known as acute inflammatory demyelinating polyneuropathy (AIDP). Various microorganisms have been implicated as the trigger for the immune response in GBS (Campylobacter jejuni, Cytomegalovirus and Epstein Barr virus, etc.). GBS is a clinical diagnosis classically presenting in the child after a recent mild infection with weakness, sensory loss, pain, and hyporeflexia in the lower extremities. MR imaging is usually ordered in such cases to confirm the diagnosis and more importantly to rule out other spinal cord or nerve root pathologies that mimic AIDP. MRI findings may be normal in pediatric patients. Hyperintensity and nerve thickening...
Clinical Neurology

Neurology

Multifocal motor neuropathy is another condition that affects the motor function predominantly and is more common in upper limbs as compared to the lower limbs. Multiple conduction blocks are noted on electrodiagnostic examinations and MRN of the extremity or the plexus shows diffuse nerve thickening and/or enlargement, not limited to the entrapment sites. There is generally good response to IVIG treatment or cyclophosphamide therapy.

Conclusion

Imaging of nerves in children is challenging due to their small size and comparative rarity of neuropathies affecting them. MR Neurography is a powerful diagnostic tool even in pediatric population. With proper communication between the referring physician and the radiologist, the diagnostic value of MRN is enhanced leading to early diagnosis and proper patient care.

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References


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