Look for the nerves! MR neurography adds essential diagnostic value to routine MRI in pediatric practice: A pictorial overview

Cherchez les nerfs ! La neurographie RM apporte des arguments diagnostiques essentiels à l’IRM de routine en pratique pédiatrique : une revue iconographique

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Available online 12 January 2011

Summary
Purpose. — This study aimed to assess the feasibility of magnetic resonance (MR) neurography in children, and the potential roles of diffusion-weighted imaging (DWI) and fiber-tracking (FT) techniques.

Methods. — Five pediatric patients (age range: 6–12 years) underwent magnetic resonance imaging (MRI) for various clinical indications: neurogenic bladder (case 1); persistent hand pain following minor trauma (case 2); progressive atrophy of the lower left extremity muscles (case 3); bilateral hip pain (case 4); and palpable left supraclavicular mass (case 5). All studies were performed using a 1.5-T Avanto MRI scanner (Siemens, Erlangen, Germany). The protocol included 3D T2-weighted STIR and SPACE imaging, T1-weighted fat-saturation post-gadolinium imaging and diffusion tensor imaging (DTI) with tractography. ADC (N × 10^{-3} mm²/s) and FA values were calculated from regions of interest (ROIs) centered on the nerves. Nerve-fiber tracks were calculated using a fourth-order Runge-Kutta algorithm (NeuroD software).

Results. — MR neurography allowed satisfactory visualization of all neural structures, and FA and ADC measurements were feasible. The final diagnoses were Tarlov cysts, median-nerve compression, sciatic perineurioma, Charcot-Marie-Tooth disease andplexiform neurofibroma in a patient with NF-1.
Introduction

Peripheral nerve imaging is useful in pediatrics primarily because clinical findings are often misleading and nerve-conduction studies are either non-specific or impossible to perform in small children [1–3]. In the pediatric literature, examples of magnetic resonance (MR) neurography are scarce. The aim of the present report is to describe the feasibility of MR neurography in children, and to discuss the potential implications for disease management and treatment planning of newer MR neurography techniques such as diffusion tensor imaging (DTI) and fiber-tracking (FT) magnetic resonance imaging (MRI).

Methods and patients

MRI technique

All studies were performed using a 1.5-T Avanto MRI scanner (Siemens, Erlangen, Germany). Different coils were combined and adapted to the various regions of interest (ROIs). For the brachial plexus, the six-element body-array coils were combined with three elements of the posterior neck-array coil, six elements of the head-array coils and three elements of the spine-array coils, thereby covering the entire field of view (FOV) with 18 coil elements. For peripheral nerves such as the median nerve, an eight-element knee-array coil was used whereas, for the lumbar region and sacral plexus, combined spine and body coils were used.

The following sequences were performed according to our standard clinical protocols: (1) axial turbo spine-echo (TSE) with T2-weighted imaging (T2-WI): TR/TE 3100/88 ms, flip angle 150°, TI 0, voxel size 1 × 1 × 7 mm, FOV 250 × 176 mm, and acquisition time 3.5 min; (2) coronal 3D with T2-WI SPACE (sampling perfection with application-optimized contrast using different flip-angle evolutions) and STIR (short tau inversion recovery): TR/TE/T1 2000/174/160 ms, turbo factor 85, TA 6–7 min, FOV 448 × 448 mm, matrix size 448 × 482, number of slices 104, iPAT factor 3, maximum-intensity projection (MIP), multiplanar reconstruction and acquisition time 7.5 min; (3) fat-saturated T1-WI: TR/TE 507/11 ms, flip angle 126°, voxel size 1.2 × 1.2 × 3 mm, gadolinium-enhanced sequences in axial, coronal and sagittal planes, and acquisition time 4.5 min; and (4) axial diffusion-weighted imaging (DWI): TR/TE 7100/92 ms, iPAT factor 2, NEX 1, FOV 256 × 256 mm, matrix 128 × 128, voxel size 3 × 3 × 3 mm, b values 0 and 900 s/mm² in 30 diffusion-encoding directions, and acquisition time 6 min. Calculations of color-coded fractional anisotropy (FA) and apparent diffusion coefficient (ADC) mapping were performed inline by the MRI scanner.

Discussion. — FA and ADC measurements are of little value because of the lack of normal reference values. Nerve-fiber tractography (FT) may be of value in the characterization of tumor pathology, and is also helpful in the planning of surgical treatments.

Conclusion. — MR neurography is feasible in pediatric patients. However, a considerable amount of work has yet to be done to establish its role in the clinical management of the wide range of peripheral nerve diseases.

Patients

Our protocol for MR neurography was used on five patients — four girls and one boy — aged 6–13 years and presenting with different clinical indications. Case 1 had undergone spine MRI for neurogenic bladder; case 2 had undergone wrist MRI for persistent hand pain after minor trauma; case 3 had undergone spine MRI to investigate progressive weakness and atrophy of the lower left extremity muscles; case 4 had undergone MRI of the hips for bilateral pain while walking; and case 5 had undergone MRI because of a palpable left supraclavicular mass.

Results

Clinical characteristics, DTI findings and DWI measurements for the five patients are summarized in Table 1.

Case 1

A 12-year-old girl underwent MRI of the spine for a neurogenic bladder with recently diagnosed renal insufficiency. MRI demonstrated sacral intradural arachnoid (Tarlov) cysts (Fig. 1, a–c). MR neurography performed at the same time showed compression of the S2 roots and slightly hyperintense nerves (Fig. 1, b and c). No other etiology for renal insufficiency was found. The mean FA of the S2 roots was 0.80 ± 0.28 and the mean ADC was 0.9 ± 0.66.

No surgical procedure was undertaken for the Tarlov cysts, but the patient underwent kidney transplantation with a good clinical outcome. The decision to avoid cyst surgery was due to technical difficulties and the lack of evidence of efficacy in the literature [5]. Although such cysts are usually asymptomatic, even without additional compressive impingement (such as disc hernia, spondylolisthesis or lumbar canal stenosis), these anomalies can be responsible for sciatic pain, motor deficits and bladder sphincter dysfunction, as seen in this case [6]. In some cases, these cysts may be related to previous trauma or arachnoiditis.
Table 1  Clinical characteristics, diffusion tensor imaging (DTI) findings and diffusion-weighted imaging (DWI) measurements of five patients.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Symptoms</th>
<th>Diagnosis</th>
<th>DTI findings</th>
<th>Mean FA</th>
<th>Mean ADC (mm^2/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Neurogenic bladder</td>
<td>Tarlov cysts</td>
<td>Fibers passing around</td>
<td>0.80 ± 0.28</td>
<td>0.9 ± 0.66</td>
</tr>
<tr>
<td>2</td>
<td>Persistent hand pain after minor trauma</td>
<td>Carpal ganglion cyst</td>
<td>Fibers passing around</td>
<td>0.51 ± 0.20</td>
<td>1.3 ± 0.52</td>
</tr>
<tr>
<td>3</td>
<td>Progressive atrophy of lower left extremity muscles</td>
<td>Sciatic perineurioma</td>
<td>Localized hypertrophy/fibers within the mass</td>
<td>0.32 ± 0.23</td>
<td>1.8 ± 0.22</td>
</tr>
<tr>
<td>4</td>
<td>Bilateral hip pain while walking</td>
<td>Charcot-Marie-Tooth disease</td>
<td>Diffuse hypertrophy/disorganization</td>
<td>0.29 ± 0.41</td>
<td>1.9 ± 0.28</td>
</tr>
<tr>
<td>5</td>
<td>Left supraclavicular mass</td>
<td>Plexiform neurofibroma</td>
<td>Fibers within the mass</td>
<td>0.24 ± 0.33</td>
<td>1.5 ± 0.16</td>
</tr>
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FA: fractional anisotropy; ADC: apparent diffusion coefficient.

Case 2

MRI was performed in a 10-year-old girl with persistent hand pain after minor trauma 2 weeks earlier. MRI fluid-sensitive sequences showed hyperintensity in the spongy parts of the carpal bones, and a hyperintense ovoid mass in the carpal tunnel (Fig. 2, a). 3D SPACE imaging together with DTI FT demonstrated compression of the median nerve by a mass (Fig. 2, b and c). The relationship between the nerve and the mass, an intraneural ganglion cyst, was clearly depicted. The mean FA of the median nerve was 0.51 ± 0.20 and the mean ADC was 1.3 ± 0.52.

Compression of the median nerve by a ganglion cyst is rare in children [7]. The ganglion cyst usually originates from the intercarpal joints.

In the differential diagnosis of a carpal-tunnel mass, hemangioma, lipoma, lipofibroma, hamartoma and intraneuronal schwannoma must be considered.

Electromyography (EMG) was not performed. Motor weakness and hand numbness were noted during the neurological examination, which was performed after the MRI results were known.

Case 3

A 7-year-old girl presented with a 2-year history of painless progressive weakness of the lower left extremity muscles, and atrophy of tibialis anterior, peroneus tertius, extensor hallucis longus and extensor digitorum longus, but no sensitivity alteration in the leg. The patient did not meet the criteria for neurofibromatosis (NF-1), and she had no family history of NF or other heritable neuropathy. Spine MRI was performed to look for any spinal causes of the gait abnormality, but electrodiagnostic studies were not performed due to the lack of patient cooperation.

On the conventional spine MRI (coronal 3D SPACE and axial T2-WI), hypertrophy of the sacral roots was noted. MR neurography depicted not only the fusiform neural hypertrophy and extent of the lesion (Fig. 3), but also allowed study of the spinal root involvement (Fig. 4), thereby helping to plan the most suitable surgical treatment for this case (sural nerve graft vs. neurolysis) [1]. The pathological nerve showed decreased FA values (0.32 on the left, 0.38 on the right), and an increased ADC (1.8 × 10^−3 mm^2/s) compared to normal nerves.
Figure 2  A carpal compression mass on axial 3D SPACE imaging (A) and on tractography (B, C) appears as an ovoid mass in the carpal tunnel (green arrows). The median nerve is not well visualized (red arrows). Tractography shows the relationship between the nerve (red arrow) and the mass (green arrow).

Figure 3  Perineurioma on 3D SPACE T2-weighted coronal reconstruction (A) and T2-weighted axial sequences (B) clearly demonstrate hypertrophy of the left sciatic nerve (yellow arrows) compared with the contralateral side (white arrow). Nerve root involvement is not clearly visualized.

Figure 4  Perineurioma on coronal post-gadolinium T1-weighted fat-saturated sequences (A) reveal fusiform neural hypertrophy (green arrows), although the nerves are difficult to distinguish from vessels (pink arrows). Fiber-tracking (B) depicts not only the extent of the lesion, but also allows evaluation of spinal root involvement (white arrowheads).

with the contralateral side ($1.6 \times 10^{-3}$ mm$^2$/s). The diagnosis of perineurioma was confirmed by biopsy.

Case 4

A 13-year-old girl presented with bilateral hip pain while walking, but no gait anomalies. Her family history was unremarkable. Bilateral hip dysplasia was detected on conventional X-rays (Fig. 5), and she was referred for hip MRI to help plan her orthopedic surgery.

3D SPACE sequences showed hypertrophy of the sacral plexus and sciatic nerves (Fig. 6, a), and FT showed hypertrophied fibers (Fig. 6, b). The mean FA of the sacral plexus fibers was $0.29 \pm 0.410$, and the mean ADC was
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Charcot-Marie-Tooth disease, as seen on a conventional X-ray, reveals bilateral hip dysplasia and dislocation of the femoral heads.

1.924 ± 0.304. MR neurography was suggestive of the hereditary neuropathy Charcot-Marie-Tooth (CMT) disease (Fig. 7). Neurological examination was significant because it revealed the loss of deep tendon reflexes, a slight decrease in vibrational sensitivity and mildly arched feet. Nerve-conduction studies demonstrated definite axon and myelin neuropathy, suggestive of hereditary neuropathy despite the lack of such a family history. Genetic testing confirmed type 1 CMT.

Case 5

A 6-year-old boy presented with a plantar nodule that had been growing slowly over the past 3 months. Physical examination showed a barely palpable left supraclavicular mass, three café-au-lait spots < 1 cm in size, no evidence of Lisch nodules, no visual dysfunction and no scoliosis. The neurological examination was unremarkable. There was no family history of neurofibromatosis, and the child was of normal stature for his age. Thorax and spine radiography studies showed no anomalies, and brain MRI showed no evidence of optic-pathway gliomas, or hemispheric cerebellar or cerebral gliomas.

MR neurography of the brachial plexus was also performed. The 3D SPACE sequence showed bilateral, multiple, dumbbell-shaped lesions involving the brachial plexus and with high signal intensity (Fig. 8). The mean FA of the plexiform neurofibroma was 0.24 ± 0.33, and the mean ADC was 1.542 ± 0.16. FT showed a tight mass of entangled fibers (Fig. 9), confirming the diagnosis of plexiform neurofibroma. The diagnosis of NF-1 was confirmed by genetic investigation.

Discussion

Our protocol for MR neurography, using a 1.5-T scanner, allowed satisfactory visualization of the nerves, including those of small size such as the median nerve. Although 3-T MRI is being increasingly performed for clinical purposes because of its potential to improve spatial and temporal resolution, MRI of the peripheral nerves at 1.5 T is preferable because it reduces B0 and B1 variability, and minimizes susceptibility artifacts [8]. Fat-saturated T1-weighted gadolinium-enhanced sequences are useful for demonstrating the anatomical relationship of nerve fascicles to a nearby mass lesion [9]. The role of gadolinium-enhanced sequences in differentiating various types of diffuse neural hypertrophy, such as the wide range of demyelinating and dysmyelinating diseases, needs to be investigated by further studies [10,11].

Pathological nerves appear brighter compared with normal ones on 3D SPACE T2-WI sequences (Fig. 4, a). This type of sequence is useful for depicting cases of neural hypertrophy, as seen in our case 3 (sciatic perineurioma) and case 4 (CMT disease). Also, a negative correlation between

Figure 5 Charcot-Marie-Tooth disease, as seen on a conventional X-ray, reveals bilateral hip dysplasia and dislocation of the femoral heads.

Figure 6 Charcot-Marie-Tooth disease on 3D SPACE T2-weighted images (A) shows striking hypertrophy of the sacral plexus and sciatic nerve. The same image fused with fiber-tracking reconstruction of the sciatic nerves (B) shows hypertrophy and disorganization of the fibers (shown in normal, vertical, blue-coded directions, as well as in horizontal red-coded and anteroposterior green-coded directions).
Figure 7  Charcot-Marie-Tooth disease in a T2-weighted axial sequence shows an hypertrophied sciatic nerve with clearly defined fascicles separated by interposed low-signal connective tissue (arrows).

Figure 8  Neurofibromatosis on coronal 3D SPACE T2-weighted imaging shows diffuse involvement of the brachial plexus, and the tortuous expansion (‘bag of worms’) appearance that is pathognomonic of plexiform neurofibroma.

diameters of spinal nerve roots and F-wave conduction velocity ($P < 0.05$) has been reported on EMG [12]. If such data are confirmed, then MR neurography may prove to be useful in many different settings. However, while nerve area or fascicle numbers are easy to evaluate, 3D SPACE on its own cannot distinguish the subtypes of CMT [13] or differentiate acquired demyelinating from congenital dysmyelinating diseases.

To achieve the eventual goal of being able to distinguish between the various hypertrophic nerve pathologies and correlate MRI findings with histopathological changes, any future line of research needs to apply DWI measurements — namely, FA values (longitudinal or transverse) and the ADC ($N \times 10^{-3} \text{ mm}^2/\text{s}$). Unfortunately, these techniques are limited by, on the one hand, multiple artifacts and by, on the other hand, the small size of nerves. A low signal-to-noise ratio (SNR) is of particular concern with peripheral-nerve DTI and especially in children, although our technique has demonstrated good quality and reproducibility. Also, a b value of 900 s/mm$^2$ was used, which lies between the 400 s/mm$^2$ used by Khalil et al. [14] and the 1025 s/mm$^2$ recommended by Andreisek et al. [15], at 1.5 T with good results.

However, normative values for the different nerves and thresholds between normal and pathological nerves are needed before DTI can be put into common use as a diagnostic tool [16,17]. At present, the median and ulnar nerves are the most often investigated nerves but, so far, no normative values have been determined in children. In addition, it is not known whether or not the age-related changes reported in white-matter anisotropy in the brain [4,17–19] are also present in peripheral nerves. In cases of unilateral pathology, it may be useful to compare findings with the non-affected contralateral side (as in our case 3).

Some reports have investigated changes in DTI values in entrapment syndromes, such as carpal tunnel syndrome, and found decreases in the mean FA [14,20], which suggest alterations in water-proton diffusion along the median-nerve axis in association with histological changes, such as segmental demyelination, wallerian degeneration and, eventually, axon damage after chronic compression. The latter may alter the diffusion of water protons along the nerve fibers because of a slight increase in diffusion vectors in a perpendicular direction. However, there may be no ADC increase [14], or a relatively smaller ADC increase, compared with the decrease in FA [20]. In our case of median-nerve compression, there were lower FA and higher ADC mean values in comparison to the normative data reported in the literature compatible with carpal tunnel syndrome.

In our case 3 with sciatic perineurioma, case 5 with plexiform neurinoma and case 4 with CMT disease, FA values were lower and ADC values higher compared with the healthy sciatic nerve in case 3 (see above). However, the precise significance of these findings has yet to be established.

FA measurements and the ratio of longitudinal and transverse diffusion have been reported in many studies as being
the most sensitive diffusion measurements for differentiating between healthy and demyelination/remyelination processes in multiple sclerosis [7,19,21]. It may also be possible to apply these concepts to peripheral-nerve demyelinating pathologies.

FT of peripheral nerves has limited use in the current pediatric practices and has yet to be validated. In our experience, the value of the technique is related to tumor pathology. Indeed, FT appears to be capable of assessing whether or not a mass is intrinsic or extrinsic to the nerve, and can precisely determine the site of the displaced, compressed or destroyed nerve fibers [8]. Fiber tractography has proved useful for differentiating a perineuroma, in which the lesion is linear, from a neurinoma (Fig. 9), a tight mass of entangled fibers (probably reflecting the fact that the tumor is not encapsulated) and a schwannoma. The information obtained by FT is also helpful in the preoperative planning procedure, such as in our case 3, where FT revealed the involvement of spinal roots and, thus, the impossibility of performing a sural nerve graft [1].

Conclusion

MR neurography is perfectly feasible even in pediatric patients and may be a powerful diagnostic tool. However, a considerable amount of work has yet to be done to establish the role of MRI in the clinical management of peripheral nerve diseases such as demyelinating and congenital dysmyelinating pathologies, particularly in children.Conflict of interest statement

The authors guarantee that the research has not been sponsored. We certify that there are no actual or potential conflicts of interest in relation to this article.

Acknowledgments

The authors thank Stefan Huwer and Heiko Meyer from the Siemens Healthcare Advanced Neuro MR development group (Erlangen, Germany) for their helpful discussions and collaborations involving the Neuro 3D prototype software.

References