Corticospinal tract mapping in children with ruptured arteriovenous malformations using functionally guided diffusion-tensor imaging

Report of 3 cases


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Arteriovenous malformations (AVMs) can lead to distortion or reorganization of functional brain anatomy, making localization of eloquent white matter tracts challenging. To improve the accuracy of corticospinal tract (CST) mapping, recent studies have examined the use of functional imaging techniques to help localize cortical motor activations and use these as seed points to reconstruct CSTs using diffusion-tensor imaging (DTI). The authors examined the role of pretreatment functionally guided DTI CST mapping in 3 children with ruptured AVMs. In 2 patients, magnetoencephalography motor activations were adjacent to the nidus and/or hemorrhagic cavity. However, in 1 child, functional MRI motor activations were detected in both hemispheres, suggestive of partial transfer of cortical motor function. In all children, quantitative analysis showed that fractional anisotropy values and fiber density indices were reduced in the CSTs of the hemisphere harboring the AVM compared with the unaffected side. In 2 children, CST caliber was slightly diminished, corresponding to no motor deficit in 1 patient and a temporary motor deficit in the other. In contrast, 1 child demonstrated marked reduction and displacement of the CSTs, correlating with severe motor deficit. Preoperative motor tractography data were loaded onto the intraoperative navigation platform to guide complete resection of the AVM in 2 cases without permanent neurological deficits. These preliminary results confirm the feasibility of CST mapping in children with ruptured AVMs using functionally guided DTI tractography. Prospective studies are needed to assess the full value of this technique in the risk stratification, prognosis, and multimodality management of pediatric AVMs.

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KEY WORDS • arteriovenous malformation • diffusion tensor imaging • magnetoencephalography • functional magnetic resonance imaging • corticospinal tract

Successful management of AVMs in children requires careful consideration of the disease’s natural history weighed against the risks of treatment. The natural history of pediatric AVMs is poorly understood, but the vast majority are considered for treatment to eliminate the cumulative lifetime risk of intracranial hemorrhage. Among the factors that impact treatment decision-making are a history of hemorrhage and proximity of the AVM to eloquent brain regions. The management of ruptured AVMs residing within the primary motor cortex or involving the CST is particularly challenging.

Microsurgery offers a higher rate of AVM cure but often at a greater risk of postoperative neurological deficit. Alternatively, stereotactic radiosurgery carries a lower risk of neurological deficit but is associated with lower cure rates and exposes the child to additional annual risks of hemorrhage until the AVM is obliterated. Despite the role that eloquence plays in AVM management, conventional MRI techniques are limited in their ability to characterize functionally eloquent pathways and their spatial relationship to AVMs.

Diffusion-tensor imaging and tractography has recently emerged as a powerful noninvasive imaging tool allowing the localization and mapping of important white matter tracts. Using the properties of water diffusion and their directionality in 3 dimensions,2 DTI has been used

Abbreviations used in this paper: AVM = arteriovenous malformation; CST = corticospinal tract; DTI = diffusion-tensor imaging; MEG = magnetoencephalography.
to evaluate white matter alterations in a number of congenital and acquired neurological conditions.\textsuperscript{6,12,13,15–17} Conventional DTI mapping and tractography techniques use anatomically selected seed points within the precentral gyrus to help guide CST reconstruction. However, in children with AVMs, intracerebral hemorrhage or components of the AVM may distort or displace regional brain anatomy, making definition of DTI seed points and fiber tracking more challenging. Additionally, AVMs may also induce reorganization or transfer of important cortical functions to neighboring or distant brain regions.\textsuperscript{1,7,11,14} Failure to account for brain distortion and shifts in cortical function may not only impact DTI mapping but also AVM risk stratification, leading to uninformed therapeutic decision-making and avoidable treatment-related morbidity. To improve the accuracy and reliability of DTI mapping, recent studies have examined the use of functional MRI or MEG to help localize eloquent cortical functions and use these as seed points to reconstruct white matter tractography. Although such approaches have been used to map CST alterations in adults and children with brain tumors,\textsuperscript{6,10} they have yet to be applied to children with AVMs.

The purpose of this case series was to retrospectively evaluate the role of functionally seeded DTI CST mapping in children with ruptured AVMs. Quantitative analysis of selected DT indices was performed to compare affected and nonaffected hemispheres and correlate the changes in CST integrity with clinical examination results. The potential role of this technology in preoperative risk assessment, prognosis, and management of children with AVMs is discussed.

\section*{Case Reports}

\section*{Case 1}

\textbf{History and Neuroimaging.} This 8-year-old boy with right-hand dominance awoke with severe headache, left-sided numbness, and vomiting. The numbness progressed to loss of fine motor control of his left hand, as well as unsteady gait and an episode of left-leg shaking. Computed tomography of the head at a different hospital demonstrated a right parietal intracerebral hemorrhage adjacent to the central sulcus. Upon transfer to Hospital for Sick Children, the patient demonstrated a mild left pronator drift. Sensory examination and reflexes were normal. Computed tomography angiography demonstrated an enhancing tangle of vessels anterior to the hemorrhage (Fig. 1). Cerebral angiography demonstrated a 2-cm AVM located in the region of the right rolandic cortex with dominant supply from branches of the middle and anterior cerebral arteries and venous drainage directed superficially to the superior sagittal sinus (Spetzler-Martin Grade II). The patient completed outpatient rehabilitation and returned to his pre-event baseline status within 4 months. Nine months later the boy underwent stereotactic radiosurgery without complication. Follow-up angiography at 30 months after radiosurgery showed a residual AVM. Prior to resection of the residual AVM, the patient underwent MEG for motor and somatosensory mapping using techniques that have been previously described.\textsuperscript{6} The hand-motor function was localized to the right precentral region anterior to the hematoma cavity, and sensory function was localized to the postcentral sulcus. Diffusion-tensor imaging was postprocessed using previously described methods\textsuperscript{7} and demonstrated reduced fractional anisotropy and a slightly reduced fiber density index of the right CSTs (Table 1). Diffusion-tensor tractography of the CSTs was also performed on BrainLAB using the MEG motor mapping as a seed point for fiber tracking. Tractography was then overlaid onto volumetric T1-weighted MR images with contrast enhancement, which demonstrated the residual nidus of the AVM abutting the posterior aspect of the CST.

\textbf{Operation and Postoperative Course.} The boy underwent a right parasagittal craniotomy under general anesthesia without the use of muscle relaxants. Prior to AVM resection, intraoperative motor mapping was performed with electrocorticography and direct cortical stimulation. Intraoperative mapping findings were concordant with findings of the preoperative MEG mapping, localizing hand function within the gyrus immediately anterior to the hemorrhagic cavity. The AVM resection was completed, guided by the corticospinal tractography that was incorporated onto the neuronavigation platform.
Case 2

History and Neuroimaging. This 11-year-old, previously healthy boy presented with acute onset right-sided hemiparesis. A noncontrast CT scan from an outside institution showed a left frontal intracerebral hemorrhage in the region of the primary motor cortex. Upon transfer to our institution, his motor weakness had improved significantly, but his motor examination demonstrated a grade of 4−/5 of the right triceps and biceps, 3−/5 of the right hip flexion, 0/5 of the right ankle dorsiflexion, and 4−/5 of the right ankle plantar flexion. A sensory examination showed decreased light touch sensation of the right foot.

Computed tomography angiography showed a 2-cm periventricular AVM with a single draining vein extending to cortex and draining superficially (Fig. 2). Cerebral angiography confirmed the presence of an AVM supplied by small branches of both the anterior and middle cerebral arteries and drained by branches of the anterior and middle cerebral arteries and drained by a single vein extending into the superior sagittal sinus. Preoperative motor mapping demonstrated asymmetry of the CSTs (yellow). Corticospinal tractography demonstrates mild displacement of the left CST (yellow) anterior to the AVM nidus and hemorrhage.

Operation and Postoperative Course. At the 4-month follow-up the patient demonstrated complete resolution of his motor deficits. The child subsequently underwent a left parasagittal craniotomy under general anesthesia without muscle relaxants. Intraoperative electrocorticography and direct cortical motor mapping confirmed the location of the motor cortex located anterior to the hemorrhagic cavity and AVM nidus. With the aid of corticospinal tractography guided neuronavigation, AVM resection was performed with special care to preserve the CSTs localized anterior to the AVM nidus. Immediate postoperative angiography showed no evidence of a residual AVM. Postoperatively, the child demonstrated mild right-foot weakness that resolved prior to hospital discharge.

Case 3

History and Neuroimaging. This previously healthy 12-year-old right-handed boy suffered acute onset headache followed by loss of consciousness and generalized tonic-clonic seizure. On initial examination, he was hemiplegic on the right side with marked dysphasia. A CT head scan demonstrated a left frontal intracerebral hemorrhage. Computed tomography angiography demonstrated evidence of an AVM in the left frontoparietal region within the hematoma (Fig. 3). Cerebral angiography confirmed a 2-cm AVM with the nidus located within the medial aspect of the left frontal lobe, fed by the left frontal opercular branches of the left middle cerebral artery and a left lenticulostriate artery. Venous drainage occurred via the left Sylvian vein, left vein of Trolard, and the left caudate vein into the deep venous system (Spetzler-Martin Grade III). The patient was initially treated conservatively and sent to

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**TABLE 1: Diffusion-tensor indices of the affected and nonaffected CSTs in children with AVMs**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Abnormal Side CST</th>
<th>Normal Side CST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FA</td>
<td>MD</td>
</tr>
<tr>
<td>1</td>
<td>0.21</td>
<td>0.84</td>
</tr>
<tr>
<td>2</td>
<td>0.23</td>
<td>0.90</td>
</tr>
<tr>
<td>3</td>
<td>0.21</td>
<td>0.88</td>
</tr>
</tbody>
</table>

* FA = fractional anisotropy, FDI = fiber density index, MD = mean diffusivity.
rehabilitation; however, he was lost to follow-up for a period of 2 years. When the patient returned to the clinic he was found to walk independently with a hemiparetic gait, had limited movement of his right hand, and had mild hesitancy of speech. Increased tone and reflexes were also observed in the right extremities. A repeat angiogram demonstrated slight growth of the AVM nidus to approximately 3 cm (Spetzler-Martin Grade IV). Sensorimotor mapping of the left hand with functional MRI revealed bilateral activations of the sensorimotor strip with larger activations in the right hemisphere. Diffusion-tensor tractography showed reduced fractional anisotropy and marked reduction in the fiber density index (Table 1).

**Operation and Postoperative Course.** As the AVM nidus was separated from the CSTs by the hemorrhagic cavity, DTI data were not incorporated into the Gamma Knife dosing plan. The patient underwent Gamma Knife surgery at a dose of 20 Gy to the 50% isodose line. At 18 months after radiosurgery, the patient remains clinically stable with stable MRI configuration of the left frontal AVM.

**Discussion**

In the present study we examined the role of noninvasive preoperative CST mapping in 3 children with ruptured AVMs. In patients with ruptured AVMs, intracerebral hematoma or AVM components may distort or displace cortical anatomy or, more importantly, lead to transfer of important cortical functions to neighboring or distant brain regions. Failure to account for these changes can result in inaccurate localization and mapping of the CSTs, resulting in errors of AVM grading and false estimations of treatment-related risk. To improve the accuracy of CST mapping in children with ruptured AVMs, we used motor activations derived from functional MRI and MEG imaging as seed points, or start points, to launch corticospinal tractography. Using this technique, quantitative analysis showed that fractional anisotropy and fiber density index values were reduced in the CSTs of the hemisphere harboring the AVM compared with the unaffected side. Although we did not observe a clear relationship between the net difference in interhemispheric fractional anisotropy values in patients with or without motor deficits, the most striking reduction in fiber density index was observed in the child with the most functional impairment.

Diffusion-tensor imaging tractography was superimposed on contrast-enhanced T1-weighted images to show the relation of the nidus of the AVM (and its associated hemorrhagic cavity) and the ipsilateral CSTs. Using this technique, the location and course of the CSTs were successfully mapped in all cases. In Cases 1 and 2 with periorolentic AVMs, the hemorrhagic cavities were found to displace the CSTs slightly anteriorly, with both AVM niduses abutting, but not invading, the posterior surface of the CSTs. In these cases, the caliber of the CSTs were only slightly diminished, corresponding to no motor deficits in 1 patient and a temporary motor deficit in the other. In contrast, tractography in Case 3 demonstrated markedly reduced caliber of the left CST, which was related to severe motor deficits in this case.

Following preoperative mapping, Cases 1 and 2 were treated using resection. In these children, preoperative functional mapping findings were confirmed by intraoperative direct cortical stimulation and electrocorticography. Both children underwent complete AVM resection with the aid of DTI tractography incorporated into the neuronavigation platform. Postoperatively, 1 child was noted to have a transient sensorimotor deficit of the hand that resolved spontaneously, while the other developed mild foot weakness that also resolved before hospital discharge. Diffusion-tensor imaging tractography was not included in the Gamma Knife surgery plan of Case 3 because the AVM nidus was separated from the CSTs by the hemorrhagic cavity. The inclusion of this case further demonstrates the feasibility of this technique in children with ruptured AVMs.

Previous studies have demonstrated the role of preoperative functional imaging in AVM risk stratification and management in adults. Gabarrós et al. reported an algorithm whereby patients with AVMs 1 gyrus removed from the mapped motor cortex or with cortical reorganization were treated with surgery; those with AVMs located within the areas responsible for motor function were considered for radiosurgery or observation, and those with AVMs located in close proximity to motor function...
were considered for surgery with awake cortical mapping. The present study offers critical information about white matter architecture that complements this approach and is especially important in children, in whom awake cortical mapping during AVM surgery is not feasible. As demonstrated in Case 1, this information is of paramount importance in children with AVMs residing within critical motor areas that have failed radiosurgery and must be treated with surgery to obtain a cure.

Preoperative functional mapping and tractography data may also be incorporated into neuronavigation platforms to assist in intraoperative decision-making during surgery. Despite acknowledged limitations such as intraoperative brain shift, accumulating evidence from the neurooncology literature suggests that both functional and DTI-based neuronavigation platforms improve the extent of resection and reduce postoperative neurological deficits in patients with brain tumors. Preliminary data from this study suggest that similar neuronavigation strategies are both feasible and valuable in children with AVMs, allowing surgeons to preserve eloquent cortex and critical white matter tracts during AVM resection.

Despite promising studies using both qualitative and quantitative DT indices to predict neurological recovery in patients with ischemic and hemorrhagic stroke, the role of DTI and tractography in predicting motor recovery following AVM hemorrhage warrants further study. The ability to predict preoperative motor recovery on the basis of CST integrity has important implications for therapeutic decision-making. Patients with CST disruption, or those in whom the probability of motor recovery is deemed to be low, should be considered for early surgery to eliminate the risk of future AVM hemorrhage. In contrast, patients in whom the CSTs are only slightly deformed or reduced in caliber may go on to achieve greater functional recovery, and thus may benefit from a period of observation or definitive treatment with radiosurgery. One study has shown that comparison of pre- and postoperative DTI may also help to predict functional recovery of neurological deficits following AVM surgery.

One important limitation of this technique concerns the accuracy of functional cortical mapping techniques. Functional MRI is based upon blood oxygen level–dependent MRI signal detection, which requires the coupling of blood flow and metabolism for accurate assessment. High-flow AVMs may disrupt this coupling, thereby rendering cortical localization with functional MRI unreliable, which in turn affects the accuracy of DTI seed point and CST reconstruction. In contrast, MEG is governed by neuronal activity instead of regional blood flow and may be less prone to hemodynamic activity associated with AVMs. For this reason, our current practice is to use MEG for motor mapping in children with AVMs, especially in those with high-flow lesions.

Taken together, our preliminary results confirm the feasibility of CST mapping in children with ruptured AVMs using functionally guided DTI tractography. Although these initial findings are promising, prospective study with a larger sample size is needed to validate the role of this technique in the risk stratification, prognostication, and multimodality management of pediatric AVMs.

Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Widjaja, Ellis, Rutka. Acquisition of data: Widjaja. Analysis and interpretation of data: Widjaja. Drafting the article: Widjaja, Ellis. Critically revising the article: all authors. Approved submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Widjaja. Study supervision: Rutka, Kulkarni, Dirks.

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