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# New Model of Minimally Invasive Experimental Spinal Cord Injury

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observed at that level, probably because bidirectional flows last longer in patients with Chiari malformations compared with those in control volunteers and are thus easier to observe. Also of concern is that errors in peak velocities can be produced if the epidural plexus flow adjacent to the CSF regions of interest is included in the measurements.

The presence of a small or abnormal posterior fossa may also contribute to Chiari symptomatology and dynamics, probably more to brain stem symptoms and abnormal brain stem motion than to CSF flow abnormalities. The role of adhesions in obstructing or redirecting flow may also be important, regardless of the amount of tonsillar descent. It may be worthwhile to verify whether the patients included in a study have specific abnormalities such as tonsillar adhesions, whether tonsillar motion is present, or whether the foramen of Luschka or Magendie is obstructed differently, thereby compounding differences between midline and lateral flows. In addition to CSF flow abnormalities, patients with Chiari malformations have greater motion of the medulla and brain stem than do control volunteers, which can also produce greater spatial flow variations. Theoretically, symptoms related to those anatomic regions could be secondary to regional dynamic tissue deformations. In general, clinical manifestations of Chiari malformations seem to be related to both CSF disturbances and direct compression of nervous tissue, although the structural abnormalities may be causative.

The craniospinal axis is a *spatially distributed system*, with an elongated extended geometry, such that the regional dynamic properties vary along its length. Changes occurring in one region may thus affect the dynamics in another region, reminiscent of referred pain syndromes. Craniospinal dissociation is such an example, with a loss of distal compliance due to a proximal obstruction. CSF flow abnormalities may originate from sites remote from regions of altered flow due to wave propagation effects. Present studies indicate that in syringomyelia, increased spinal pulse pressures may lead to abnormal transmedullary pressure gradients and force movement of interstitial fluid across the spinal cord. The resulting spinal pressure waves and associated CSF flow velocities may develop increased peaks; however, other parameters, such as rate of change, propagation, or duration of these pulses, may also be important. Importantly, prolongation of CSF systole, associated with decreased spinal compliance due to mechanical obstruction, may result in abnormal pulse pressures and pulse propagation along the neuraxis, contributing to the pathogenesis of syringomyelia. Future examination of flow indices may thus need to include spatially and/or temporally separate effects, and more detailed approaches, such as multidimensional vector fields, may be useful to more accurately identify the pathophysiology (4). Combined measurements, involving both CSF flow and neuraxis motion, may thus provide the most specific and comprehensive indices with which to evaluate patients with Chiari malformations, with or without syringomyelia.

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# New Model of Minimally Invasive Experimental Spinal Cord Injury

In this issue of the *AJNR*, Dr. Purdy and colleagues present a new canine model of experimental spinal cord compression injury. They fluoroscopically manipulated a balloon catheter intrathecally from the lumbar region to the thoracic region and then inflated the balloon to create the injury. Animals underwent imaging with a 1.5-T magnet at the time of balloon inflation. This technique could have advantages over other widely used experimental spinal cord compression injury models, such as the weight-drop method, transection, and maintained compression.

The weight-drop method results in contusion injury. Laminectomy is performed over the spinal cord region of interest, and a known weight is dropped from a known height onto the exposed spinal cord. This method is widely used in the rat because of its

morphologic, histologic, and functional similarities to human spinal cord injury (1). Additionally, modifications to this system have allowed precise measurements of biomechanical physical indices, such as spinal cord displacement and force curves.

Despite that only a small minority of injuries (such as knife wounds) result in a clean transection of spinal cord tissue, the use of a transection model is important in testing new treatment strategies designed to elicit axon regrowth and regeneration. The experimental advantage of this model is that axon regrowth and regeneration can be inferred with histologic axon tracing techniques showing axons extending beyond the transection site. In contusive models, initial axon transection may or may not have occurred.

Experimental spinal cord compression injury models of maintained compression of the spinal cord use weights placed on the spinal cord for variable lengths of time. These models also require laminectomy. A review by Anderson and Stokes (2) suggests that compression injury results in a block of local blood flow, causing disruption of axonal conduction and functional deficits. In addition to degree of compression, the speed or dynamics of compression are also important; the spinal cord may have no permanent deficits if slow compression is applied, whereas an equal but dynamic compression will result in permanent deficits and extensive histologic damage. This type of model allows one to dissociate the ischemic effects of spinal cord injury from the dynamic effects, thereby allowing for the evaluation of treatment regimens directed at the ischemic and reperfusion damage. The model presented by Purdy et al seems to fall more into the maintained compression category but with several added advantages.

The use and timing of a decompressive laminectomy in the setting of acute spinal cord injury is controversial, and in cases of chronic compressive myelopathy, decompressive laminectomy may be the treatment of choice. Experimental laminectomy, therefore, provides a confounding situation both when evaluating the effects of injury and treatment and when translating findings to the clinical arena. The effects of a decompressive laminectomy in the experimental setting have not been well studied; however, decompression of an injured spinal cord may ameliorate the ischemic changes of spinal cord compression injury by decreasing compressive forces on an edematous spinal cord. The CSF flow dynamics may also be altered by a laminectomy, and in the setting of chronic spinal cord compression injury, changes in CSF flow have been postulated to result in further damage to the spinal cord. The model presented by Purdy et al removes this problem by limiting surgical intervention to a lumbar puncture remote from the site of injury.

The use of MR imaging at the time of spinal cord compression injury may help in understanding the hemodynamics of this injury. The use of perfusion MR imaging techniques in the model presented by Purdy et al could help quantitate ischemic thresholds for spinal cord compression injury on the basis of compression. The effect of vascular permeability after compressive spinal cord compression injury has been studied and may be an important factor in secondary injury and in correlating with the extent of injury. A recent article by Bilgen et al (3) reported the use of in vivo dynamic contrast-enhanced MR imaging studies to evaluate the permeability of the blood-spinal cord barrier breakdown after contusive spinal cord compression injury to the rat. Bilgen et al noted a correlation between the restoration of the blood-spinal cord barrier and improvement in neurobehavioral scores.

Because ischemia is thought to be an important cause of myelopathy in association with chronic spinal cord compression, the use of diffusion MR imaging may be helpful in evaluating the acuteness and severity of spinal cord damage. If this model could be modified to emulate chronic spinal cord compression (perhaps with detachable balloons), the ischemic changes in compressive myelopathies due to spinal cord stenosis, as well as treatment effects (such as decompressive laminectomy), could also be evaluated.

As Purdy et al point out, the canine model may be easily translated to a clinical setting because it uses a standard 1.5-T magnet. The use of a standard imaging unit can be important in testing sequences in a controlled setting before applying them to humans. The "standard," however, continues to change. Clinical 3-T magnets are now easily available and should provide improved resolution of the spinal cord. The use of small-bore, high-field-strength magnets continues to be necessary to test new sequences and hypotheses with high resolution in a controlled experimental setting. There is a large body of spinal cord compression injury basic science and behavioral research involving rodents and cats, thereby making it easier to evaluate and to compare new MR imaging techniques if these animals initially undergo imaging in a small-bore magnet. On a practical level, using large numbers of dogs to evaluate a new injury technique is difficult because of the expense and space required as compared with smaller animals. As the authors noted, their model could also be used in other animal models.

As Anderson and Stokes (2) point out, a single ideal experimental model of spinal cord compression injury is not possible because there is no stereotypical human spinal cord compression injury. This article provides a first look at a canine model of compressive spinal cord compression injury with possible advantages over other techniques, including lack of invasive surgical intervention and the ability to perform MR imaging at the time of injury. The model does still require validation with proof of reproducible histologic and behavioral

findings. Its strengths, however, certainly warrant further investigation.

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