Expert Commentary

Neuroimaging Advances in Cerebral Palsy

The role of neuroimaging has taken on increasing importance in the diagnosis and management of children with cerebral palsy and other childhood neurologic disorders.

Noninvasive techniques, such as magnetic resonance imaging, magnetic resonance spectroscopy, and diffusion-tensor imaging (DTI), now are being used not only to improve diagnosis, but also to delineate specific patterns of brain maldevelopment and injury and to customize the choice of medical and rehabilitative interventions.

BY ALEC HOON, M.D., M.P.H.

Cerebral palsy (CP) affects 2-3 per 1,000 live births, and refers to a heterogeneous group of disorders of brain dysgenesis or injury, in which the primary feature is difficulty with movement.

Although there are many prenatal, perinatal, and postnatal etiologies and risk factors, the most common cause of CP in the United States is white matter injury associated with preterm birth.

The risk of severe white matter injury, commonly termed periventricular leukomalacia (PVL), is 5%-15% in children born weighing less than 1,500 g. By contrast, the risk for CP is significantly less in infants born at term.

Although CP is a "diagnosis," it is primarily a descriptor of motor function, with a variety of underlying risk factors and specific causes, and is of great benefit in promoting management in community and educational programs.

For example, children with spastic diplegic CP may look the same on neurological examination, but may have different etiologic antecedents, including brain injury associated with prematurity, brain malformation, specific genetic disease such as arginase deficiency, or HIV/AIDS.

For the pediatrician evaluating a child who presents with significant motor (or generalized) delay, a brain magnetic resonance imaging is an excellent initial diagnostic test of choice.

Among all children diagnosed with cerebral palsy, 70%-90% will have abnormal magnetic resonance imaging findings. Neuroimaging, therefore, plays a crucial role in the identification of etiology and has important ramifications for management, which may range from specific medical-surgical treatments to motor and/or sensory-based therapies.

Understanding the specific structural abnormalities involved is important in determining management, as well as prognosis and recurrence risk, in individual families. For example, a term-born child with hypoxic-ischemic encephalopathy (acute asphyxia) may have injuries in discrete locations in the thalamus and basal ganglia. Because these brain regions are of primary importance in hand use and speech, children with lesions localized there may have functional problems in these areas, but preserved intelligence.

Therefore, the recognition of this pattern of brain injury would support detailed psychoeducational testing to probe for what might be unrecognized cognitive abilities, masked by limitations in speech and writing, and used to optimize educational potential.

In children with PVL, typical magnetic resonance imaging findings include irregularly enlarged ventricles, volume loss, and/or gliosis in periventricular white matter. Although PVL is well seen on conventional magnetic resonance imaging, these images cannot demonstrate the variability of injuries in specific white matter tracts.

To delineate the distribution of those injuries, researchers are increasingly using the advanced magnetic resonance technique of DTI. Using diffusion-tensor imaging, researchers at the Kennedy Krieger Institute and Johns Hopkins University, Baltimore, have together demonstrated that children born preterm with CP have variable injuries in both central motor and sensory pathways (Am. J. Neuroradiol. 2007;28:1213-22; see images at right).

Prior to the analysis presented in this paper, the prevailing thought had been that the brain injury in children with CP associated with PVL primarily affected descending motor pathways.

It is worth noting that two neurologists in the 1950s reported data consistent with the current findings, but this is the first time a noninvasive in vivo imaging technique has demonstrated injury in sensory pathways.

The importance of these findings is that we now can begin to think of tailoring interventions to activate both motor and sensory pathways on the basis of imaging findings.

It's no longer a generic, one-size-fits-all therapeutic approach. Instead, one child might receive certain motor-based therapies, another could be given motor and sensory therapies, and a third child might receive primarily sensory stimulation as treatment.

In the small group of children with normal magnetic resonance imaging studies, in addition to the reassurance this provides to families, there are individual patients who have a genetic disorder termed dopa-responsive dystonia, also known as Segawa disease, who may respond quite dramatically to levodopa/carbidopa (Sinemet).

Personally, I've seen five children in 20 years with this condition, but it's important to consider this disorder in those with CP and a normal magnetic resonance imaging, as these children can go from wheelchair to walking with timely diagnosis and treatment.

Combining careful history, examination, and testing with an emerging knowledge of genetic and epigenetic factors, we are likely to identify other similar genetic disorders in the future.

Neuroimaging may also have a role in measuring the effectiveness of treatment interventions.

CP is no longer thought of as a static disorder, for which not much can be done beyond weekly therapy and annual visits to the orthopedist.

Rather, there is increasing recognition that sustained, regular therapy, along with judicious use of medications, can promote functional gain as well as maintain health and wellness over time.

A recent study by the Life Expectancy Project in San Francisco reported that children with CP who walked and climbed stairs without difficulty at age 10 years were less likely to decline 15 years later.

Those children who ambulated with some difficulty at age 10 years had a significant chance of improvement and only a small chance of becoming nonambulatory, whereas those who used a wheelchair at age 10 years were more likely to lose ambulatory ability (Dev. Med. Child Neurol. 2007;49:647-53).

This highlights the need to promote activity-based therapies throughout childhood.

Neuroimaging techniques such as diffusion-weighted magnetic resonance imaging may also have a role in identifying infants who would benefit from neuroprotective strategies, such as rapid cooling of the asphyxiated newborn and cell-based therapies that may someday be used to lessen injury in some children with CP.

The thinking is that the injury to the brain may be ongoing, rather than fixed.

Although some of these therapies may be years off, the pediatrician plays a central role in the care of children with CP in providing a "medical home."

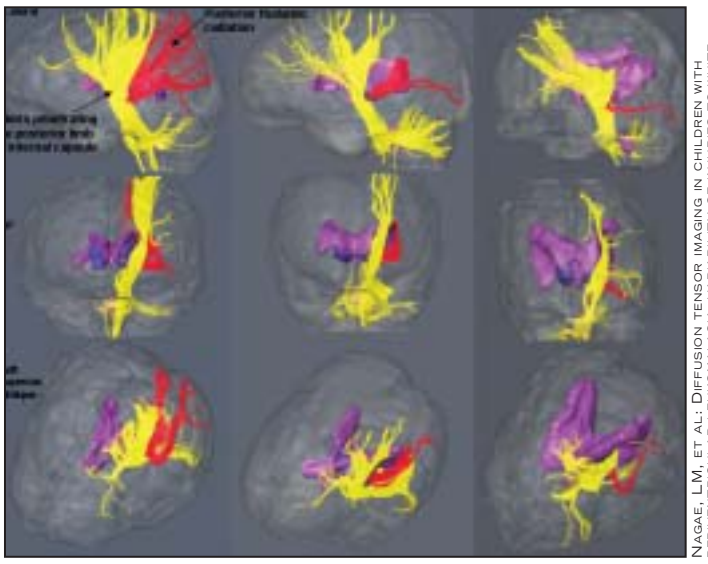
From my vantage point, CP diagnosis is best conducted at an academic, tertiary, or CP center from which recommendations can be formulated, with these recommendations implemented locally.

The pediatrician is really at the center of the wheel in terms of care coordination of the children with CP. By facilitating communication among caregivers, subspecialists, therapists, and community providers, the pediatrician is in an ideal position to optimize care and promote health and well-being.

In summary, the accurate classification of brain injury is integral to addressing the wide spectrum of developmental outcomes and therapeutic interventions in children with CP.

Diffusion-tensor imaging and other novel advanced neuroimaging techniques will enable clinicians to individualize management strategies on the basis of etiology and neurologic examination, as well as family- and child-specific factors.

A multimodal neuroimaging approach, incorporating both conventional and new advanced techniques, will improve our understanding of brain development and CP pathogenesis and set the stage for an exciting era of targeted interventions. ■



Nagae, LM, et al: Diffusion tensor imaging in children with periventricular leukomalacia: variability of injuries to white matter tracts. AJNR Am J Neuroradiol. 2007 Aug;28(7):1213-22. ©AJNR

DTI shows motor pathways (yellow) and thalamo-cortical sensory tracts (red) in an unaffected child (left) and two children with spastic CP in association with preterm birth (middle and right). CP's primary injury is in the red fibers.

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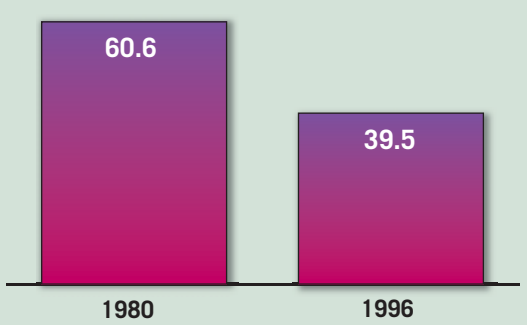
DATA WATCH

Cerebral Palsy Birth Prevalence Dropped In Very-Low-Birth-Weight* Infants in Europe

(rate per 1,000 liveborn VLBW infants)



*Infants weighing less than 1,500 g.
Note: Based on a study of 1,575 VLBW infants in 16 European centers.
Source: Child Care Health Dev. 2007;33:648-9

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