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Emerging concepts in the pathophysiology of recovery from neonatal brachial plexus injury

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Neonatal brachial plexus injury is a common problem in pediatric neurology, with an incidence of 0.6 to 2.5 per 1000 live births.[1-5] Full recovery occurs in 69 to 95% of the patients.[1,3-5] Improvement is rapid, with complete resolution of weakness in about 75% by 3 to 4 months of age.[1-4] However, 3 to 16% of these infants remain profoundly weak[2-5] and later in life have functional disability in the affected arm.[2-4,6] Skills of daily living are often impaired and progressive bone and joint deformities may develop.[5,6] The introduction of the operating microscope and the advent of microsurgical technique have rekindled interest in neurosurgical treatment of brachial plexus injury, including cases of nerve root avulsion.[7-8] In appropriately selected patients, innovative techniques of neurolysis and nerve grafting now offer hope for the severely affected child.[8-9] However, the benefit of neurosurgical intervention remains limited. The weak can be made stronger, especially in deltoid and biceps movement, but normal function is not achieved.

Two articles in this issue of *Neurology* increase our understanding of the pathophysiology of brachial plexus injury, help explain why the efficacy of surgical intervention is limited, and suggest new treatment strategies. Rollnik et al. describe six children (age 2 to 4 years) with severe biceps–triceps cocontractions attributed to aberrant spontaneous or postoperative nerve regeneration after neonatal brachial plexus injury.[10] They were treated over 8 to 12 months with injections of botulinum toxin into the triceps muscle. No severe adverse events were noted. All six demonstrated increased active range of motion at the elbow and improved elbow flexion. Hand to mouth movements became possible in five of the six. Cocontractions did not recur during a 1-year follow-up. Although such aberrant regeneration afterneonatal brachial plexus injury is relatively uncommon,[11] the associated cocontractions contribute to functional disability. Thus, botulinum toxin is a welcome addition to the treatment modalities available for affected children. It should be emphasized, however, that intensive physical therapy must be combined with the injections to increase strength and range of movement.

In a second article, Brown et al. show that persistent disability after neonatal brachial plexus injury is due, at least in part, to defective motor unit recruitment into voluntary movements.[12] Motor skills, strength, and physiologic measures, including maximal evoked muscle compound action potential (M-wave) amplitude, were studied in 16 patients (age 4 to 14 years) and compared with those of controls. Thirteen had deficits in motor skills without corresponding decreases in muscle strength or innervation. The data provide clear evidence of defective voluntary recruitment of motor units. The authors found no indication that the impaired motor unit recruitment resulted from upper motor neuron lesions. Instead, they hypothesize that the cause was an apraxia. They speculate that due to limb paralysis at a critical time in development of precise visually guided reaching, motor regions of the brain failed to construct normal motor programs for the affected limb.

These two studies are certainly provocative. The Brown et al.[12] hypothesis of impaired motor program development is consistent with the well-known importance of normal visual input for the development of sight. Furthermore, their hypothesis is supported by the rapidly growing evidence for activity-dependent plasticity in sensorimotor areas of the brain and spinal cord. Even in adults, representation

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in sensorimotor cortex is affected by motor training, as well as by manipulations that change sensory input and affect motor performance.[13] Spinal cord function is also shaped by experience during early development, as well as throughout life.[14,15] Such evidence strengthens the Brown et al.[12] hypothesis that the motor disability in neonatal brachial plexus injury results from an apraxia: in the absence early in life of normal movements and their accompanying patterns of proprioceptive and cutaneous sensory input, the brain and spinal cord do not undergo the activity-dependent changes that lead to normal motor neuron recruitment into skilled movements. The finding of Rollnik et al.[10] that biceps–triceps cocontractions had not recurred 1 year after the last injection of botulinum toxin is also consistent with this hypothesis. The lasting improvement suggests that the cocontractions were due to a central abnormality rather than to aberrant peripheral regeneration, and that the more normal movement allowed by the injections produced activity-dependent plasticity that eliminated the central abnormality or canceled its functional effect.

These extremely interesting studies need to be confirmed. They should encourage further clinical and laboratory investigations that focus on the nature, etiology, and treatment of the hypothesized apraxia. PET scanning or functional MRI may be particularly useful for exploring the issue of defective motor programming in neonatal brachial plexus injury.

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