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Rewiring to Regain Function in Patients with Spastic Hemiplegia

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Spastic hemiplegia results from several relatively common disorders, including stroke, traumatic brain injury, and cerebral palsy. Frequently, upper-limb function is impaired. In this issue of the *Journal*, Zheng et al.[1] report a new approach to the treatment of this condition: the use of a contralateral C7 nerve transfer from the nonparalyzed side to the paralyzed side in order to engage the unimpaired cerebral hemisphere.

Nerve transfers have long been performed as treatment for lesions affecting the lower motor neurons, mostly involving the brachial plexus. Gu and colleagues at Huashan Hospital, Fudan University, in Shanghai have pioneered nerve transfers, particularly those in which contralateral C7 and phrenic nerves are used as donor nerves for injuries to the brachial plexus.[2,3] They showed that the contralateral C7 nerve could be sacrificed with few if any long-term adverse effects and that the procedure could result in useful recovery of distal hand function.[4,5] The distance for nerve regeneration from the contralateral side of the neck to the opposite distal limb has been shortened by modifications in transposition techniques. Studies of brain plasticity in patients who have undergone surgery led to observations of cortical reorganization and bilateral motor-cortex control.[6,7] Despite these advances, contralateral C7 nerve transfer in adults with injuries to the brachial plexus remains controversial because of the risk–benefit ratio and the inherent challenges of the long distance and time needed for regeneration (estimated to occur at a rate of an inch per month) and the degree of cortical reorganization required.

Nerve transfers are now being introduced for patients with upper-limb paralysis resulting from injuries to the upper motor neurons — most often injuries to the spinal cord but also cerebral injuries. For example, a 4-year-old with cerebral palsy who was treated by the Huashan group with contralateral C7 nerve transfer to the middle trunk of the brachial plexus had some alleviation of spasticity and increased strength.[8] This technique was then demonstrated in a small trial involving six adult patients with hemiplegia,[9] which set the stage for the current, larger trial.

Zheng et al. report a prospective, randomized, controlled trial involving patients with severe spastic hemiparesis (but not hemiplegia) whose neurologic condition had plateaued after 5 years of rehabilitation. Magnetic resonance imaging (MRI) of the head revealed isolated injury to the brain hemisphere contralateral to the paralyzed hand, and transcranial magnetic stimulation was used to document exclusive control of the affected limb by the ipsilesional (contralateral) hemisphere. The 18 patients in the surgery group underwent a direct neurorrhaphy (i.e., suturing of cut nerves) of the contralateral C7 nerve to the C7 nerve on the paralyzed side through a prespinal route and then received rehabilitation therapy. A group of 18 matched control patients received rehabilitation therapy only.

Patients who underwent the surgery had only transient neurologic sequelae from the sectioning of the C7 nerve contralateral to the paralysis and had significantly greater improvement in the paralyzed limb, as measured on the Fugl–Meyer (motor recovery) and Modified Ashworth Scale (spasticity) scales at 12 months as compared with baseline, than did patients in the control group. Physiological connectivity was shown between the ipsilateral cerebral hemisphere and the paralyzed hand in the surgery group by means of electrophysiological testing, transcranial magnetic stimulation of the cortex, and functional MRI.

In our opinion, the results of the trial are exciting but need clarification and confirmation. The time frame for improvement is the major question: that distal muscles are functionally reinnervated in such a short time seems unlikely to us. An alternative hypothesis to explain the functional improvement is that there was reduction in spasticity caused by the C7 neurotomy on the paralyzed side: the neurotomy may have led to a reduction in limb spasticity and improved function through the normal motor pathways of the C5, C6, C8, and T1 nerves, and the effect may have been augmented by rehabilitation. The C7 neurotomy itself, associated with an immediate reduction in spasticity, represents a major advance for some patients with brain injury who have poor function and spasticity. A reduction in spasticity may also result in improved efficacy of the damaged motor cortex, an effect that may be enhanced by ongoing physical therapy. An improvement in function at 10 months cannot be readily explained as being predominantly a result of the contralateral nerve transfer, because nerves do not regenerate that quickly, fully, or consistently. Another trial from these investigators involving patients with brachial plexus injury with 6.9 years of follow-up showed that 49% of patients had motor recovery.[10] The presence of physiological connectivity observed in the trials does not necessarily equate with functional recovery.

Future studies of contralateral C7 nerve transposition in hemiplegic patients should include a group in which the patients undergo C7 neurotomy alone (i.e., without the nerve transfer) along with rehabilitation. Because of the high volume for this type of procedure at Huashan Hospital, the results obtained by these surgeons may not be easy to reproduce elsewhere. These surgeons are currently hosting workshops to train others in their techniques. Factors other than technical ones, including differences in body-mass index and limb length across different populations, may lead to different surgical outcomes.

The creative use of a strategy involving the peripheral nervous system, whether a nerve transfer or a neurotomy, for problems with the central nervous system represents a fresh approach and provides opportunities for insights into basic neuroanatomy and neurophysiology. Future research will need to address other ways to optimize physiological change — to enhance or speed up nerve regeneration, improve plasticity, and maximize rehabilitation.

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