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Innovations Influencing Physical Medicine and Rehabilitation

New Treatment Approaches on the Horizon for Spastic Hemiparesis

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Abstract

This article presents 2 recent articles that propose novel interventions for treating spastic hemiparesis by changing biological infrastructure. In 18 patients with unilateral spastic arm paralysis due to chronic cerebral injury greater than 5 years' duration, Zheng et al transferred the C7 nerve from the nonparalyzed side to the side of the arm that was paralyzed. Over a follow-up period of 12 months, they found greater improvement in function and a reduction of spasticity compared to rehabilitation alone. Using functional magnetic resonance imaging, they also found evidence for physiological connectivity between the ipsilateral cerebral hemisphere and the paralyzed hand. In the second article, Raghavan et al examine the concept of stiffness, a common symptom in patients with spastic hemiparesis, as a physical change in the infrastructure of muscle. Raghavan's non-neural hyaluronan hypothesis postulates that an accumulation of hyaluronan within spastic muscles promotes the development of muscle stiffness in patients with an upper motor neuron syndrome (UMNS). In a case series of 20 patients with spastic hemiparesis, Raghavan et al report that upper limb intramuscular injections of hyaluronidase increased passive and active joint movement and reduced muscle stiffness. Interventions that change biological infrastructure in UMNS is a paradigm on the horizon that bears watching.

Introduction

For a long time, managing impaired voluntary movement associated with an upper motor neuron syndrome (UMNS) has relied on therapeutic exercise, electrical stimulation, orthotics, and more recent rehabilitation engineering approaches such as robotics. Managing involuntary phenomena (eg, stretch-sensitive spasticity, cocontraction, dystonia, and non—stretch sensitive flexor reflex afferent activity) has relied, for the most part, on pharmacologic treatments such as oral, intrathecal, and intramuscular therapies as well as therapeutic exercise, orthotics and, to a lesser extent, surgery. A reigning paradigm underneath most of these approaches has been the belief that plastic changes can be wrought in nervous and musculoskeletal systems to bring about clinical change. In a broad sense, these various approaches are meant to "feed" a nervous system that, expectantly, will use the "food" to heal itself. Nevertheless, we are dealing with damage to biological infrastructure and, in the view of this author, most current treatment approaches, applied externally to damaged biological systems, offer limited help. This article extracts highlights from 2 recently published approaches that diverge from the current paradigm. These articles examine interventions aimed at solving the problematic aspects of spastic hemiparesis by interventions that change biological infrastructure. The author of this article has reviewed and paraphrases much content from the 2 articles because he wished to convey the novelty of their paradigms that emphasize interventions that change biological infrastructure.

Part 1: Changing Peripheral Nerve Infrastructure

Zheng et al recently published an article on C7 nerve transfer in patients with chronic UMNS [1]. Long-term disability is commonly caused by UMNS pathology affecting the cerebral hemispheres such as cerebral palsy, stroke, and traumatic brain injury [2], with hand use being particularly affected by UMNS [3]. It is well known that the corticospinal tract decussates in the

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medulla, so that a lesion affecting one side of the body is typically located in the central nervous system on the other side (above the medullary pyramids). It has been noted that during recovery, the cerebral hemispheres, both *ipsilesionally* and *contralesionally*, appear to undergo neural reorganization. (The term *contralesional* refers to the cerebral hemisphere on the same side of paralysis; eg, a right hemiparesis implies that the right hemisphere is contralesional, the lesion being in the left ipsilesional hemisphere. The terms *ipsi*- and *contralateral* are also used clinically, referring to anatomical structures on a side of the body, for example, a contralateral right hemiparesis might imply a lesion in the left hemisphere and so would an ipsilateral hand paralysis imply a contralateral lesion.] There is literature to suggest that the ipsilateral (contralesional) hemisphere may be involved in recovery of hand function after stroke with UMNS [4-8]. However, direct connections between the ipsilateral (contralesional) hemisphere and the paralyzed hand may be sparse in humans, consequently placing limits on compensatory motor behavior [9,10].

Zheng et al conducted a randomized, controlled, 12-month longitudinal trial involving a group of 36 patients with cerebral injury. Half the group underwent grafting of the C7 spinal nerve on the unaffected side of the body. The C7 spinal nerve accounts for approximately 20% of the fibers of the brachial plexus. The authors hypothesized that the paretic hand might operationally link to the contralesional hemisphere after transfer of the C7 spinal nerve from the unaffected to the affected side. This approach had been used elsewhere with brachial plexus injuries where nerve grafting depended on development of a unitary anatomic and physiologic connectivity of a peripheral nerve anastomosis. Somewhat in contrast, a nerve graft in the case of a cerebral lesion would seem to depend on 2 connections. In order for an affected arm to work after C7 nerve transfer, physiologic connection of the anastomosed nerve to the peripheral nerve innervating the UMNS limb had to be established. In addition, a second physiologic connection had to form between the grafted peripheral nerve and the contralesional cerebral hemisphere ipsilateral to the upper limb affected by UMNS.

Study participants with spastic hemiparesis had stopped improving after a minimum of 5 years of physical therapy. Among the inclusion criteria, muscle power and touch sensation were reduced but not absent. Transcranial magnetic stimulation (TMS) of the contralesional hemisphere had to result in activation of the unaffected extensor carpi radialis whereas participants with TMS applied to the ipsilesional hemisphere causing activation of the affected extensor carpi radialis were excluded. Participants with systemic disease such as diabetes or cardiopulmonary disease, developmental delay, severe fixed contracture, joint deformity, or poor cognition were excluded. Half the group served as a control, the other half underwent C7 nerve transfer from the unaffected side to the affected side. Blinded, nonstratified randomization was performed and was not known to members of the staff until assignment for intervention was made.

The major intervention of the trial was a surgical transfer of the C7 nerve on the unaffected side to the same nerve on the affected hemiparetic side. The authors indicate that a surgical incision was made at the superior aspect of the sternum and the donor C7 nerve on the unaffected side was mobilized. The donor C7 nerve, sectioned as distally as possible but before it combined with other nerves, was then routed through a path prepared between the spinal column and the esophagus. The recipient C7 nerve on the affected side was sectioned and mobilized proximally as much as possible and the donor C7 nerve from the unaffected side was then anastomosed with the C7 recipient. No surgery was performed on the control group but both groups received similar rehabilitation therapies 4 times a week for 12 months at a single facility. Treating physical therapists were aware of treatment assignments. Therapy included similar active exercise, passive range of motion, occupational therapy, functional training, physical therapy, acupuncture, massage, and the use of orthoses. The only between-group difference was the use of an immobilizing cast during the postoperative period for patients undergoing surgical intervention.

The primary outcome measure was change in total score on the Fugl-Meyer upper extremity scale from baseline to a 12-month endpoint. Secondary outcomes included changes in active range of motion and the Modified Ashworth Scale (MAS) for elbow, forearm, wrist, thumb, and digits 2 through 5. A positive outcome was considered a significant improvement in at least 1 of the 5 joints tested over baseline scores. Functional tasks included activities such as dressing, tying shoes, wringing out a towel, and operating a mobile phone. Other secondary outcomes included evoked motor responses obtained by electrical stimulation at the Erb point on the unaffected side from extensor carpi radialis (ECR) on the affected side. In addition, TMS over each hemisphere was performed with recording of the motor response of ECR on the affected side. Functional magnetic resonance imaging measurements were obtained with the patient at rest and during active extension of the wrist on the affected side. Adverse events were documented and changes in muscle strength, tactile sensation threshold, and 2-point discrimination of arm and hand on the side of the donor C7 nerve were monitored over the 12-month period.

Descriptive characteristics related to patients was as follows: study participants with age range between 12 and 45 had spastic hemiparesis due to stroke, traumatic brain injury, cerebral palsy or encephalitis. There were no significant differences between the groups in Fugl-Meyer or Ashworth scores at baseline, with the