Effects of Somatosensory Stimulation on Use-Dependent Plasticity in Chronic Stroke

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Background and Purpose—There is a need to develop strategies to enhance the beneficial effects of motor training, including use-dependent plasticity (UDP), in neurorehabilitation. Peripheral nerve stimulation (PNS) modulates motor cortical excitability in healthy humans and could influence training effects in stroke patients.

Methods—We compared the ability of PNS applied to the (1) arm, (2) leg, and (3) idle time to influence training effects in the paretic hand in 7 chronic stroke patients. The end point measure was the magnitude of UDP.

Results—UDP was more prominent with arm stimulation (increased by 22.8%) than with idle time (by 2.9%) or leg stimulation (by 6.4%).

Conclusions—PNS applied to the paretic limb paired with motor training enhances training effects on cortical plasticity in stroke patients. (Stroke. 2006;37:246-247.)

Key Words: nerve stimulation ■ neuronal plasticity ■ stroke ■ stimulation, transcranial magnetic

Use-dependent plasticity (UDP) is instrumental in motor learning and may play a role in recovery of function after brain lesions.1 Given the influence of somatosensory input on motor function,2 it is possible that somatosensory stimulation (SS) potentiates plastic changes associated with use in stroke patients. We evaluated the effects of SS on the ability of stroke patients and healthy subjects to express UDP in the hand.3 In our UDP protocol, a rapid training period consisting of voluntary thumb movements results in a change in the cortical network representing the thumb that encodes the kinematic details of the training and represents a motor memory influenced by long-term potentiation–like mechanisms.4,5 We tested the hypothesis that SS applied to the hand preceding motor training would enhance training effects on UDP in stroke patients and healthy subjects.

Methods

Seven patients (4 men; 66.7 ± 4.3 years of age) with single ischemic stroke >6 months before testing were enrolled. Medical Research Council scores (hand muscles) at ictus were <2, but patients recovered to the point of being able to perform isolated thumb movements. Six healthy subjects (4 men; 32 ± 3.5 years of age) were enrolled as additional control. All gave informed consent, and the protocol was approved by the institutional review board.

Patients participated in 3 different sessions randomly ordered in a crossover design and separated by ≥24 hours (a safe period to avoid carryover effects6). UDP was tested after 2-hour stimulation of (1) ulnar, median, and radial nerves in the paretic hand (arm stimulation); (2) tibial, superficial peroneal, and sural nerves in the paretic leg (leg stimulation; only stroke subjects); and (3) no stimulation (idle time; Figure and also see supplemental Figure I, available online at http://stroke.ahajournals.org). Trains of electrical stimulation consisting of 5 pulses at 10 Hz (1-ms duration each) were delivered every second using a stimulator (Grass; Astro-Med, Inc) at an intensity adjusted to elicit compound muscle action potentials up to 100 μV.6 For electromyographic recordings, disposable electrodes were placed over the belly of abductor pollicis brevis, abductor digiti minimi, and extensor digitorum communis muscles in the upper extremity (arm stimulation) and tibialis anterior muscle and abductor hallucis muscle in the lower extremity (leg stimulation).

We determined the maximal thumb movement rate that each patient could sustain over 30 minutes. UDP was tested after thumb movements cued by an auditory signal in a direction opposite to the baseline transcranial magnetic stimulation (TMS)–evoked movement direction for 30 minutes at each subject’s maximal rate. Healthy subjects had a constant rate of 1 Hz.4,5 On each day, subjects received 1 of the 3 interventions (arm, leg-only patients, and idle time; see online supplement, available at http://stroke.ahajournals.org). Motor training was the same in all sessions.4,5 To describe intervention effects on UDP, we defined a training target zone (TTZ) as a window of ±20° centered on the training direction. Our end point measure of UDP was the increase in the proportion of TMS-evoked movements that fell within the TTZ.

Statistical Analysis

Data were analyzed blindly off-line. Increase in the proportion of TMS-evoked movements in the TTZ was analyzed with a 1-way repeated-measures ANOVA with factor stimulation (3 levels in patients; 2 levels in healthy subjects). Movement threshold, amplitude of motor-evoked potential (MEP), and training kinematics were analyzed using factorial ANOVA with factor stimulation. Fisher post hoc tests were performed. Data are expressed as mean ± SE and considered significant if P < 0.05.
Results
Motor and movement threshold, amplitude of MEP training antagonist, MEP training agonist at baseline, and training kinematics were comparable across interventions and within groups (supplemental Table I, available online at http://stroke.ahajournals.org).

Motor training alone with idle time was unable to elicit UDP (Figure), consistent with previous results. In stroke patients, arm stimulation enhanced training effects eliciting clear UDP (0.23 ± 0.07 increase in the proportion of TMS-evoked thumb movements in the TTZ in reference to baseline; P < 0.05) similarly to healthy subjects (0.19 ± 0.09). Within-subject comparison revealed that UDP increased in 5 stroke patients and remained unchanged in 2. Leg stimulation failed to elicit UDP. The magnitude of UDP elicited by arm stimulation was more prominent than any changes elicited by leg stimulation or idle time (P < 0.05).

Discussion
SS preceding motor training increased the magnitude of UDP in patients with chronic stroke and healthy subjects in the absence of global measurable differences in motor cortical excitability.

Reorganizational changes occur in the central nervous system throughout the lifespan and may sustain functional recovery after brain lesions. It has been proposed that somatosensory input, with its ability to drive plastic changes in the motor cortex, could modulate UDP. For instance, stimulation of the somatosensory cortex in kittens enhanced excitatory postsynaptic potentials in the motor cortex and stimulation of muscle, tactile, and joint afferents activate motor cortical areas in monkeys. Stimulation of whiskers in rats enhances c-fos expression, which has been postulated to upregulate the expression of neurotrophins that may be involved with dendritic and axonal sprouting. SS enhances excitability of the stimulated body part representation in the motor cortex in healthy subjects and results in improvements in motor performance in stroke patients. Our results demonstrate that this intervention may enhance the beneficial effects of a single motor training session on UDP in stroke patients. Combination of SS with training protocols could conceivably be applied in the future to improve the effects of customary rehabilitative interventions.

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References
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