



AOTA Evidence Briefs

Stroke: Focused Questions

**A product of the American Occupational Therapy Association's Evidence-Based Literature Review Project*

SFQ 3

What conditions have been shown to be associated with cortical reorganization?

In the past several years, advances in technology have allowed study of the awake, functioning brain. Many studies using this technology have demonstrated in humans, rats, and monkeys that, after injury to the **sensorimotor** (see *Glossary*) cortex, the remaining tissue in both the injured and the intact hemispheres undergoes substantial functional reorganization. Further, “it is well established that the brain undergoes experience-dependent changes throughout the life of an animal or human” (Friel, Heddings, & Nudo, 2000, p. 197—Level II). Motor recovery has been shown to parallel the changes in functional organization (Heddings, Friel, Plautz, Barbay, & Nudo, 2000—Level III). Studies indicate that synapses in the cortex can be remodeled by experience, sensory input, and learning (Heddings et al., 2000; Johansson, 2000).

Cortical reorganization may be the principal process responsible for recovery of function after stroke, but to what extent can intervention facilitate such reorganization? To date, studies of specific therapeutic interventions are few (Johansson, 2000). Interventions or conditions that have been documented to be associated with cortical reorganization after stroke are included in this review. They are presented by type of intervention.

Findings of Selected Studies

Immobilization

Immobilization appears to reduce the cortical area that serves the part immobilized. In a study (described more fully later) of squirrel monkeys that underwent **ischemic infarct** (see *Glossary*) of the primary motor cortex, Friel et al. (2000—Level II) allowed some of the animals to recover spontaneously and put others in a restrictive jacket, which forced them to use their impaired hand. The group that wore the restrictive jacket displayed a reduced representation in the cortical area of their immobilized, less-affected hand, as did the group allowed to recover spontaneously.

Decreased cortical representation after immobilization also has been observed in humans. In a study of constraint-induced therapy (CIT; described more fully later), Liepert, Miltner, et al. (1998—Level III) found that the cortical maps of the restrained arm of patients in the chronic stage of stroke recovery lost representation as a result of the restraint. Liepert, Tegenthoff, and Malin (1995—Level II) mapped the motor cortices of 22 patients with orthopedic problems requiring immobilization of the ankle and 10 healthy people who served as a **control group** (see *Glossary*). In patients with immobilization of at least 4 weeks' duration, the average size of the motor cortex area of the immobilized anterior tibialis was reduced **significantly** (see *Glossary*) compared with the nonimmobilized side. There was a significant decrease in the ratio of the cortical area of the injured leg to the cortical area of the unaffected leg, compared with that ratio in the control group after the first 9 days of immobilization, during which the ratios were normal. There was a significant correlation between immobilization time and reduction of the cortical maps.

Immobilization appears not to be beneficial when the goal is to increase cortical area that is related to limb performance.

Passive Movement

Carel et al. (2000—Level II) investigated the effects of 1 month of training consisting of passive movement of the wrist, compared with rest (the control condition), on the cortical maps of 12 healthy young adults. The training group received passive wrist flexion and extension for 20 minutes per day, 5 days a week, for 4 consecutive weeks. Surface **electromyography** (see *Glossary*) confirmed that the movements were not accompanied by muscle activity.

The researchers found that the training group evidenced increased activity in the supplementary motor area (SMA) and in the contralateral primary sensorimotor area (S1M1), compared with the control group, although the significance and the **effect size** (see *Glossary*) were not reported. All the participants who underwent the training showed the increased activity in the SMA and the contralateral S1M1. The researchers concluded that prolonged passive training can change the S1M1 and the SMA.

Because the report of this study failed to present the data statistically and because the study was carried out on only a small sample of normal, young, untreated adults, passive movement to reorganize cortical maps cannot be recommended at this time. Further study is needed.

Findings of Selected Studies

Repetitive Use

Plautz, Milliken, and Nudo (2000—Level II) examined the effect of repetitive use without learning. They studied the behavioral performance of squirrel monkeys before and after training that followed a surgically imposed infarction of the primary motor area (M1) of the cortex. The training task was one for which the monkeys already possessed the needed motor abilities—that is, retrieval of a food pellet from a well large enough that they could use their whole hand, as they normally do. Their motor behavior (patterns of movement, error rate, and efficiency) remained stable over the study's 3 time periods (1–4 days following the **lesion** (see *Glossary*), 5–8 days following the lesion, and 9 days following the lesion to the end of training). The end of training for each monkey was when it achieved 12,000 finger flexions of the affected hand. Only speed of performance increased, and that occurred between the first and second time periods.

This indicated that learning had not taken place and therefore the independent variable (repetitive use without learning) had been implemented. They examined the topographic organization of the cortical maps, the overall size of the maps, and the relative size of the individual representations that constituted the maps of the monkeys under study. There were no systematic task-related changes in movement representations following the training (repetitive practice of a known movement).

The researchers compared these results with those of an earlier study (Nudo, Milliken, Jenkins, & Merzenich, 1996) in which both behavioral changes and motor cortex reorganization were demonstrated when squirrel monkeys were required to learn to retrieve food pellets from a small well using one or two fingers, instead of their whole hand, which is their habitual behavior. The only difference in these two studies was the size of the wells that held the food pellets. Plautz and colleagues (2000) concluded, “The present study demonstrates that not all repetitive behavioral experiences result in cortical map modifications. Only when the subject acquires a novel skill does the cortical map reorganize. Use alone does not modify the cortical representations” (p. 51).

Learning

Learning has consistently shown the effect of increasing the cortical map associated with the learned behavior. Friel et al. (2000—Level II) stated that, throughout a person's life, there are extensive changes in cortical representations based on that person's sensory and motor experiences. They went on to say, “Numerous studies of both somatosensory and motor cortex show that cortical representations of specific body parts change as a function of skill acquisition” (p. 197).

Karni, Meyer, Jezzard, Adams, Turner, and Ungerleider (1995—Level I) examined what cortical changes occurred in humans' motor cortex as a result of long-term practice to learn a complex motor sequence. The report is sketchy, but essentially the researchers studied the motor learning of 10 healthy young adults and examined the cortical representation of the learned sequence in the M1 region of 6 of the participants. The 10 participants were randomized to one

of two groups: (a) oppose the thumb of the nondominant hand lightly to the fingers according to sequence A: 4 (little), 1 (index), 3 (ring), 2 (middle), 4 or (b) oppose the thumb of the nondominant hand lightly to the fingers according to sequence B: 4, 2, 3, 1, 4. The other sequence (B for the A group, A for the B group) was used as a control condition, executed without practice. The participants practiced their assigned sequence 10–20 minutes per day for 5 weeks; compliance was not reported. The speed (the number of completed sequences performed in a 30-second interval) increased significantly from the 1st week to the 5th week. The accuracy (decrease in the number of sequences that contained errors) also improved significantly over this period. There was **no significant** (see *Glossary*) improvement for the control sequence, although it contained the same submovements. Furthermore, there was no transfer of learning of the practiced sequence to the contralateral (dominant) hand. After 3 weeks, the activation map evoked by the trained sequence was consistently larger than for the control sequence, irrespective of the order in which the sequences were executed. The researchers concluded that the extent of representation of the trained sequence in M1 does indeed expand with learning.

Classen, Liepert, Wise, Hallett, and Cohen (1998—Level III) tested the ability of 9 healthy adults to alter their cortical maps by practicing movements diametrically opposite to the movements usually governed by a particular cortical area. The researchers mapped the area associated with thumb extension and abduction. Then the participants practiced unidirectional, stereotyped thumb movements in the direction of flexion and adduction for 30 minutes, paced at 1 per second by a metronome. The data to be analyzed were collected from approximately 5 movements each minute. When measured, movements were averaged across participants, the mean was 138 ± 31 movements.

Analysis indicated that the movement patterns in the cortex changed in the direction of training (flexion and adduction rather than extension and abduction). The change lasted for 15–20 minutes following training, and then the pattern returned to the original. The researchers concluded that reorganization of the neuronal network mediating thumb movements occurred and that the neuronal network encodes certain kinematic aspects (initial direction and velocity) of the practiced action.

Constraint-Induced Therapy (Forced Use)

CIT is a special case of the learning condition. Via this therapy, patients who have some voluntary control relearn to use their affected extremity. Edward Taub, the developer of this therapy, believes that CIT overcomes the phenomenon of “learned nonuse,” in which ineffective and unrewarded use of an impaired limb causes people eventually to abandon use of it (Friel et al., 2000—Level II). Johansson (2000) noted that “changes in [brain] activation pattern can be induced by forced training of the paretic hand even 4 to 15 years after stroke onset” (p. 226).

Findings of Selected Studies

Using small samples, Liepert and his colleagues conducted several studies of cortical reorganization associated with CIT. All the studies required the participants to have some voluntary extension of the wrist and fingers of the paretic hand.

Liepert, Miltner, et al. (1998—Level III) studied the effects of CIT on the cortical maps of 6 stroke patients in the chronic stage of recovery (6 months–17 years after onset). CIT involved restraining the unaffected arm and hand and training the affected arm 6 hours a day, 5 days a week, for 2 weeks to learn to handle objects and do various activities. After training, the size of the cortical area of the abductor pollicis brevis, the muscle being monitored, was significantly enlarged, whereas that of the healthy abductor pollicis brevis was decreased. These changes in the affected and unaffected sides of the brain combined to yield a dramatic increase in the ratio of the size of the cortical activation area of the affected arm to that of the unaffected arm from 0.6 before treatment to 1.44 after treatment. Daily motor function improved significantly, as measured by the Motor Activity Log (MAL), a subjective estimation of the amount of use and quality of movement of the affected upper extremity. There was no correlation between the amount of MAL improvement and the extent of the increase of area size.

In the researchers' view, the study demonstrates that CIT improves motor performance and that therapy induces changes in the motor cortex of the affected hemisphere. Improvement occurred even in participants who had received physical therapy right up to the time of starting the study.

Liepert, Bauder, Miltner, Taub, and Weiller (2000—Level III) tested whether CIT would cause changes in the cortical areas of 13 stroke patients who were an average of 4.9 years after onset. Two weeks of CIT was preceded by 2 weeks

of no treatment to control for spontaneous recovery. CIT consisted of wearing a resting hand splint and a sling on the unaffected arm for 90% of waking hours and 6 hours a day of training the affected arm to do a variety of tasks requiring the use of one hand. The tasks were graded with the goal of improving the quality of movement.

The researchers reported a “massive” increase in the cortical representation of the paretic hand 1 day after treatment compared with 1 day before treatment. This increase persisted through a 4-week follow-up. There was significantly greater use of the affected arm 1 day after treatment compared with 1 day before treatment, as measured by the MAL. This use also persisted through the 4-week follow-up.

Liepert, Uhde, Gräf, Leidner, and Weiller (2001—Level III) tested whether modified CIT would induce motor cortex reorganization, compared with conventional physical therapy, in 9 stroke patients 4 to 8 weeks after onset. Modified CIT involved immobilization of the unaffected arm in a forearm splint for a period of time each day for 1 week. The amount of time was individually negotiated with each patient. The report of the study makes no mention of training. Conventional physical therapy involved therapy to improve gait performance, to improve balance, and to regain activities of daily living such as dressing and feeding and also training to improve cognitive functions. All the participants underwent both therapies sequentially, but the sequence was not randomized.

There was no change in the motor output area after conventional therapy, but the maps of the motor output area were significantly greater after CIT. There was no significant improvement on the Nine-Hole Peg Test after conventional therapy, but there was significant improvement after CIT.

Liepert, Graef, Uhde, Leidner, and Weiller (2000—Level III) examined whether one 30-minute session of CIT would affect the motor cortex representation of the affected hand of 9 patients 4–8 weeks after ischemic stroke. Immediately following treatment, the cortical maps showed the motor output area of the affected hemisphere to be significantly greater than before treatment. Seven of the participants improved on the Nine-Hole Peg Test of dexterity. One day after treatment, however, the motor output area had shrunk back to its size before treatment.

In a study of 9 squirrel monkeys, Friel et al. (2000—Level II) found restraint of the unaffected upper extremity without training not to be significantly different from no intervention. The monkeys underwent small ischemic lesions in their motor cortex. Then they were assigned to one of three conditions: (a) no treatment; (b) restraint of the unaffected arm and hand with no training; and (c) restraint of the unaffected arm and hand with training. Training involved two 30-minute sessions a day, 7 days a week, until the monkeys achieved a predetermined level of skill. This took 15–55 days.

There were no significant differences among conditions on the behavioral testing (number of finger flexions per retrieval of food pellet), but this was probably because the lesions were small and produced mild deficits. All monkeys, even those in the no-intervention group, returned to normal levels of pellet retrieval by 4 weeks after the lesion. A significant effect was found on the percentage of change in total hand area representation in the motor cortex, however. Both the no-intervention and the restraint–no training group lost more than 50% of the area that controls the affected hand that was not damaged by the lesion, whereas the restraint–training group gained 9%. A further analysis of the statistical data showed that the significant differences occurred between the restraint–training group and the no-intervention group and between the restraint–training group and the restraint–no training group. There was no significant difference between the no-intervention group and the restraint–no training group. When the researchers divided the representational area into digit and hand/forearm areas, they saw that the no-intervention group lost 74% of the digit representation, the restraint–no training group 64%, and the restraint–training group 3%—a significant difference. The researchers concluded that, after small cortical lesions to the motor hand representation in the M1 area of the cortex, additional loss of hand representation occurs unless animals receive skill training of the impaired hand. Increased use of the hand by constraint of the unimpaired hand is not sufficient to retain representational area.

Enriched Environment and Enriched Rehabilitation

Enriched environment and enriched rehabilitation also are special cases of the learning condition. In the case of enriched environment, an animal is provided with opportunities to learn new motor skills by engaging with interesting objects in the environment. Through such engagement, the animal is encouraged to use the affected arm. This contrasts with CIT, a case of enriched rehabilitation, which forces use of the affected arm.

Findings of Selected Studies

Biernaskie and Corbett (2001—Level I) studied the effects of enriched rehabilitation on functional recovery and on the growth of **dendrites** (see *Glossary*) within the hemisphere that remained intact after surgical lesion. Half of the 57 rats received a surgical lesion of their cortex in the area of the middle cerebral artery distribution; the other half received a sham operation, without a cortical lesion. The enrichment consisted of enticing the rats to reach with the affected paw to get mini-M&Ms during 4 weeks of training, 6 hours a day, 5 days a week. Between training sessions, the rats were returned to a cage containing other rats and many intriguing rat toys. In other words, the rats were provided with meaningful occupation. Before assignment to condition, the ischemic rats were paired for level of function, and then both the ischemic and the sham rats were randomly assigned to enriched or standard treatment. So there were 4 groups: ischemic enriched, ischemic standard, sham enriched, and sham standard. “Standard” was defined as each rat being housed alone, with food pellets put on a little staircase in the cage twice a day for 5 days. The researchers controlled for potential effects of sugar and chocolate by feeding all rats M&Ms equal to the amount retrieved and eaten by the ischemic-enriched rats.

After treatment, the sham groups were not significantly different (i.e., they showed no effect of enriched rehabilitation), so their scores were combined for analysis. On a skilled-reaching test, the ischemic-enriched rats scored significantly better than the ischemic-standard rats. Further, the ischemic-enriched rats showed approximately 30% recovery at 4 weeks after the start of therapy, but the ischemic-standard rats showed no improvement. This improvement for the ischemic-enriched rats transferred to a task that required similar levels of precision—beam walking—but not to a task that had different motor demands—postural support in the upright position. There was significant dendritic growth for the ischemic-enriched rats compared with the other 3 groups. The researchers concluded that enriched rehabilitation providing positive reinforcement (a food reward) for using the impaired limb encouraged the animals to use “spared” (motor function that was not affected by the lesion) or residual motor function/or prompted development of compensatory motor strategies, resulting in lessened functional impairment.

According to Johansson (2000),

There is substantial evidence that the postoperative environment can influence the outcome after experimental brain damage [in rats]. After an experimental brain infarction, rats housed in an enriched environment with the opportunity for various activities and interactions with other rats performed significantly better than rats housed in standard laboratory environments. A comparison between enriched environment, social interaction, and physical activity in the form of wheel-running indicated that social interaction was superior to wheel-running and that an enriched environment which allowed free physical activity combined with social interaction resulted in the best performance. (p. 225)

Johansson continued,

Housing animals in an enriched environment with the opportunity to perform various activities, but no specific training significantly improved functional outcome without increasing [brain] tissue loss. However, if the enriched environment was combined with more specific training (which forced use of only the affected limb and therefore overuse) from 24 hours after the insult, an increased tissue loss occurred. (p. 227)

There are no studies of humans in enriched environments. Overuse has not been a clinical issue with human stroke patients, as it was with the rats Johansson wrote about. Neither are there studies concerning overuse of paretic limbs after stroke.

Summary

The conditions that have been shown to be associated with cortical reorganization are learning (increasing the cortical map associated with learned behavior), including CIT and enriched environment; immobilization (decreasing the cortical map); and repetitive use without learning (decreasing the cortical map associated with learned behavior). The effect of passive movement is inconclusive.

Clinical Application

The studies cited here provide evidence to support use of activities in therapy that require skill acquisition, rather than repetition of already well-learned movements, if the goal is increasing the cortical map associated with the learned behavior and improved skilled use of the affected upper extremity. Furthermore, because immobilization of limbs has been shown to decrease the cortical maps associated with learned behavior, therapy after immobilization is recommended to restore the diminished cortical maps.

Glossary

control group—a group that received special attention similar to that which the treatment group received but did not receive the treatment.

dendrites—balancing protoplasmic processes that conduct impulses toward the body of a nerve cell.

effect size (Cohen's r)— a measure of clinical significance. It provides information about the magnitude of effect of the treatment. Although related to significance, it is not as influenced by the size of the sample. Therefore, it is possible to have an outcome on which the treatment had a large effect (e.g., the treatment group improved a lot more than the control group) and still have a nonsignificant result. If the results have a large effect but no significance, this means that this effect may be sample specific and not generalizable outside the study. There are many different types of effect sizes. What is reported here is Cohen's r . Cohen's r can be interpreted in a manner similar to a Pearson's correlation coefficient:

Effect size r	Size of the effect
<0.10	Negligible
0.10 – 0.29	Small
0.30 – 0.49	Medium
>0.50	Large

Note: Cohen, J. (1977). *Statistical power analysis for behavioral sciences*. New York: Academic Press.

electromyography—a method of recording the electrical activity of contracting muscle.

functional magnetic resonance imaging (fMRI)—magnetic resonance imaging (MRI) is a computer-enhanced radiologic procedure for clearly examining the structures of the body. fMRI is the same procedure applied to the head and conducted while the subject is doing some functional task. The fMRI indicates which brain areas are active or inactive for particular tasks or parts of a task.

ischemic infarct—death of tissue resulting from mechanical obstruction (mainly arterial narrowing of blood supply).

lesion—“an abnormal change in structure of an organ or part due to injury or disease” (*Merriam-Webster Medical Dictionary*, s.v.).

nonsignificant (or no significance)—A statistical term that refers to study findings that are likely to be due to chance differences between the groups rather than to other factors (e.g., the treatment of interest). A nonsignificant result is not generalizable outside the study. Like significance, a nonsignificant result does not indicate the clinical effect. Often studies will show nonsignificant results, yet the treatment group's mean will be better than the control group's. This is usually referred to as a *trend in the right direction*. Because significance is closely determined by sample size, nonsignificant results would often become significant if the sample size were increased.

sensorimotor—“of, relating to, or functioning in both sensory and motor aspects of bodily activity” (*Merriam Webster's Collegiate Dictionary*, 10th ed., s.v.).

significance (or significant)—a statistical term; refers to the probability that the results obtained in the study are not due to chance but to some other factor (such as the treatment of interest). A significant result is one that is likely to be generalizable to populations outside the study.

Significance should not be confused with *clinical effect*. A study can be statistically significant without having a very large clinical effect on the sample. For example, a study that examines the effect of a treatment on a client's ability to walk, may report that the participants in the treatment group were able to walk significantly longer distances than the control. However, if you read the study you may find that the treatment group was able to walk, on average, 6 feet, while the control group was able to walk, on average, 5 feet. While the outcome may be statistically significant, a clinician may not feel that a 1-foot increase will make his or her client functional.

References

Articles Ranked for Level of Evidence

- Biernaskie, J., & Corbett, D. (2001). Enriched rehabilitative training promotes improved forelimb motor function and enhanced dendritic growth after focal ischemic injury. *Journal of Neuroscience*, *21*, 5272–5280.
Level IC1: Randomized controlled trial, less than 20 participants per condition, high internal validity, external validity not reported.
- Karni, A., Meyer, G., Jezard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature*, *377*, 155–158.
Level IC3c: Randomized controlled trial, less than 20 participants per condition, low internal validity, low external validity.
- Friel, K. M., Heddings, A. A., & Nudo, R. J. (2000). Effects of postlesion experience on behavioral recovery and neurophysiologic reorganization after cortical injury in primates. *Neurorehabilitation and Neural Repair*, *14*, 187–198.
Level IIC1: Nonrandomized controlled trial—two groups, less than 20 participants per condition, high internal validity, external validity not reported.
- Plautz, E. J., Milliken, G. W., & Nudo, R. J. (2000). Effects of repetitive motor training on movement representations in adult squirrel monkeys: Role of use versus learning. *Neurobiology of Learning and Memory*, *74*, 27–55.
Level IIC2: Nonrandomized controlled trial—two groups, less than 20 participants per condition, moderate internal validity, external validity not reported.
- Liepert, J., Tegenthoff, M., & Malin, J. P. (1995). Changes of cortical motor area size during immobilization. *Electroencephalography and Clinical Neurophysiology*, *97*, 382–386.
Level IIC3a: Nonrandomized controlled trial—one group (one treatment) pretest and posttest, less than 20 participants per condition, low internal validity, high external validity.
- Carel, C., Loubinoux, I., Boulanouar, K., Manelfe, C., Rascol, O., Celsis, P., et al. (2000). Neural substrate for the effects of passive training on sensorimotor cortical representations: A study with functional magnetic resonance imaging in healthy subjects. *Journal of Cerebral Blood Flow and Metabolism*, *20*, 478–484.
Level IIC3c: Nonrandomized controlled trial—two groups, less than 20 participants per condition, low internal validity, low external validity (see *Glossary*).
- Heddings, A. A., Friel, K. M., Plautz, E. J., Barbay, S., & Nudo, R. J. (2000). Factors contributing to motor impairment and recovery after stroke. *Neurorehabilitation and Neural Repair*, *14*, 301–310.
Level IIIC2: Nonrandomized controlled trial—one group (one treatment) pretest and posttest, less than 20 participants per condition, moderate internal validity, external validity not reported.
- Liepert, J., Bauder, H., Miltner, W. H. R., Taub, E., & Weiller, C. (2000). Treatment-induced cortical reorganization after stroke in humans. *Stroke*, *31*, 1210–1216.
Level IIIC2c: Nonrandomized controlled trial—one group (one treatment) pretest and posttest, less than 20 participants per condition, moderate internal validity, low external validity.
- Liepert, J., Graef, S., Uhde, I., Leidner, O., & Weiller, C. (2000). Training-induced changes of motor cortex representations in stroke patients. *Acta Neurologica Scandinavica*, *101*, 321–326.
Level IIIC2c: Nonrandomized controlled trial—one group (one treatment) pretest and posttest, less than 20 participants per condition, moderate internal validity, low external validity.
- Liepert, J., Uhde, I., Gräf, S., Leidner, O., & Weiller, C. (2001). Motor cortex plasticity during forced-use therapy in stroke patients: A preliminary study. *Journal of Neurology*, *248*, 315–321.
Level IIIC2c: Nonrandomized controlled trial—one group (one treatment) pretest and posttest, less than 20 participants per condition, moderate internal validity, low external validity.
- Classen, J., Liepert, J., Wise, S. P., Hallett, M., & Cohen, L. G. (1998). Rapid plasticity of human cortical movement representation induced by practice. *Journal of Neurophysiology*, *79*, 1117–1123.
Level IIIC3c: Nonrandomized controlled trial—one group (one treatment) pretest and posttest, less than 20 participants per condition, low internal validity, low external validity.
- Liepert, J., Miltner, W. H. R., Bauder, H., Sommer, M., Dettmers, C., Taub, E., et al. (1998). Motor cortex plasticity during constraint-induced movement therapy in stroke patients. *Neuroscience Letters*, *250*, 5–8.
Level IIIC3c: Nonrandomized controlled trial—one group (one treatment) pretest and posttest, less than 20 participants per condition, low internal validity, low external validity.

References

Articles for Focused Questions (not ranked)

Johansson, B. B. (2000). Brain plasticity and stroke rehabilitation: The Willis Lecture. *Stroke*, *31*, 223–230.

Nudo, R. J., Milliken, G. W., Jenkins, W. M., & Merzenich, M. M. (1996). Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. *Journal of Neuroscience*, *16*, 785–807.

Further Reading

Bütefisch, C., Hummelsheim, H., Denzler, P., & Mautriz, K-H. (1995). Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. *Journal of the Neurological Sciences*, *130*, 59–68.

Hummelsheim, H. (1999). Rationales for improving motor function. *Current Opinion in Neurology*, *12*, 697–701.

Johnson, S. H. (2000). Imagining the impossible: Intact motor representations in hemiplegics. *NeuroReport [Cognitive Neuroscience and Neuropsychology]*, *11*, 729–731.

Ohlsson, A. L., & Johansson, B. B. (1995). Environment influences functional outcome of cerebral infarction in rats. *Stroke*, *26*, 644–649.

Page, S. J., Levine, P., Sisto, S., & Johnston, M. V. (2001). A randomized efficacy and feasibility study of imagery in acute stroke. *Clinical Rehabilitation*, *15*, 233–240.

Staines, W. R., McIlroy, W. E., Graham, S. J., & Black, S. E. (2001). Bilateral movement enhances ipsilesional cortical activity in acute stroke: A pilot functional MRI study. *Neurology*, *56*, 401–404.

This work is based on the evidence-based literature review completed by Catherine A. Trombly, ScD, OTR/L, FAOTA.

For more information about the Evidence-Based Literature Review Project, contact the Practice Department at the American Occupational Therapy Association, 301-652-6611, x 2040.

