Effect of Lesion Location on Upper Limb Motor Recovery After Stroke

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Background and Purpose—The purpose of this study was to assess the effects of stroke involvement of primary and secondary hemispheric motor systems and corticofugal tracts on arm and hand recovery.

Methods—Forty-one patients participating in an inpatient stroke rehabilitation database, admitted 17±2 (SEM) days after initial unilateral hemispheric ischemic stroke, with neuroimaging studies performed >48 hours after stroke and with minimal upper limb (UL) movement (admission Fugl-Meyer UL motor scores ≤9; normal score, 58) were studied. Patients were divided into 3 groups according to their UL discharge Fugl-Meyer score: 0 to 9, no/poor recovery; 10 to 18, well-defined flexion-extension synergies; and >18, synergies + isolated movements. Lesions affecting the following structures were recorded: primary motor cortex, premotor area, supplementary motor area, anterior half of the middle third of corona radiata (secondary motor efferents), posterior half of the middle third of corona radiata (primary motor efferents), genu, anterior and posterior limbs of the internal capsule (PLIC), basal ganglia, and thalamus. χ² Analysis and ANOVA were used to study the significance of stroke location on UL motor recovery.

Results—The effect of involvement of primary, premotor, or supplementary motor areas on motor recovery did not reach statistical significance. Patients with purely cortical stroke were likely to recover UL isolated movement (3 of 4) compared with purely subcortical (1 of 17) or mixed cortical-subcortical stroke location (2 of 20) (P=0.009). Of those with cortical, subcortical, or mixed cortical plus subcortical lesions sparing the PLIC, 5 of 13 recovered isolated UL movement (P=0.01). Only 1 of 28 patients with involvement of the PLIC plus adjacent corona radiata, basal ganglia, or thalamus recovered isolated UL movement (P=0.01). Patients with small lacunar strokes affecting only the PLIC did not have sufficient motor deficits 2 weeks after stroke to meet inclusion criteria.

Conclusions—The probability of recovery of isolated UL movement decreases progressively with lesion location as follows: cortex, corona radiata, and PLIC. This is consistent with our current understanding of redundant cortical motor representation and convergence of corticofugal motor efferents as they pass through the corona radiata to the PLIC. (Stroke. 2001;32:107-112.)

Key Words: hemiplegia • prognosis • rehabilitation • stroke outcome

Transcranial magnetic stimulation (TMS)¹,² and functional MRI (fMRI)³ support the concept of neuroplasticity as one of several mechanisms responsible for motor recovery after stroke. After infarcts involving the primary motor system, the TMS coordinates that produce flexor pollicis brevis movement may be displaced anterior from the primary motor cortex (MI) to the premotor area (PMA).⁴ PET studies have shown similar findings.⁵ More extensive lesions show fMRI activation of ipsilateral PMA and supplementary motor area (SMA), plus activation of contralateral MI and PMA.⁶ Patients with stroke involving the PMA have been shown to have reduced functional outcome when compared with patients in whom the PMA is spared.⁷ These observations imply that attention to the presence or absence of stroke involvement of MI, PMA, SMA, transcallosal fibers in the centrum semiovale, and subcortical internal capsule outflow from these key areas, as seen on standard CT or MRI, might predict motor recovery after stroke.

CT evidence of involvement of the supratentorial corticospinal pathways has been shown to predict the presence or absence of arm weakness after stroke.⁸ In the presence of weakness, it is assumed that upper limb motor recovery after stroke is also influenced by lesion location, specifically by involvement of cortical or subcortical structures related to primary and/or secondary motor systems. In primates, the size and location of lesions within the primary cortical hand area determines whether motor recovery will occur by reacquisition of preinfarct movement strategies or by development of compensatory movement techniques.⁹,¹⁰ In humans, it may be inferred that recovery of isolated or synergistic upper limb movements after stroke may also be influenced by lesion location.
In an inpatient stroke rehabilitation population, we have observed that patients with purely cortical stroke have better motor outcome than patients with purely subcortical stroke. Furthermore, patients with mixed cortical plus subcortical stroke tended to do better than patients with purely subcortical stroke despite the expected larger size of mixed lesions. Although subcortical strokes are normally smaller than cortical strokes, they are more likely to involve both primary and secondary motor pathways. The descending axons from MI, PMA, and SMA must converge as they approach the internal capsule. For this reason, even small subcortical lesions can be devastating.

There is general consensus concerning the course of the corticospinal pathway from the primary motor cortex, through the posterior limb of the internal capsule, to the lower motor neurons. Under normal circumstances, corticospinal control of voluntary hand movements is derived from contralateral cortical areas. This appears to change in pathological states.

Functional MRI and PET have shown that primary motor areas contralateral to the lesion can be activated after injuries to the internal capsule. Uncrossed anterior corticospinal tract fibers may be involved in this process. Transcallosal motor interconnections have also been proposed to modulate this phenomenon, although the interaction between right and left corticospinal tracts appears to be modulated at multiple levels along the neuroaxis. Early in the development of the macaque monkey, corticospinal tract axon collaterals synapse at several subcortical levels before reaching the α-motor neurons. Most of these collateral connections disappear by the early postnatal period, but remaining functionally inactive pathways might be activated under pathological circumstances.

The influence of SMA and PMA corticofugal fibers on lower motor neurons is less well understood than that of MI. Axons from SMA neurons have both direct and indirect connections with the lower motor neurons. The SMA is heavily interconnected with MI, and it appears to be involved in planning and pacing complex motor activities. The SMA also coordinates the performance of bimanual motor tasks. The PMA sends fewer direct fibers to the lower motor neurons but has strong connections with the mesencephalic rubrospinal system and with the pontomesencephalic reticulospinal system, which in turn send fibers to the vestibulospinal system. All these brain stem nuclei project to lower motor neuron groups. The PMA is important for the control of visually guided hand movements and for circumstance-related changes in motor strategies. Both the SMA and PMA are known to have either facilitatory or inhibitory effects on lower motor neurons.

Supplementary motor corticofugal efferents appear to travel through the anterior limb of the internal capsule. The bilateral supplementary motor areas are known to be heavily interconnected through the corpus callosum. The transcallosal supplementary motor system provides for potential cortical control of voluntary movement through the contralateral internal capsule. The corticofugal outflow from PMA is usually described as unilateral and has been shown to run through the genu of the internal capsule.

The neuroanatomic considerations discussed above suggest that the pattern of motor recovery observed after stroke may be dependent on which component of the motor system is more severely involved. In most cases, motor recovery after stroke follows a predictable sequence. Fragmented synergistic motor patterns, sometimes restricted to shoulder shrugging, are the first movements to reappear. Progressively, mass flexion and extension synergies of shoulder, elbow, and wrist become more complete. As the recovery process continues, non–synergy-dependent movements, such as flexion at the shoulder, extension at the elbow, and pronation-supination at the wrist, begin to reappear. Finally, isolated movements of the wrist and fingers may be observed. As a rule, motor recovery follows a proximal-to-distal direction. Motor assessment techniques, such as the Fugl-Meyer scale, have tried to translate this progressive motor recovery sequence into ordinal scores.

In the majority of stroke patients, the upper limb is more severely involved than the lower limb, as most strokes occur in the territory of the middle cerebral artery. From an initial state of flaccid weakness after stroke, some patients regain varying degrees of isolated upper limb movements, some recover only mass flexion-extension synergistic movements, and some do not recover any significant voluntary upper limb movements. From the previous neuroanatomic considerations, it is hypothesized that sparing of specific brain regions must occur to allow for recovery of synergistic or isolated voluntary upper limb movements. It is generally assumed that those recovering isolated upper limb movements have small, incomplete lesions affecting MI or the corticospinal tract. Those who recover only synergistic upper limb movements are assumed to have relatively complete lesions affecting MI or the corticospinal tract but have preservation of SMA and PMA efferents to reticulospinal, rubrospinal, and vestibulospinal nuclei in the brain stem. Patients without significant upper limb motor recovery presumably have lost primary motor, premotor, and supplementary motor control of lower motor neuron groups.

Diaschisis has been implicated in the presence and severity of motor impairment after stroke. It is defined as a decrease in neuronal activation distant from the area of injury. The downregulation of neuronal activity is supposedly due to a decrease in afferent input normally received from the area of infarction. This phenomenon has been best described in the cerebellar hemisphere contralateral to a supratentorial corticospinal tract injury. Resolution of diaschisis is a potential confounding factor when assessing the relation between lesion location and subsequent motor recovery after stroke. It is thought to resolve with time and to be responsive to environmental stimulation and to the action of monoamine agonists.

Neuronal dysfunction due to the ischemic penumbra surrounding an area of infarction magnifies the apparent clinical severity of the stroke. Neuronal recovery in the ischemic penumbra is thought to explain rapid improvement of neurological impairment over the first several days post stroke.

We studied the effect of stroke involvement of MI, PMA, SMA, centrum semiovale, anterior limb of the internal capsule, genu of the internal capsule, posterior limb of the
internal capsule (PLIC), basal ganglia, and thalamus in patients with versus patients without recovery of voluntary synergistic or isolated upper limb movements. To minimize the effects of motor recovery due to reversal of diaschisis or to recovery of neuronal function in the ischemic penumbra, we studied the effects of lesion location on patients with plegic shoulder-arm-hand muscles persisting for an average of 17 days after stroke.

**Subjects and Methods**

Our study population consisted of patients consecutively admitted to the Burke Rehabilitation Hospital over a 2-year period for rehabilitation after stroke. They are part of the Burke Stroke Data Base. Forty-one patients met our inclusion criteria: (1) they had a first, single, unilateral, hemorrhagic, ischemic stroke; (2) they had previously been independent in the community; (3) they had a virtually plegic upper limb at the time of rehabilitation hospital admission, as defined by a Fugl-Meyer upper limb motor score (UM) of ≤9 (maximal deficit, 0; normal, 56) (in the UM Fugl-Meyer motor scale, excluding the points corresponding to deep tendon reflexes and coordination, a score of 9 would correspond to incipient flexion/extension synergistic movements in which the individual components of synergies were only partially executed); (4) they had neuroimaging studies performed ≥48 hours after the stroke, which were available for our review; and (5) there were no other focal abnormalities present on neuroimaging besides the index stroke. The acute inpatient rehabilitation treatment was uniform and was provided by the same rehabilitation team. The patients’ daily therapy schedule consisted of two 45-minute physical therapy sessions, two 45-minute occupational therapy sessions, and one 30-minute speech therapy session. If indicated, additional speech therapy, recreational therapy, and a cognitive stimulation program were added. The nursing staff promoted practice and reinforcement of skills learned during scheduled therapy sessions. Social workers coordinated the discharge planning process. Dieticians assisted with each patient’s specific dietetic needs. Team leadership and medical management was provided by neurologists who specialized in neurological rehabilitation.

Motor assessment was performed with the upper limb subset of the Fugl-Meyer scale, which was prospectively collected for all patients, in a standardized manner, on admission and at discharge. The upper limb motor subset is composed of tests for deep tendon reflexes, synergistic mass movements, gross non–synergy-dependent movements, fine isolated muscle movements, and coordination testing. For this study, we excluded the points corresponding to deep tendon reflexes and coordination. The UM score ranged from 0 (plegic) to 56 (normal).

Our selection criteria required that all patients have no movement or only minor movement of their affected upper limb on admission, as defined by a UM score of ≤9. Their upper limb movements were, at best, characterized by minimal shoulder shrug, possibly with some associated elbow flexion, representing very incipient shoulder-elbow synergistic movement. At discharge, patients were divided into 3 cohorts: (1) patients whose upper limb remained virtually plegic (UM score ≤9); (2) patients with well-defined upper limb mass flexion and extension synergy-dependent movements (UM score 10 to 18); (3) patients with recovery of isolated upper limb movements (UM score ≥19).

The presence of severe sensory deficits was assessed by the limb-placement task. In this test, the patient is asked to touch the affected index finger with the nonaffected index finger while the latter is sequentially placed in all 4 spatial quadrants. The patient’s eyes are occluded during the test. Severe sensory deficit was defined as a reproducible placement error of ≥6 inches.

Neuroimaging studies were reviewed by the authors. Interrater reliability was established with the use of Matsui and Hirano’s Atlas to identify areas of interest. We assessed involvement of cortical motor structures, namely MI, PMA, and SMA. We looked for involvement of the middle third of the corona radiata because it carries the bulk of movement-related fibers. The anterior half of the middle third of the corona radiata appears to carry efferent fibers from secondary motor cortices on their way to the internal capsule or to the corpus callosum. The posterior half of the middle third of the corona radiata carries efferent fibers from the primary motor strip to the posterior limb of the internal capsule. Involvement of the anterior limb, genu, and posterior limb of the internal capsule was also assessed, as was involvement of the basal ganglia and thalamus.

Categoric data were analyzed with the χ² statistic. Interval-scale data were analyzed across patient cohorts by 1-factor ANOVA. Cohort comparisons were considered significantly different if the statistical probability was ≤0.05. Results are presented as mean±SEM whenever a variance is indicated. All statistical analyses were performed with StatView for Windows, version 4.57, Abacus Concepts Inc.

**Results**

The demographic characteristics of our population are shown in Table 1. The mean age is as expected among stroke patients. There were more female than male subjects. The distribution of handedness was close to that of the general population. Both right and left hemispheres were involved with similar frequency. Patients were admitted to the rehabilitation unit an average of 17±2 days after their stroke. Their mean Functional Independence Measure (FIM) score on admission was 43±2, indicating severe disability. The patients’ Mini Mental State Examination (MMSE) score on admission was 16.8±1.7, and their score on the cognition subset of the FIM was 17.9±1.2.

On average, the patients were discharged after 44.7±2 SEM days of inpatient rehabilitation, a mean of 62±3 days after stroke. At the time of inpatient rehabilitation discharge, 30 of the 41 patients had not had any significant upper limb motor recovery and still had a virtually plegic upper limb; 5 patients had recovered well-formed synergistic upper limb movements; and 6 patients had recovered at least some degree of isolated upper limb movements (Table 2).

After assessing stroke involvement of the target neuroanatomic areas previously mentioned, we observed that the posterior limb of the internal capsule was the only structure that was significantly associated with poor recovery of isolated upper limb movements. Only 1 of the 28 patients with PLIC involvement recovered isolated upper limb movement by the time of discharge, whereas 5 of the 13 patients

| TABLE 2. Plegic Upper Limb: Motor Outcome at Hospital Discharge |
|----------------------------------|---------------|--------------|----------|--------|
| No Minor | Synergy | Isolated | Total |
| 30 | 5 | 6 | 41 |
without involvement of the PLIC recovered isolated upper limb movements \( (P=0.01, \chi^2) \). If involvement of the posterior half of the middle third of the corona radiata was added to that of the PLIC, no recovery of isolated upper limb movements was observed in our population \( (P=0.04, \chi^2) \) (Table 3).

It should be stressed that our population was not composed of patients with isolated PLIC involvement caused by small lacunar strokes. These patients are expected to have good motor outcome because the PLIC is only partially affected. All our patients with PLIC involvement \( (n=28) \) had extension into adjacent structures: corona radiata \( (26 \text{ of } 28) \), basal ganglia \( (22 \text{ of } 28) \), or thalamus \( (3 \text{ of } 28) \). Our patients with PLIC involvement have what has been called a “lagoonal” stroke,\(^{11}\) which extends beyond the internal capsule into surrounding structures.

Involvement of the anterior limb of the internal capsule showed a trend toward poor prognosis for upper limb motor recovery, but this observation did not reach statistical significance.

The effect of involvement of primary, premotor, or supplementary cortical motor areas on upper limb motor recovery after stroke did not reach statistical significance, although patients in whom the primary motor strip was the only cortical structure involved tended to do better. Recovery of isolated upper limb movements occurred in all 7 of these patients as opposed to 23 of the 34 patients with both primary and secondary motor cortices affected. This may be a consequence of the larger size of the combined lesions.

To obtain larger study groups for analysis, we collapsed lesion locations into 3 groups: cortical only, subcortical only, and mixed cortical plus subcortical involvement. There were 4 patients with purely cortical stroke, 17 patients with purely subcortical stroke, and 20 patients with mixed cortical plus subcortical stroke. Three of the 4 patients with purely cortical stroke had recovered isolated upper limb movements by the time of their discharge from inpatient rehabilitation. No more than 10% of the patients with purely subcortical or mixed cortical plus subcortical stroke had recovered isolated upper limb movements by the time of their discharge from inpatient rehabilitation \( (P=0.009, \chi^2) \) (Table 4).

Although all patients had very low UM scores on admission \( (<9 \text{ points}) \), these scores were lower for patients who went on to have no significant upper limb motor recovery \( (0.6\pm0.2) \) than for patients who recovered flexion-extension synergistic movements \( (3.8\pm1.7) \) or for patients who recovered isolated upper limb movements \( (3.7\pm1.4) \) \( (P=0.0007, \text{ ANOVA}) \).

We observed that some patients in our population also had a virtually plegic lower limb in addition to a plegic upper limb. A plegic lower limb was defined by the same criteria used to define a plegic upper limb. A Fugl-Meyer lower limb motor score of \( \leq7 \) of 26 possible points defined lower limb plegia. Among the 41 patients in our population, 26 had a plegic lower limb. The remaining 15 patients’ affected lower limb, though weak, was not plegic. The posterior limb of the internal capsule was equally involved in both of these subgroups. When upper limb motor recovery was analyzed, patients with both upper and lower limb plegia tended toward a lower likelihood of isolated upper limb movement recovery when compared with their counterparts in whom only the upper limb was plegic. The same pattern was observed concerning recovery of synergistic upper limb movements (Figure). These differences, however, did not reach statistical significance \( (\chi^2) \).

Age, sex, handedness, side of stroke, cognitive status on admission, admission FIM, and interval after stroke did not significantly influence motor recovery in our study population.

**Discussion**

For patients with plegic or nearly plegic upper limbs, motor recovery was best for those with purely cortical (SMA, PMA, or MI) involvement. Motor recovery declined progressively with involvement of the corona radiata or PLIC. This is consistent with our current understanding of a hierarchical but redundant cortical motor control system. Cortical lesions affecting MI, PMA, or SMA span both the middle cerebral cortex and primary motor area.
and anterior cerebral artery distributions. Involvement of all 3 motor control areas by 1 vascular lesion is rare. PET, fMRI, and TMS studies all indicate that motor recovery from a lesion affecting MI is partially mediated by increased activation of ipsilateral PMA and SMA.

Corticofugal outflow from MI, PMA, and SMA are thought to be through PLIC, genu, and ALIC, respectively. Purely cortical strokes therefore do not totally interrupt cortical input to more primitive rubrospinal, reticulospinal, and vestibulospinal motor control systems.

Of the multiple cortical and subcortical structures studied, only PLIC was found to be independently related to recovery of isolated UL movement. This may imply that although the majority of PMA and SMA corticofugal efferents course through the genu and ALIC, those fibers relevant for UL motor recovery course more posterior through the PLIC in association with the primary motor corticospinal tract. Our observations support the general consensus that recovery of ipsilateral PMA and SMA.

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Fibers from MI and other cortical areas contributing to the corticospinal tract converge in the posterior half of the middle third of the corona radiata before entering the PLIC. We observed that lesions affecting both these structures at the same time led to poorer motor recovery than was seen with either lesion alone. This could represent a “double-crush” phenomenon because the stroke is affecting corticospinal efferent fibers at 2 different levels. The “double-crush” phenomenon is well documented in peripheral nerve dysfunction but not usually considered relevant in central nervous system lesions.

Another possible explanation for the importance of the PLIC and corona radiata in UL motor recovery is that involvement of these structures might interfere with activation of secondary motor control systems. Secondary motor circuits might depend on a “drive” from primary motor collaterals or from afferent sensory input. Both of these facilitatory systems would be interrupted by lesions involving the centrum semiovale or posterior limb of the internal capsule. Both PET and fMRI show evidence of ipsilateral and contralateral cortical activation associated with recovery of isolated finger movement after subcortical stroke. Areas of activation include MI, PMA, SMA, insula, cingulate gyrus, and prefrontal cortex bilaterally. This widespread cortical activation may be “driven” by afferent sensory and/or primary motor collaterals.

We have implied thus far that the poor motor recovery seen in patients with initially plegic upper limbs and PLIC lesions is probably due to interruption of primary and secondary motor corticofugal efferents. However, interruption of thalamicortical somatosensory afferents, also traveling through the PLIC, may adversely affect motor recovery as well. The deleterious effect of sensory deafferentation on the quality of movement in the forelimb of nonhuman primates has been well documented. Both in monkeys and in humans, this effect can be reversed by binding the unaffected limb and forcing the use of the affected limb. Severe somatosensory deficits are also associated with worse functional outcome after stroke. Sensory input may be an important drive for cortical reorganization. Enhanced sensory input by means of robot-assisted movement of the paretic upper limb after stroke has been shown to improve motor recovery.

Thalamic lesions may lead to upper extremity weakness. Involvement of the thalamus has been shown to negatively affect motor recovery when associated with lesions of the posterior limb of internal capsule. The role of sensory deafferentation in this setting has not yet been defined. Because we had only 3 patients with thalamic involvement, our power to show similar relations is limited.

Involvement of the basal ganglia, either in isolation or in association with lesions of the posterior limb of internal capsule, did not significantly influence motor recovery. This is in agreement with previous publications.

In summary, for patients with a virtually plegic upper limb 2 weeks after stroke, recovery of isolated limb movement can be predicted on the basis of lesion location: (a) 75% for those with lesions restricted to the cortex (MI, PMA, or SMA); (b) 38.5% for those with subcortical or mixed cortical plus subcortical lesions not affecting the PLIC; and (c) 3.6% for those with involvement of the PLIC plus adjacent corona radiata, basal ganglia, or thalamus. Patients with small lacunar strokes affecting only the PLIC did not have sufficient motor deficits 2 weeks after stroke to be included in our study population.

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References


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