Compensatory Contribution of the Contralateral Pyramidal Tract after Stroke

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Abstract

Stroke is a leading cause of long-term disability with early accelerated followed by gradual recovery during the first 6 months after the ictus. The most important mechanism concerning early recovery is thought to be brain plasticity provided by anatomical and functional reorganization of the central nervous system after injury. Recent advances in noninvasive, functional brain imaging techniques provided some insight indicating the contribution of ipsilateral uncrossed corticospinal tracts in motor recovery after stroke. Since motor tracts vary considerably among subjects, the ratio of contralateral corticospinal tract fibers and their interhemispheric control versus the amount and function of ipsilateral corticospinal tract fibers may affect the scale of motor recovery after stroke. Further studies are needed to clarify the mechanisms of motor recovery after stroke in humans.

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Brain injury after stroke causes damage to intrinsic neural networks affecting the function of motor, sensory, cognitive and other functional domains. Motor dysfunctions including dysphagia, hemiparesis and gait disturbance are important aspects of activities of daily living and affect the long-term psychosocial welfare. It is well known that some deficits, such as hemiparesis or imbalance, often recover spontaneously, suggesting that inherent plasticity within neural networks compensates for lost motor function.

While many patients achieve independence in their activities of daily living after 6 months, the most significant recovery in motor function happens within the first month regardless of the initial stroke severity. Mild to moderate stroke patients recover within the first month, while moderate to severe stroke patients continue to recover for prolonged periods after stroke [1].

Several mechanisms have been proposed to explain the pattern of recovery after stroke. We believe that the main mechanism implicated in early recovery after
stroke is an inherent blueprint of pre-existing anatomical pathways and functional rearrangement of networks within the central nervous system. This rebuilding process may involve various mechanisms, including (1) redundant pathways that perform similar functions being able to substitute one another if one pathway has been damaged, (2) unmasking of silent pathways, and (3) sprouting of fibers from surviving neurons with formation of new synapses [2–4]. The temporal profile of recovery observed very likely reflects the variant mechanisms involved. Short-term changes are probably related to functional enforcement of existing circuits, such as unmasking of silent synapses [5, 6], whereas long-term changes involve other processes, such as axonal regeneration or synaptic sprouting. When damage to the system is only partial, complete recovery may occur within the system. More extensive damage, however, requires the recruitment of a functionally related system.

**Role and Plasticity of the Pyramidal Tract**

The pyramidal tract, which is mainly involved in motor function, consists of descending nerve fibers that originate in the cerebral cortices (Brodmann’s areas 4, 6 and others) and extend longitudinally through the bulbar pyramid into the spinal cord. Anatomically, 75 and 90% of the corticospinal fibers cross the midline in the lower medulla or upper cervical cord forming 3 separate corticospinal tracts on each side [7]. The largest one is, naturally, the lateral corticospinal tract that crosses in the medullary decussation and extends caudally in the dorsolateral fasciculus to the last sacral segment. The fibers of this tract terminate mainly on the ipsilateral motoneurons of the ventral horn of the spinal cord. The anterior or ventral corticospinal tract consists of fibers that do not cross in the medullary decussation and extend caudally only until the upper thoracic cord. These fibers are known to decussate at various levels of the cervical cord through the anterior white commissure to largely terminate on contralateral motoneurons within the medial portion of the ventral horn. Additionally, a third uncrossed corticospinal tract, which varies individually in size and may be a compact, well-delineated tract, is known to exist [7]. Whereas the function of this third tract has not been elucidated, it may be dormant, and activated only in case of damage to the central motor control system. We speculate some role within early motor recovery after stroke in humans.

It is well established that motor recovery in children goes beyond that seen in adults. In fact, prenatal brain damage, such as congenital hemiplegia, induces extensive reorganization of the corticospinal tract particularly of transient projections to the ipsilateral spinal cord. Studies using transcranial magnetic stimulation (TMS) revealed that topographic rearrangement of representations from the primary motor cortex occurs in both, paretic and nonparetic limbs in patients with congenital hemiplegia [8, 9].
Preserved Ipsilateral Corticospinal Tract Function Is a Plausible Mechanism of Motor Recovery after Stroke

Brain plasticity implies adjustment of neural function over time, which in turn results in behavioral adaptation after brain injury. Behavior-related plasticity can be quantified by repeated computation of the distribution of neural activity following sequential task repetitions. Comparison of patterns of activation as a function of time identifies brain areas in which time-related modification of activity appears. This concept has been applied to functional brain imaging studies examining changes of brain function during the acquisition of motor skills [10]. Similarly, the recovery of brain function after stroke has been studied using noninvasive functional imaging techniques, such as positron emission tomography, functional magnetic resonance imaging (fMRI) and electrophysiological techniques represented by TMS. In the early 1990s, the significance of bilateral cerebral and cerebellar regional activation involving the ipsilateral sensorimotor cortex and motor pathways in motor recovery of stroke patients was discovered [11–13]. Technological improvements in MRI methodology made fMRI the predominating functional brain study since the late 1990s. The principle of fMRI is based on blood oxygenation levels in comparable brain regions between rest and activated states. When neurons become active, local blood flow to those brain regions increases, and oxygenated blood displaces deoxygenated blood around 2 s later. This rises to a peak over 4–6 s before falling back to the original level (and typically undershooting slightly). Deoxygenated hemoglobin is paramagnetic as opposed to oxygenated hemoglobin being resistant to magnetism. This difference leads to an improved MR signal that can be mapped to reveal which neurons are active at a time. Using blood-oxygenation-level-dependent technology, it could be shown that the contralateral primary sensorimotor cortex is activated during passive movement of the paretic limb in patients with hemiparetic strokes [14]. The results indicated that in patients recovering from hemiparesis contralateral motor pathways became involved in the reorganization of motor function possibly involving the contralateral brain regions via uncrossed corticospinal tracts or other indirect uncrossed pathways. In contrast, stroke patients with infarcts not involving the primary motor cortex exhibit a linear relationship between recovery scores and task-related brain activation in many parts of the associated motor system [10]. It can be speculated that differences among patients are likely the result of variable anatomical damage and cognitive parameters such as motivation, concentration and attention. Moreover, TMS studies revealed that motor evoked potential amplitude correlates with the extent of hand motor recovery after subcortical stroke when stimulating the affected side of the cerebral cortex [15, 16]. In summary, motor recovery is best when motor cortices remain structurally preserved, functionally connected, and can magnify information processing. While there is no doubt about the contribution of cerebral reorganization to functional recovery after stroke, the processes and factors affecting it remain elusive. A detailed sequential analysis of stroke patients re-
covering from motor deficits with highly sophisticated functional imaging techniques may help to reconcile therapeutic strategies to enhance motor recovery in the future.

**Role of the Ipsilateral Corticospinal Tract in Patients with Motor Recovery after Stroke**

Recently, several patients with a prior recovered hemiparesis after stroke were reported to experience worsening of their motor function after a new contralateral stroke recurrence. The important unifier is the lesion site in all these cases [17–20]. These cases reveal that the ipsilateral, uncrossed corticospinal tract may have helped to com-

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**Table 1. Clinical features of the patients who showed hemiparesis ipsilateral to the lesion side caused by the second stroke attack**

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>Age, years</th>
<th>Sex</th>
<th>Symptoms of 1st SA</th>
<th>Lesion site of 1st SA</th>
<th>Type of 1st SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim [17], 1999</td>
<td>64</td>
<td>male</td>
<td>Rt hemiparesis + sensory deficit</td>
<td>Lt IC + basal ganglia</td>
<td>hemorrhage</td>
</tr>
<tr>
<td></td>
<td>68</td>
<td>male</td>
<td>Rt hemiparesis + sensory deficit</td>
<td>Lt IC + thalamus</td>
<td>infarction</td>
</tr>
<tr>
<td></td>
<td>53</td>
<td>female</td>
<td>Rt hemiparesis + sensory deficit</td>
<td>Lt IC + thalamus</td>
<td>infarction</td>
</tr>
<tr>
<td>Ago et al. [18], 2003</td>
<td>59</td>
<td>male</td>
<td>Lt hemiparesis</td>
<td>Rt IC + basal ganglia</td>
<td>hemorrhage</td>
</tr>
<tr>
<td>Song et al. [19], 2005</td>
<td>62</td>
<td>female</td>
<td>Lt hemiparesis</td>
<td>Rt IC + thalamus</td>
<td>hemorrhage</td>
</tr>
<tr>
<td></td>
<td>41</td>
<td>male</td>
<td>Lt hemiparesis</td>
<td>Rt CR</td>
<td>infarction</td>
</tr>
<tr>
<td>Yamamoto et al. [20], 2007</td>
<td>74</td>
<td>male</td>
<td>Rt hemiparesis + aphasia</td>
<td>Rt CR</td>
<td>infarction</td>
</tr>
<tr>
<td></td>
<td>76</td>
<td>male</td>
<td>Rt hemiparesis + aphasia</td>
<td>Lt CR + T-P lobes</td>
<td>infarction</td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>male</td>
<td>Rt hemiparesis + dysarthria</td>
<td>Lt CR + T-P lobes</td>
<td>infarction</td>
</tr>
<tr>
<td>Our case, 2013</td>
<td>83</td>
<td>female</td>
<td>Lt hemiparesis</td>
<td>Rt CR</td>
<td>infarction</td>
</tr>
</tbody>
</table>

SA = Stroke attack; Rt = right; Lt = left; mRS = modified Rankin Scale score; IC = internal capsule; CR = corona radiata; T-P = temporoparietal; O = occipital; F-P = frontoparietal.
Compensatory Contribution of the Contralateral Pyramidal Tract after Stroke

In what follows, we will present the features of this patient in more detail. An 83-year-old right-handed female with hypertension was admitted to our institute (National Cerebral and Cardiovascular Center) because of suddenly developed left hemiparesis, dysarthria and sensory disturbance; 1.5-tesla MRI revealed an acute small infarcted lesion in the left corona radiata on diffusion-weighted images (fig. 1a). Previously, the patient had experienced left hemiparesis caused by right corona radiata infarction as shown on a brain computed tomography scan (fig 1b). The previous left hemiparesis fully recovered within several months after the first stroke, and no residual motor weakness remained. Her recurrent left hemiparesis recovered once again fairly well (modified Rankin Scale score: 2) after the second stroke. We

<table>
<thead>
<tr>
<th>mRS score after 1st SA</th>
<th>Duration between two SAs</th>
<th>Symptoms of 2nd SA</th>
<th>Lesion site of 2nd SA</th>
<th>Type of 2nd SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>3 months</td>
<td>exacerbation of Rt hemiparesis</td>
<td>Rt thalamus + O lobe</td>
<td>infarction</td>
</tr>
<tr>
<td>1</td>
<td>7 years</td>
<td>exacerbation of Rt hemiparesis</td>
<td>Rt F-P lobes</td>
<td>hemorrhage</td>
</tr>
<tr>
<td>1</td>
<td>1 year</td>
<td>exacerbation of Lt hemiparesis</td>
<td>Rt pons basis</td>
<td>infarction</td>
</tr>
<tr>
<td>2</td>
<td>5 years</td>
<td>exacerbation of Lt hemiparesis</td>
<td>Lt CR</td>
<td>infarction</td>
</tr>
<tr>
<td>2</td>
<td>1 month</td>
<td>exacerbation of Lt hemiparesis</td>
<td>Lt CR</td>
<td>infarction</td>
</tr>
<tr>
<td>0</td>
<td>1 month</td>
<td>recurrence of Lt hemiparesis</td>
<td>Lt CR</td>
<td>infarction</td>
</tr>
<tr>
<td>2</td>
<td>11 years</td>
<td>exacerbation of Rt hemiparesis</td>
<td>Rt thalamus</td>
<td>infarction</td>
</tr>
<tr>
<td>1</td>
<td>11 years</td>
<td>exacerbation of Rt hemiparesis</td>
<td>Rt CR</td>
<td>infarction</td>
</tr>
<tr>
<td>1</td>
<td>4 years</td>
<td>exacerbation of Rt hemiparesis</td>
<td>Rt CR + basal ganglia</td>
<td>infarction</td>
</tr>
<tr>
<td>0</td>
<td>3 years</td>
<td>recurrence of Lt hemiparesis</td>
<td>Lt CR</td>
<td>infarction</td>
</tr>
</tbody>
</table>

pensate motor recovery after the earlier stroke. Table 1 shows the previous case reports including a patient that we recently investigated.
Fig. 1. a, b Our patient’s neuroimages. a Diffusion-weighted image reveals the recent infarct lesion in the left corona radiata (arrow). b Brain computed tomography scan reveals the past infarct lesion in the right anterior corona radiata (arrow). c A plausible mechanism of motor recovery in our patient. The right pyramidal tract had been damaged in the corona radiata at the initial infarction and left hemiparesis occurred (A). However, her motor deficit was fully recovered by the compensatory role of the left, contralesional corticospinal tract (B). Recently, a second infarction damaged the left corticospinal tract in the left corona radiata, resulting in left hemiparesis (C). Rt = Right; MO = medulla oblongata; CST = corticospinal tract.
suspect that the left hemiparesis caused by the first stroke at the right corona radiata recovered completely due to the compensation with the uncrossed left-sided corticospinal tract. During the second stroke at the left corona radiata, the compensating uncrossed left-sided corticospinal tract was damaged, and hence left hemiparesis again manifested. Interestingly, the patient did not show right hemiparesis during the second stroke in spite of damage to the left corona radiata. Presumably, the second stroke affected only the left-sided uncrossed corticospinal tract and did not involve crossing the corticospinal tract controlling right motor function (fig. 1c).

Several possible explanations have been proposed in terms of the relationship of the ipsilateral corticospinal tract with motor recovery following stroke. (1) The ratio of uncrossed corticospinal fibers in the whole pyramidal tract seems to vary between 10 and 25%, but there is considerable variability of the ratio [7]. A higher ratio may correspond to a superior recovery of hemiparesis after stroke. Reports of ipsilesional hemiparesis after cerebral injury in some patients imply the possibility of primarily dominant ipsilateral corticospinal fiber architecture [21, 22]. (2) The lesion size and topography of brain injury are crucial for motor recovery. At least 60% of neural fibers of the pyramidal tract originate in the primary motor cortex, premotor frontal and supplementary motor areas. Most of the corticospinal fibers from the primary motor cortex cross at the decussation, while corticospinal fibers from premotor, frontal and supplementary motor cortices connect with the ipsilateral primary motor cortex, contralateral homologous areas, and to various levels of the spinal cord via both sides of the corticospinal tract [23]. Furthermore, premotor frontal and supplementary motor areas promote reticulospinal tract function via rich projection from those cortical areas to brainstem reticular formation [24]. Fibers of the reticulospinal tract descend to the spine and send axonal branches to spinal gray matter to control proportional movements of proximal limb muscles. Motor deficit caused by the localized lesion at the primary motor cortex is considered to show good recovery in adults as well as children. (3) The activity of motor cortices can be modulated via transhemispheric connection to the contralateral motor cortices [25]. Low-frequency repetitive TMS applied to the motor cortex inhibits motor cortical excitability in the homonymous motor representation of the opposite hemisphere. Therefore, the presence of a balance of reciprocal inhibitory projections between both hemispheres has been proposed. Recent studies have suggested that this balance is disturbed during voluntary movement of the paretic hand in patients with cortical infarcts. Specifically, more severely paretic patients demonstrate greater interhemispheric inhibition between the primary motor cortices than those less affected [26]. Therefore, it is conceivable that decreasing the inhibiting effect of the ipsilateral, intact, motor cortex may enhance motor recovery of the paretic hand. Recent case studies have revealed that inhibitory regional TMS of the unaffected hemisphere is effective even in chronic stroke patients with severe motor deficits [27]. Similarly, regional TMS of the contralesional primary motor cortex can improve motor function in patients with subcortical infarction, presumably by balancing neural activity in both hemispheres documented by fMRI [28]. The durability of these effects...
and enhanced clinical outcomes remain to be shown. Brain activation patterns observed with constraint-induced movement therapy (which forces the use of the paretic limb by movement restriction of the intact extremities) also support the concept of hemispheric neural activity balance [29]. Alternatively, the concurrence of compensatory uncrossed corticospinal tracts and interhemispheric inhibition may limit the potential for recovering motor function after stroke.

Using TMS and fMRI (simple finger tapping) techniques, two patterns of corticospinal reorganization have been proposed in congenital hemiparesis [30]. The premotor pattern observed in patients with only minor lesions and mild hand paresis shows activation of the premotor areas in the affected hemisphere. The primary pattern observed in the more severely affected patients shows activation of the primary sensorimotor region in the contralateral hemisphere. While the premotor pattern may forecast beneficial reorganization, the primary pattern may reflect detrimental adaptations, such as disinhibition of ipsilateral pathways and interhemispheric inhibitory connections. Clinical observation suggests that both patterns occur simultaneously supporting a potential contradiction of anatomical and functional preconditions for motor recovery. We suggest that the clinical observations along with the activation patterns observed in recent fMRI studies limit a role for ipsilateral corticospinal tract reorganization in motor recovery after stroke. The degree of motor recovery depends foremost on the extent of the damage, while early recovery is destined by the individual makeup of uncrossed versus crossed projections.

Conclusion

The role of the ipsilateral, uncrossed pyramidal tract in motor recovery after stroke remains elusive. Interaction of this tract with environmental factors, drugs and genes is still unknown. From the clinical point of view, we suspect that the ipsilateral, uncrossed corticospinal tract may be a compensatory asset in motor recovery of hemiparesis in some stroke patients. Further research is needed to substantiate this proposed mechanism to determine the impact of rehabilitation approaches for motor deficits.

References

Compensatory Contribution of the Contralateral Pyramidal Tract after Stroke

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