Recovery of the paretic upper limb early after stroke

van Kordelaar, J.

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Summary

Recovery of the paretic upper limb early after stroke: restitution or substitution of motor control?

SUMMARY

Eighty percent of all stroke survivors have impaired arm function immediately after stroke. Depending on the initial severity of the upper limb paresis, 30 to 66 % of these patients never regain any upper limb function, whereas only 5 to 20 % fully recovers. Most of the improvements in upper limb function occur typically in the first 10 weeks after stroke. However, the mechanisms underlying motor recovery of the paretic upper limb after stroke are poorly understood. As a consequence, it is largely unclear how therapeutic strategies in neurorehabilitation should be improved to enhance motor recovery early after stroke. To understand the mechanisms underlying motor recovery after stroke it is important to investigate how quality of motor control changes as a function of time poststroke. Previous studies showed that, during functional tasks, patients often show qualitatively different movement patterns compared with healthy individuals. These different coordination patterns are assumed to reflect adaptive motor learning strategies whereby patients learn to compensate for existing motor deficits. However it is unclear how these adaptation strategies emerge and therefore it is unclear *what* patients actually learn when they regain upper limb function after stroke.

The current thesis is part of the translational research programme EXplaining PLastiICITy after stroke (acronym: EXPLICIT-stroke). EXPLICIT-stroke is funded by ZonMw (grant no: 89000001) and is registered with the Netherlands National Trial Register (trial no: NTR1424). The aim of the current thesis is to investigate how adaptive strategies to compensate for existing motor impairments (i.e. substitution) complement true motor recovery by which movement patterns change towards those observed prior to injury (i.e. restitution). The quality of motor control during functional reach-to-grasp task was measured using intensively repeated three-dimensional (3D) kinematic measurements in the first 5 weeks with follow up measurements at week 8, 12 and 26 after stroke.

Chapter 2 shows that 3D kinematic data could accurately and reliably be measured within multiple measurement environments including a motion laboratory, a treatment room and a home situation. By using this mobile 3D kinematic motion tracking device, the presented case report shows that changes in quality of motor

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control as a function of time poststroke could be detected. Early after stroke task performance was mainly driven by adaptive motor control, that is, the elbow was 'locked' in a flexed position within the flexion synergy, whereas the reaching movement was mainly controlled by a displacement of the trunk in a forward direction. Over time poststroke the elbow was progressively released during the reaching task, whereas forward trunk movements simultaneously diminished. This change in quality of motor control was accompanied by improvements in speed and timing of grasping movements of the fingers with respect to displacement of the hand.

In chapter 3 the interaction between compensatory trunk movements and couplings between shoulder and elbow movements, i.e. synergies, is investigated in a group of 46 patients at on average 26 weeks after stroke. Principal component analysis (PCA) was applied to identify dominant couplings between joint rotations during reach-to-grasp. The results of this study show that horizontal shoulder abduction was mainly coupled to elbow flexion. Since these joint rotations are the most dominant aspects of the basic flexion synergy, this finding suggests that the basic flexion synergy was the most dominant component that differentiated between patients in this study. This study also suggests that lateral trunk rotation is coupled to upward shoulder rotation in the second principal component, whereas forward and axial trunk rotation is coupled to elbow flexion in the third principal component. Importantly, the identified movement components can predict whether patients are able to fully dissociate from the basic flexion synergy as established with the upper limb section of the Fugl-Meyer Motor Assessment (FMA). This finding supports the hypothesis that basic limb synergies, as clinically determined with FMA, directly determine the degrees of freedom that patients are able to control for. Hence, these synergies may directly determine the adaptive coordination strategies needed to accomplish meaningful tasks such as reaching and grasping after stroke.

Chapter 4 applies PCA to investigate how the control over de various degrees of freedom in the paretic upper limb changes as a function of time in 31 patients with stroke. This study shows that the presence of the basic flexion synergy, reflected by a coupling between horizontal shoulder abduction and elbow flexion, during a reach-to-grasp movement decreased mainly within the first 5 weeks after stroke.

This finding suggests that restitution of motor control by which patients regain control over the degrees of freedom of the paretic upper limb is mainly determined within the first 5 weeks after stroke. These early improvements in the control over the degrees of freedom paralleled improvements in FMA scores, suggesting that the change in quality of motor control is critically dependent on the change in the ability to dissociate from the basic limb synergies. At 26 weeks, however, PCA shows that dissociations from the basic flexion synergy were still not complete in 12 out of 31 patients as compared with healthy subjects. This finding suggests that motor strategies remain often adaptive, even in patients with an initial favourable prognosis for recovery of upper limb function after stroke.

Based on a group of 44 patients, chapter 5 shows that in parallel to the early improvements in the control over the degrees of freedom, smoothness of hand transport and grasp movements during reach-to-grasp improves strongly and significantly during the first 8 weeks after stroke. Smoothness is regarded as a feature of skilled and well controlled movements. Therefore, the strong improvement of smoothness in the first 8 weeks after stroke suggests that movements are controlled more efficiently as patients regain control over the degrees of freedom in the paretic upper limb. The lack of smoothness early after stroke suggests that patients make more movement errors which have to be corrected using feedback mechanisms based on afferent sensory information. As a function of time poststroke the ability to plan movements correctly in advance probably may reduce the reliance on feedback mechanisms which may ultimately lead to the observed improvements in smoothness.

However, the neuronal substrate underlying smoothness of motor control after stroke is unclear. Therefore, chapter 6 describes in a group of 17 patients how smoothness of grasping movements, established with 3D kinematics, was related to cortical activation patterns, as established with fMRI during a finger flexion-extension paradigm. It appeared that activation levels in secondary sensorimotor areas and the cerebellum were significantly and positively related to smoothness of the paretic upper limb after stroke. This finding is interpreted as an indication that secondary sensorimotor areas are not able to take over lost neuronal function when the primary motor area, the cortico-spinal tract or both are damaged. Moreover, it suggests that these areas are activated to assist in feedback motor control when feedforward control by the primary motor system is disrupted.

The time-dependent improvement in the ability to perform smooth and dissociated upper limb movements, as presented in the current thesis, may be the result of spontaneous neurological recovery, which is assumed to occur within the first 10 weeks after stroke. Although spontaneous neurological recovery is still poorly understood, it is often assumed that salvation of penumbral tissue and alleviation of diaschisis play an important role during the first days to weeks after stroke. In addition, it is assumed that the brain is able to reorganize its structure as well as its function based on experience and motor learning. However, the meaning of learning-dependent mechanisms in the brain for motor recovery after stroke is still unclear. In fact, the relation between activation levels in secondary sensorimotor areas in the brain and lack of smoothness, as presented in chapter 6, suggests that additionally recruited sensorimotor areas reflect compensatory movements strategies based on feedback mechanisms, rather than true motor recovery.

The most important clinical implication of the current thesis is that the aim of therapeutic interventions within neurorehabilitation should depend on time poststroke. Until week 8 after stroke, it is recommended that interventions should be aimed at reducing motor impairments and improving quality of motor control, whereas after the first 8 weeks, treatment strategies should be aimed at optimizing coordination strategies within task-specific contexts, while allowing compensation movements.

However, favourable effects of early intensive neurorehabilitation to enhance motor recovery after stroke remain to be proven. The time-dependent improvements in quality of motor control during the first 8 weeks after stroke suggest that recovery of quality of motor control is mainly defined by spontaneous neurological recovery. There are currently only a limited number of RCTs that investigated whether therapies aimed at restoring motor functions and improving quality of motor control can enhance motor recovery beyond mechanisms of spontaneous neurological recovery. Previous research showed that the ability to extend the wrist and fingers strongly determines the functional outcome of the paretic upper limb after stroke. In patients who can show some finger extension in the first week after stroke, the translational research programme EXPLICIT-stroke investigates the effects of modified constraint-induced movement therapy (mCIMT) during the first 5 weeks on motor recovery of the paretic upper limb after stroke. In patients who cannot extend the fingers in the first week after stroke, it is investigated whether EMG-triggered neuromuscular stimulation (EMG-NMS) of the wrist and finger extensors during the first 5 weeks after stroke has a favourable effect on motor recovery of the paretic upper limb after stroke.

Finally, neurorehabilitation should develop novel and innovative methods to enhance quality of motor control early after stroke. However, it is still unclear whether, for instance, transcranial direct current stimulation or pharmacological interventions combined with intensive mCIMT or robot-assisted treatment may lead to enhanced true neurological recovery. Therefore, translational research programmes such as EXPLICIT-stroke are essential to investigate the effects of such innovative strategies and, in addition, to understand the mechanisms that are responsible for these effects. The most important challenge that neurorehabilitation is currently facing is to enhance true neurological recovery, particularly with respect to the cortico-spinal tract, in order to improve quality of motor control beyond mechanisms of spontaneous neurological recovery.