CHAPTER 8

General discussion
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Main findings

The present thesis focused on two conceptually conflicting approaches for upper limb rehabilitation after stroke, namely unilateral and bilateral training. The main goals were to assess the relative effectiveness of unilateral and bilateral upper limb training at a group level and as a function of patient characteristics, and to determine what changes in underlying mechanisms are associated with functional improvement after stroke. The thesis was built around the ULTRA-stroke (acronym for Upper Limb Training After stroke) program, a single blind randomized clinical trial (RCT) that was run at the rehabilitation center Reade in Amsterdam from May 2009 until December 2012. In this RCT the merits of a modified version of Constraint-Induced Movement Therapy (mCIMT) were compared with those of modified Bilateral Arm Training with Rhythmic Auditory Cueing (mBATRAc) and an equally intensive (i.e., dose-matched) conventional treatment (DMCT) in patients recruited between one to six months after stroke.

First, an overview and qualitative evaluation of the clinical applicability of bilateral upper limb training devices was presented in Chapter 2. The most important finding was that the existing evidence for the clinical efficacy of the discussed bilateral upper limb training devices for rehabilitation after stroke is rather limited and not yet of such caliber that the devices in question and the concepts on which they are based are firmly established. A second systematic review, including a meta-analysis on the data of nine RCTs comparing the effects of unilateral and bilateral upperlimb training after stroke, was presented in Chapter 3. There were no significant differences between the two approaches except one. For patients with a mild upper limb paresis starting the intervention in the chronic phase after stroke a marginally positive effect in favor of unilateral training was found. However, the obtained effects were small and below the conventional threshold of a clinically meaningful change. The results of these reviews provided insufficient insights into the differential effects of unilateral and bilateral training, how they influence the mechanisms of upper limb recovery, and which post-stroke conditions are indicative of either approach.

The findings of both reviews underscored the need of the ULTRA-stroke translational research program, which is described in detail in Chapter 4. The program entailed an RCT recruiting patients with an upper limb paresis one to six
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months after a first-ever stroke in one of the hemispheres; a group of patients for which no previous unilateral versus bilateral comparison studies were found in the systematic review. In this RCT the relative effectiveness of equally intensive mCiMT, mBATRAC, and DMCT were assessed, and the associated functional and neurophysiological changes induced by these interventions were investigated. The clinical results of the ULTRA-stroke trial were presented in Chapter 5. All groups demonstrated significant improvement on the Action Research Arm Test (ARAT; the primary outcome measure) from baseline to post-intervention, which sustained from post-intervention to follow-up. Clinically, there were no significant differences between groups in change scores on the primary and secondary outcome measures reflecting (I) body functions and structure, (II) activity, and (III) participation. These results indicate that mQMT and mBATRAC were not superior to DMCT or each other in improving upper limb function, thereby confirming the results of our meta-analysis.

For a better understanding of the associated mechanisms of upper limb function improvement after unilateral and bilateral training, the effects on bimanual coupling strength were also investigated as part of the ULTRA-stroke program. In Chapter 6 a series of rhythmic interlimb coordination tasks were described, which were used to discern intended and unintended coupling effects between the hands. There were no significant between-group differences in change scores from baseline to post-intervention and from post-intervention to follow-up regarding intended and unintended interlimb coupling. Unilateral and bilateral training (and DMCT) led to similar changes in bimanual coupling. From the data of the same set of tasks, significant differences were found at post-intervention for changes in parameters reflecting control over the paretic hand in favor of the group receiving mBATRAC. At first sight these improvements seem to indicate a beneficial influence of bimanual neural coupling. However, a more likely explanation may be found in the fact that mBATRAC involved rhythmic hand movements that were very similar to those required in the various kinematic tests, suggesting that the improvements were merely due to practicing rhythmic movements with the paretic hand rather than a significant improvement in bimanual neural coupling. Moreover, these significant improvements in control over the paretic hand did not translate into better clinical outcomes in favor of bilateral training as presented in Chapter 5.

The focus of research was then shifted from the discrepancy between unilateral and bilateral training to the relation between observed and perceived upper limb recovery. In particular, it was investigated in Chapter 7 whether objectively meaningful improvements in upper limb motor capacity, following the ARAT, were matched by subjectively meaningful improvements in upper limb performance, following the Motor Activity Log quality of movement (MAL-QOM) subscale and
the Stroke Impact Scale hand domain (SIS-Hand), after a period including six weeks of upper limb therapy and a follow-up period. Remarkably, there was not always an obvious, significant association between objectively and subjectively measured improvements. This indicates that capacity and self-perception measures represent different constructs, and suggests that conclusions following the results of RCTs strongly depend on the selection of the (primary) outcome measures. The selection of a wide range of outcome measures, including objective and subjective measures, is therefore recommended for future RCTs. Furthermore, none of the characteristics directly related to the upper limb could be used as determinant for the (non)matchers. Conversely, the concord and disagreement between meaningful changes could be predicted based on the knowledge of the patient’s level of education and mood at baseline. Patients with a lower level of education and a higher mood score showed significantly more often a match between the perceived improvement according to SIS-Hand and the capacity improvement measured with the ARAT when compared to those with a higher education and lower mood score at baseline. The relevance of the predictive values of these two determinants remains speculative and requires further investigation.

The remainder of this concluding Chapter provides a critical reflection on the research as described in the present thesis, as well as a discussion of clinical implications and future considerations.

Communalities of unilateral and bilateral upper limb training

Based on the results reported in the present thesis, it appears that the selection of intervention type is less important than the active involvement of the paretic upper limb in therapy. One common denominator of the three interventions in the ULTRA-stroke trial was the active training of the paretic upper limb and the instruction to engage the paretic upper limb in daily activities (be it unilaterally as in mCMT or bilaterally as in mBATRAC). Although active exercise of the paretic upper limb is unambiguously coerced in (m)CMT (as a result of the constraint placed on the non-paretic upper limb; cf. forced-use),11,29 active exercise of the paretic upper limb is a key-factor in mBATRAC as well. In addition, the control treatment in the ULTRA-stroke trial also entailed active exercise of the paretic upper limb. In all likelihood, it was the mere use of the paretic upper limb that resulted in beneficial effects in all intervention groups, although any additional effects of spontaneous mechanisms of recovery, such as reperfusion of penumbral tissue and alleviation of diaschisis, cannot be ruled out.54,189

Another communality of the interventions in the ULTRA-stroke trial was the intensity of the treatments. Similar to the active involvement of the paretic upper
limb in therapy, treatment intensity may be a far more important determinant of treatment success than specific features that distinguish the training approaches. The results of the ULTRA-stroke trial find support in several other studies presenting comparable functional improvements after interventions of equal intensity, some comparing unilateral and bilateral training, and others comparing either unilateral or bilateral training with conventional treatment. Alternatively, one of the criticisms of the largest CMT-trial so far (the EXCITE trial; acronym for Extremity Constraint Induced Therapy Evaluation trial) is that the interventions were not dose-matched, with patients in the CMT group receiving a higher-intensity training. This raises the question whether the high-intensity or other key features of CMT were the driving force that led to the differences in outcomes in favor of CMT in that study. Without consistent findings from large scale RCTs and a better understanding of the mechanisms of recovery, the optimal intensity of training will remain a topic of debate. Meanwhile, the individual patient who desires a tailored intervention program, faces additional factors that influence the provided treatment intensity, such as his or her individual characteristics, other disorders as a result from the stroke, and the rules and regulations of the healthcare system.

**Distal control**

Stinear and colleagues developed an algorithm for predicting the potential for recovery of upper limb function after stroke. According to this algorithm, patients who retained voluntary finger extension (reflecting a high degree of CST integrity) should receive unilateral training (targeting the ipsilesional hemisphere) and patients with little or no distal movement (reflecting poor or no CST integrity) would benefit more from bilateral training. The meta-analysis presented in Chapter 3 provides only limited support for these suggestions. In the ULTRA-stroke trial the same inclusion criteria related to distal control were applied as in the EXCITE-trial, i.e., 10° of active wrist extension and 10° of active extension of at least two fingers and the thumb of the paretic upper limb. After the pretests, the patients were stratified into lower- and higher-functioning subgroups. Consequently, besides the group analyses, additional analyses could be performed on these subgroups (Chapter 5). These analyses revealed no indications that unilateral training had a larger positive impact on upper limb function in the higher-functioning group and that bilateral training had a larger positive impact on upper limb function in the lower-functioning group. However, these subgroup analyses have to be treated with considerable caution given the small sample sizes.

Furthermore, in the ULTRA-stroke trial the training of distal extension in the two experimental interventions was emphasized. In this regard, mBATRAC deviated...
from the original, proximally oriented BATRAC. Given the alleged importance of an early return of distal control\textsuperscript{35-38} and based on a meta-analysis on upper limb robotics,\textsuperscript{61} distally oriented training was expected to be more effective than a proximally oriented approach in terms of regaining upper limb capacity. Moreover, there is very limited evidence available for interventions to improve hand function,\textsuperscript{5} and there were no previous trials in which wrist and finger extensors were targeted specifically by unilateral or bilateral training. However, this emphasis on distal training did not lead to a significant difference in upper limb function improvement in favor of the experimental interventions compared to the control treatment. Possibly, differences between intervention outcomes may be detected when distal extension training is started earlier post-stroke, when homeostatic neuroplasticity is most apparent\textsuperscript{276,277} and assumed to support motor learning and neural repair.\textsuperscript{35-38,108} Alternatively, the potential for recovery of distal control (and upper limb function) may be determined at the moment of stroke onset.\textsuperscript{36,39} This would render an attempt to positively influence the potential of functional hand recovery, for example through distal training, unattainable, and may be the reason for the relative absence of interventions showing a consistent pattern of improvement in hand function.\textsuperscript{5}

**Interhemispheric interactions**

An additional factor that may affect upper limb training after stroke (although not directly investigated in the present thesis) is interhemispheric inhibition. After a stroke, the balance of excitatory and inhibitory interactions between both hemispheres is disrupted, with the unaffected hemisphere having a larger inhibitory drive over the affected hemisphere than vice versa.\textsuperscript{278,279} Increasing the excitability of the affected hemisphere, in order to enhance functional recovery, may be achieved through electro-(magnetic) stimulation.\textsuperscript{280-287} However, both (m)CIT and bilateral training have also been proposed to increase excitability in the lesioned hemisphere and thus rebalance the interhemispheric inhibition. With (m)CIT, the reduced somatosensory input from the constrained non-paretic upper limb is presumed to lead to a decrease in excitability of the non-lesioned hemisphere followed by disinhibition of the lesioned hemisphere.\textsuperscript{122,193,194,288} On the other hand, bilateral training, in particular when involving mirror-symmetric movements, allegedly modulates the inhibitory processes through bilaterally shared movement commands (through which the two upper limbs are coupled and controlled as a single unit\textsuperscript{16,289}) and movement-elicited (re)afference.\textsuperscript{16,22,78,290} Whether these proposed mechanisms were in operation in patients in the ULTRA-stroke trial cannot be derived from the results presented in the present thesis. However, intended and unintended bimanual coupling were investigated and the results showed that the degree of coupling between the hands was not significantly higher
after bilateral than after unilateral training and control treatment (Chapter 6). This implies that bilateral and unilateral training may invoke similar changes in bilateral coupling. However, how these changes in coupling are effectuated by training, and relate to the rebalancing of interhemispheric inhibition, is unclear and remains to be investigated.

**Methodological considerations**

The limitations of each of the studies presented in this thesis have been described in the individual chapters. However, there are some general methodological concerns that deserve further discussion. A primary concern is related to the small numbers of patients. In the systematic review and meta-analysis of unilateral and bilateral upper limb training comparison studies only a small number of studies were included, due to the strict selection criteria used (e.g., RCTs only), the relatively short history of bilateral training, and probably as a result of publication bias. This prevented a thorough sensitivity analysis to investigate characteristics that may influence the relative effect of unilateral and bilateral upper limb training, except for the severity of the upper limb paresis and the time of intervention after stroke. Moreover, the data in the meta-analysis were obtained predominantly from patients with chronic stroke suffering from a mild upper limb paresis. Only a few patients with severe upper limb paresis were included and no patients who started the intervention between one to six months after stroke. The lack of data from the latter group in the meta-analysis highlighted the need of the ULTRA-stroke trial.

The sample size in the ULTRA-stroke trial may appear small but the recruited number of patients was based on a power analysis performed before the start of the trial, which indicated that 15 patients per treatment group were required. Expecting a drop-out of less than 25%, 20 patients per group were recruited. These were all patients with an initial favorable prognosis for upper limb outcome. Hence, the between-subject variances were low (due to existing homogeneity of the sample), which reduced the number of required patient numbers, and made the group sizes sufficiently large for the overall analyses. Furthermore, based on the obtained differences in the post-intervention ARAT scores, thousands of participants would be required to achieve a significant difference between groups. One should have considerable reservations about recruiting such a large sample, given the associated ethical and practical issues, while the relevance to stroke rehabilitation is expected to be minimal.

The second general issue concerns outcome measures and clinical relevance. Outcome measure selection is a process of deliberate consideration. There is no single measure that evaluates all aspects related to upper limb paresis after stroke.
Therefore, a number of outcome measures were selected in the ULTRA-stroke trial in an attempt to cover all three levels of the WHO-ICE, using the ARAT as primary outcome measure. The ARAT is a widely used capacity measure of upper limb function with excellent dimension properties\textsuperscript{159,208} and high concurrent validity with the WMFT.\textsuperscript{155} However, for the interpretation of changes over time, a statistically significant difference on the ARAT does not necessarily mean that the changes have clinical relevance or are meaningful to the patient. To cope with this issue, the minimal clinically important difference (MCID) was introduced. The MCID is often set at 10% of the total range of a measure's scale. However, most capacity measures do not have equal distances between each of the scale’s elements. Alternatively, MCIDs can be estimated with distribution- and anchor-based methods. The disadvantages of a distribution-based method are that the MCID varies between samples and that it has no clinical justification. The anchor-based method, on the other hand, varies with the anchor. The anchor is usually a subjective response to a question related to the patient’s well-being, for example whether or how much improvement is perceived. Hence, the anchor itself is a self-perception measure and therefore prone to changes in a patient’s health status perspective over time (i.e., response shift).\textsuperscript{248-251} In the studies presented in the present thesis, MCIDs were selected of which the estimates related most to the patients’ characteristics.

Another concern to be discussed is the methodology used to investigate the intervention effects on bimanual coupling strength (Chapter 6). The methods used in this study differed on a number of characteristics from the original protocol introduced by Riddervold and colleagues.\textsuperscript{50} The main reason for the methodological disparity is that in the ULTRA-stroke program patients with an upper limb paresis were tested instead of healthy subjects. This required a reduction of the number of tasks to shorten the assessment time and the creation of sinusoidal passive movement trajectories for two tasks instead of using the patients’ own recorded movements, which were often too irregular. As a consequence of these irregularities, it was impossible in the analysis to calculate the discrete relative phase between both hands based on the moments of peak flexion and peak extension. Instead, a continuous analysis approach was used in which the cross-correlation coefficient of the continuous movements was calculated. Due to the changes made in the protocol and analysis, it was not feasible to address the different sources of interlimb interactions.\textsuperscript{66} However, with this alternative analysis approach it was possible to determine the movement pattern in terms of its relative phase, and to determine changes in coupling strength. Furthermore, the same data still allowed for the extraction and analysis of two additional indicators of control over the paretic hand: amplitude and movement harmonicity.
Further considerations

For the individual patient it is important that an intervention is tailored to his or her characteristics, health condition, contextual factors, personal desires, needs, and goals. It is the clinician's responsibility to provide such a tailored intervention and it is the researcher's obligation to investigate the evidence of clinical practice in terms of efficacy and efficiency as well as to investigate possible reasons why clinical practice is or is not effective and efficient. The difficulty in this matter lies in demonstrating that the intervention substantially influences the natural dynamics of recovery in the desired direction. However, a proper insight into the process of recovery after stroke is lacking.

This paucity of insight calls for a step back from the ULTRA-stroke program and requires a broader view of some fundamental issues in upper limb recovery after stroke. First, it is important to investigate whether an intervention indeed has any (positive) influence on the natural processes of recovery. Unfortunately, in what is considered the typical stage of rehabilitation (from stroke onset up to three to six months after stroke) it is unethical to compare one group of patients receiving an upper limb intervention with a group receiving a sham or placebo intervention. Given the similarity in outcomes (in selected groups of patients) after different, yet dose-matched interventions, including conventional treatment, it is impossible to determine whether the specific properties of these treatments have surplus value beyond spontaneous recovery after stroke.

One particular factor that is suggested to be effective for (re)learning skills in stroke rehabilitation is the intensity of task specific training. Irrespective of the type of exercise performed in the intervention, previous research suggests that greater treatment intensity will lead to better outcomes (cf. the success of original CIMT). For this reason, one may ask oneself whether a dose-matched trial in which three hours per week exercise therapy is offered next to usual care is sufficient to reveal meaningful differences in clinical outcomes. Moreover, properly conducted dose-response trials are lacking in stroke rehabilitation.

Also the timing of the intervention plays a role. There is strong neurobiological evidence for a critical time window early after stroke onset, in which homeostatic neuroplasticity is most apparent and assumed to support motor learning and neural repair. It is in this time window that interventions are expected to optimally stimulate the recovery process. Therefore, as stated before, differences between intervention effects are most likely to be detected within this critical time window. However, with regard to the intensity of the intervention, it has been suggested that in the acute phase after stroke high-intensity practice may be less favorable. This suggestion is based on one study in humans, which reported less...
motor improvement after higher-intensity CIMT (i.e., three as opposed to two hours per day, five days per week for two weeks) very early after stroke. Several animal studies have found that intensive practice of the affected limb in rats is harmful if initiated too soon after stroke,\textsuperscript{293-296} when the penumbral tissue is presumably still vulnerable.\textsuperscript{297} In addition, it has been suggested that the effects of early practice may depend on cortical or subcortical involvement. Detrimental effects of overuse of the affected limb were found in rats with an exclusively cortical infarction, whereas in rats with an exclusively subcortical infarction harmful effects of disuse, not overuse were found.\textsuperscript{298} Nevertheless, harmful effects of early intensive practice in humans have not been reported.\textsuperscript{137}

The foregoing discussion does not imply that gains cannot be made at much later stages after stroke. There are examples of patients improving upper limb function years after stroke onset.\textsuperscript{29,69,299} However, it is not by definition that the specific properties of the intervention caused these improvements. First, these improvements may suggest that the full potential was not realized earlier. Second, the circumstances are very likely to be different from earlier after stroke, allowing for more time to practice. And third, these improvements (after intensive training) may simply reflect motor learning similar to that seen in healthy subjects.

The final issue discussed here is the discrepancy between the results of large scale RCTs and meta-analyses on the one hand and the importance of an intervention tailored to the patient’s critical individual characteristics on the other hand. It is plausible that one intervention is more beneficial than another on average in a group comparison, but at the same time has no effect or is even detrimental for a subset of the investigated sample. RCTs do not take into account the individual patient, which is a major disadvantage of this type of research. For example, the relationship between the individual functional outcomes and collateral neuropsychological deficits\textsuperscript{300-302} and emotional disturbances,\textsuperscript{303} and motivational state\textsuperscript{304} may provide a better insight into the mechanisms of an intervention. Note that the Virtual International Stroke Trials Archive (VISTA) specifically accommodates for additional individual meta-analyses using data from completed clinical trials.\textsuperscript{305}

**Implications for clinical practice**

Although null results in intervention comparison studies are usually not desired, they provide important information for both scientists and clinicians. Null results spur the scientist to further investigate the parallels of the interventions that led to the beneficial effects, for example the paretic upper limb’s active involvement in therapy and in daily activities. Alternatively, they should also challenge scientists to investigate whether there were indeed differences between the assumed underlying
mechanisms of the interventions, for example with kinematics, electromyography (EMG) and brain dynamics studies. For now and until future research suggests otherwise, the results presented in the present thesis indicate that modesty with regard to claims of superiority of one type of intervention over the other appears to be appropriate. This means that clinicians may expect similar results when applying either a unilateral or a bilateral intervention, and are therefore advised to consult with the patient which approach best fits the patient’s motivation, needs, and goals. However, based on the results of our meta-analysis, a unilateral approach (i.e., (m)CIMT) deserves a careful recommendation for patients with a mild upper limb paresis in the chronic phase after stroke. In intervention selection there will always be practical and financial considerations, as well as personal preferences (of both patients and clinicians). For example, (m)CIMT is notorious for its restrictive device, although a restraint may be of lesser importance. On the other hand, (m)BATRAC has the potential of tediousness. However, this drawback can be alleviated with the help of patient-relevant music and/or a computer game to enhance compliance.

Future directions
There is a definite need to better understand what it is exactly that patients learn from an upper limb intervention and how the underlying learning process evolves over time. To this end, patients should not only be tested before and after an intervention, but also serially during the intervention (cf. the Explicit-stroke trial). With tests only before and after an intervention much information about the time course may be lost. With the help of serial tests changes during the intervention can be monitored, which may have implications for the intervention. It is plausible that the content and intensity may have to be changed based on the progress made by the patient. In addition, the patient’s health status perspective may change over time, including the course of the intervention. Consequently, future trials should include subjective, self-perception measures as primary outcomes in addition to the commonly used objective, observational capacity measures. This implicates that researchers should consider the MGDs of both subjective and objective measures of upper limb function in their power calculations for patient recruitment in trials. Similarly, clinicians are advised to set rehabilitation goals that can be measured not only with capacity measures but also with self-perception measures of upper limb function in consultation with the patient.

Changes should not only be tested with clinical outcomes of impairment, activity performance, and activities of daily living, but also by using kinematic measures. After stroke, restitution by neural repair and substitution of function by compensatory movements both contribute to the process of upper limb function.
recovery. These compensatory movements demonstrate the redundancy in motor control and reflect an adaptive control strategy to compensate for motor deficits in the paretic upper limb. Clinical outcome measures are far less capable of distinguishing between restitution of function and compensatory movements than kinematic measures.\(^{312,313}\) With the help of kinematic measurements (possibly in combination with EMG recordings\(^{314-316}\)) the changes in coordination of the paretic upper limb movements can be investigated in parallel with the non-linear improvements in functional ability and shed light on what actually changes during recovery.\(^{317-320}\)

The incorporation of measures of neural reorganization will provide further essential information. For example, Whitall and colleagues compared the effects of unilateral and bilateral upper limb training in patients with chronic stroke.\(^{25}\) In their RCT patients also underwent functional magnetic resonance imaging (fMRI) examinations before and after the intervention. Although the clinical results were similar after both types of intervention, the neuroplastic mechanisms were not. Bilateral training led to a greater increase of activation in the ipsilesional precentral gyrus and contralesional superior frontal gyrus (associated with improved upper limb function). This corresponds with the conclusion of a review of clinical recovery and neuroplasticity, which states that no single pattern of neuroplastic change is observed during recovery, although neuroplasticity seems to depend on the content and intensity of the intervention, in addition to the deficits caused by the initial lesion.\(^{321}\) This is an interesting conclusion, because it implies that there is valuable information to be gathered from the relations between the pattern of neuroplastic change, the applied intervention, and the initial lesion and deficits. In the ULTRA-stroke trial examinations of treatment-induced neuronal reorganization were also included. To this end magneto-encephalographic (MEG) recordings were used. MEG is a very suitable tool for studying patterns of correlated (synchronized) neurological activity within and across hemispheres. Synchronization of neural activity is deemed crucial for information processing in the nervous system.\(^{322}\) The MEG recordings prior and after the interventions were conducted with the intention to investigate treatment-induced changes in these patterns, as well as changes in spectral power in the movement-related frequency bands. With additional EMG recordings from the upper limbs the examination of cortico-cortical synchronization of neural activity can be supplemented with an examination of cortico-spinal synchronization.\(^{322,323}\) Unfortunately, however, at the time of completing this thesis, the analysis of the MEG and EMG recordings was still incomplete. From the analysis, cortical reorganizations primarily in the ipsilesional hemisphere (i.e., increased phase synchronization between regions surrounding the lesion) are expected after mCIMT, whereas cortical reorganizations with a stronger coupling between the lesioned and the contralesional hemisphere are expected.
after mBATRAC (i.e., a greater increase in the degree of phase synchronization between the hemispheres). However, with the results of the bimanual coupling study in mind, the results of the MEG study may be different from what is expected. Nevertheless, the results are anticipated to provide a better insight into the changes in neurodynamics, which can be related to the area of the lesion, the initial deficits, and functional improvements after the intervention. The information derived from these analyses may complement prediction models and help improve algorithms, such as proposed by Stinear and colleagues.39

Taken together, it is reasonable to expect that the additional information from serial testing, kinematic analyses, and measures of neural reorganization will help clinicians in selecting an appropriate intervention.

**Concluding remark**

The ULTRA-stroke program was a translational research program that provided valuable information for upper limb rehabilitation after stroke and is expected to yield further useful results in the near future. This research shows that conceptually different rehabilitation approaches can lead to similar clinical outcomes. Likewise, even kinematic analyses can present comparable results after different types of training. Therefore, modesty with regard to claims of superiority of one type of intervention over the other seems to be called for in intervention selection.