

# Intensity of practice after stroke: More is better

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## Summary

The present debate paper addresses four relevant issues related to the impact of intensity of practice after stroke. First, the best way to define intensity of practice is discussed. Second, the paper describes the evidence that exists for a dose-response relationship in stroke rehabilitation. Third, the relevance of an appropriate patient selection for a meaningful intensive practice is explored. Finally, the feasibility of intensive practice by: (1) early started mobilization of stroke patients (2) ability to practice in groups, (3) using forced use paradigms such as constrained induced movement therapy for the upper limb, (4) using robotics and (electronic) devices that help patients to practice on their own and (5) preventing poor compliance in terms of practice in therapeutic sessions by identifying factors that predict poor adherence are discussed.

## Introduction

In biology it is well accepted that deliberate practice for the purpose of acquiring and maintaining expert performance in sports [1], chess playing [2], typing [3] and learning to play a musical instrument [3, 4] follows a dose-response relationship. In other words, more time dedicated to learning a specific skill is associated with improved performance. Rehabilitation can be largely regarded as a process in which patients are taught to accomplish complex motor tasks such as walking, dressing and washing, one may infer that intensive training by hemiplegic patients with stroke should follow the same biological rules.

## Evidence for intensity of practice

Two systematic reviews [5, 6] have suggested that an early start of intensive stroke rehabilitation may be associated with greater and faster improvement of activities after stroke. For this purpose articles from MEDLINE, CINAHL, Cochrane Central Register of Controlled Trials, PEDro, DARE and PiCarta and references presented in relevant publications were examined as well as abstracts in proceedings. Both research groups found small but statistically significant SESs in favour of the group that spent more treatment time focused on the activities of daily living (ADL). In a sensitivity analysis, larger overall effect sizes were found in studies that weighted individual effect sizes by the differences in volume of exercise between experimental and control groups [10]. However, methodological limitations of the primary studies, differences in organisational settings, as well as a marked heterogeneity of patient characteristics, proved to be major confounding factors [5]. This finding confirms the results of

a meta-analysis by Ottenbacher and Janell [7], which combined the findings of 36 studies on the effects of stroke rehabilitation wards and on different methods of rehabilitation in one summary effect size, with a magnitude of 0.4. They concluded that programmes with focused stroke rehabilitation may improve functional performance for patients who have sustained a stroke.

Until the end of 2004, 20 randomised clinical trials (RCTs) involving 2686 patients had been conducted in the acute or subacute, post-acute and chronic stages after stroke [8]. Some trials were restricted to a specific type of patient, such as those with first-ever ischemic stroke, whereas others applied less restrictive inclusion criteria with respect to type, localisation and number of previous strokes. Outcomes of these trials were all evaluated by standardised ADL measures. Pooling reported differences in ADL by applying a random effects model yielded a small, but statistically significant SES in favour of more intensive therapy (SES [fixed]: 0.13 Standard Deviation Units [SDUs]; CI: 0.06–0.23;  $Z = 3.252$ ,  $p < 0.001$ ). This SES denotes an overall change of about 5% in favour of more intensive therapy, which corresponds to a 1-point change on the 20-point scale of the Barthel Index score. While one may question the clinical significance of such a finding, even this small change in ADL score is likely to have a disproportionate impact from an epidemiological point of view, considering that more than 80% of all patients with stroke receive some form of exercise therapy [8]. The evidence for a dose-response relationship does not seem to be confined to the intensity of ADL practice, but such a relationship has also been observed in related domains in stroke rehabilitation, such as aphasia therapy [9, 10].

How much practice is needed to improve functional recovery is a key issue to be solved in rehabilitation medicine. On average, the intensive rehabilitation groups in these RCTs received about 959 minutes more training by therapists than the control groups (i.e., about 48 minutes of physical therapy and 23 minutes of occupational therapy per day for about 3 months) [8]. There were, however, considerable differences between trials with respect to the total amount of additional therapy provided, as well as in the timing and focus of the interventions. Some trials concentrated on gait training, others on dexterity, and some restricted their efforts to facilitating ADLs in general. The additional time of therapy for the experimental groups ranged from 132 to 6186 minutes. The association between effect size and additional time given to the experimental groups was 0.39 in favour of studies with a larger treatment contrast ( $p < 0.05$ ), thus supporting the existence of a dose-response relationship between more practice time and better outcomes. Differences were found, however, between studies comparing the effects of intensity

in the chronic stage of stroke (SES [fixed]: 0.04 SDU; CI: 0.14–0.29;  $Z = 0.45$ ;  $p = 0.29$ ) and those comparing effects within six months of stroke onset (SES [random]: 0.17 SDU; CI: 0.02–0.26;  $Z = 3.49$ ,  $p < 0.001$ ) [8]. Current findings suggest that higher training intensities are more likely to speed up functional recovery after stroke, rather than to produce additional activities [11, 12]. It should be noted, however, that the absence of significant SES values for the three studies that investigated augmented exercise therapy time in the chronic phase may have been caused by insufficient statistical power.

### Patients qualifying for intensive deliberate practice

Effectiveness as reported in randomised controlled trials is not only defined by the effectiveness of the task-oriented intervention programme, but also to a large extent by the identification of those patients who will benefit most from intensive practice. The latter in particular seems to be critical for an understanding of the effects of augmented exercise training of the upper limb, for which a dose-response relationship has not been found [8, 12]. Thus far, most large RCTs agree that the impact of upper limb training on functional outcome is greatest for those who have some residual willed movement of the paretic hand at the baseline [13, 14, 15, 16, 17]. This finding suggests that for patients who are expected to achieve at least some dexterity within 4 weeks, every opportunity should be encouraged to regain function in the affected upper limb. In contrast, those patients for whom a poor motor recovery without return of dexterity is anticipated at 4 weeks post stroke, treatment should be focused on achieving and maintaining a comfortably mobile arm and hand, whereas compensation strategies with the non-paretic arm should be considered [18].

The above-mentioned limited time window for recovery of the upper paretic limb is not a new finding; it has already been confirmed by a number of descriptive [19] and prognostic studies [20–23] in the past. All these studies, which focused on the effectiveness of upper limb training, claimed that the absence of a measurable grip function within about four or five weeks post stroke coincides with a poor functional recovery of the hemiplegic arm at six months. Obviously, the limited time window for the prediction of regaining dexterity in relation to the effects of upper limb training treatment after one month, such as neuromuscular stimulation [23] or exercise therapy [13, 14], suggests that regaining dexterity is restricted to those patients with a favourable prognosis (i.e., a partial intact corticospinal tract system). It is not without reason that some willed extension of the wrist and fingers is often used as an inclusion criterion for patients in upper limb trials, such as those involving constraint-induced movement therapy (CIMT), in order to select those patients who are able to improve dexterity [15]. Another important advantage of selecting only those patients with some willed wrist and finger extension for such trials is that it reduces the heterogeneity between subjects and thus decreases the risk of type II error by lack of statistical power [7, 24].

### Feasibility of intensive practice in the present-day health care system

Rehabilitation facilities are under financial pressure, and most inpatient facilities are feeling the impact in terms of decreased length of stay and reduced staff to provide daily assistance. In other words, there is a mismatch between, on the one hand, the evidence from RCTs showing that augmented practice improves functional recovery, and, on the other hand, the actual therapy time provided by most therapists in our health care system. A recent observational study in stroke units has shown that patients with stroke spend most of the hours in each workday alone and physically inactive [25]. In this observational behavioural mapping study on 64 patients with stroke in five acute stroke units, patients were monitored on workdays from 8 a.m. to 5 p.m. (i.e., the most active part of a patient's day) by 1-minute observations every 10 minutes. Patients were observed for two consecutive days at a mean time interval after stroke of 5.6 days (range, 0 to 13 days). Bernhardt and colleagues<sup>42</sup> observed that during working days, patients spent more than 53% of their time resting in bed and were alone for 60.4%, whereas 28% of the time was spent sitting up out of bed. Only 13% of their time was filled with activities that could potentially prevent complications and improve mobility. Therapist contact constituted only 5.2% of the day. In addition, therapy time in most settings is restricted from Mondays to Fridays. With respect to frequency of exercise, a recent quasi-experimental study suggested that continuing rehabilitation treatment programmes for seven days instead of five days per week might be more effective in terms of ADL outcome [26]. For example, Sonoda and colleagues [26] showed that the gain achieved by continuing therapy during weekends resulted in a shorter length of stay and lower costs compared to conventional five-day treatment programmes. However, randomised clinical trials to demonstrate the effectiveness of continuing therapy for patients with stroke through weekends are largely lacking [44], and the evidence of therapy on weekends is still weak [26–27]. Despite the financial pressure to increase efficacy without increasing costs, a number of studies have shown that augmentation of task-oriented practice is often possible by increasing (1) the ability to practice in groups [28], (2) using forced use paradigms such as constrained induced movement therapy for the upper limb [15], (3) using robotics [29] and (electronic) devices that help patients practice on their own [30, 31] and (4) preventing poor compliance in terms of practice in therapeutic sessions by identifying factors that predict poor adherence [32].

The most pragmatic way to make more efficient use of available staff is by implementing group training programmes. Recently, a number of studies have shown that circuit-training programmes in which patients are allowed to train functional tasks in different workstations is an effective and efficient way to improve gait-related activities in subacute and chronic stroke [28]. Meta-analysis of 14 RCTs in which work stations were applied by gait-oriented training showed a significant medium effect of gait-oriented training interventions on both gait speed and walking distance, whereas a small, nonsignificant effect size was found on balance.

Although functional mobility was positively affected, no evidence was found that activities of daily living, instrumental activities of daily living, or health-related quality of life were significantly affected by gait-oriented training [28].

Another way to increase intensity is to implement a constraint-induced movement therapy paradigm for the upper limb in which patients are forced to use the upper limb for two [15] to six hours or more per day while performing daily tasks. For example, a recent study showed that forced use therapy without shaping therapy of the upper limb for 2.7 hours per day for two weeks improved dexterity by about 11% as measured on the ARAT [33].

Another development that is in line with the above-mentioned studies is that of new assistive technologies, including robotics, that allow patients to practice more intensively on their own [29]. As the body of evidence grows that more intensive therapy influences recovery favourably, robotics may offer an opportunity to meet an important treatment gap in the future [29]. A recent conducted meta-analysis involving 10 RCTs (N = 218 patients), showed a nonsignificant heterogeneous SES in terms of upper limb motor recovery. However, sensitivity analysis of studies involving only shoulder-elbow robotics subsequently demonstrated a significant homogeneous SES for motor recovery of the upper paretic limb [29]. No significant SES was observed for functional ability (ADL). Unfortunately, none of the studies were dose-matched suggesting that the dose of therapy may be responsible for better outcomes. On average robot-assisted therapy in the experimental groups was given about 48 minutes. This was about 2 times the intensity of the control group (i.e., 29 minutes) [29].

Besides staff shortages that affect the ability to provide intensive practice, insufficient compliance in terms of participating in physical treatment sessions is also likely to reduce the effectiveness of rehabilitation programmes. For example, Lenze et al. showed in a prospective observational study that, after controlling for baseline functional status, patients who missed more than 25% of OT and PT treatments showed 25% less improvement based on the discharge functional status according to the FIM instrument [32]. Unfortunately, the reasons why some patients show poor compliance are unknown. Future studies should investigate the determinants of compliance and to the identification of participants who are susceptible to poor participation in rehabilitation programmes [32]. Besides access to practice offering proper instruction to patients about the effectiveness of continuing to practice, and counselling partners and family members as to how to coach patients to practice are crucial elements in the augmentation of autonomous practice [34].

## Conclusions

Although precision is lacking in determining the required exact dose of practice for functional effects to take place, a minimal dose of at least 16 hours augmentation has been suggested in a recent systematic review of 20 RCTs. To date, the choice of time spent in applied exercise training programmes in all RCTs has been pragmatic and mainly based on existing local treatment policies. Besides therapy dosage,

reported effects seem to be largely dependent on adequate control for therapy time in the control group in order to augment treatment contrast, as well as on the appropriate selection of patients with some potential for functional change. The latter precondition in particular is critical for upper limb training, in which the increased probability of return of dexterity seems to be largely defined in the early stages after stroke. Therefore, understanding the effects of intensity of practice requires knowledge about functional prognosis as well as the mechanisms underlying the non-linear recovery pattern after stroke. In particular, repeated measurement designs suggest that intensive-task oriented exercise training is able to enhance or speed up recovery in the first six months after stroke onset. This also implies that controlled designs in which patients are measured at baseline and at the end of the intervention (e.g., six months post stroke) might be not appropriate. Future studies should be focused on a better understanding of what actually changes in patients when they improve, and should study the way in which these longitudinal changes in impairments, such as strength, are related to functional improvements. Currently, there are strong indications that functional recovery is more than the restoration of impairments alone, but is to a large extent due to strategies incorporating the compensation of existing impairments. In particular, longitudinal studies investigating the biological regularities of improvements in motor control may contribute to a better understanding as to why patients show a certain adaptive motor control and how improvements in impairments are accompanied by improved skills.

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