Activity-Based Therapies in Stroke Neurorehabilitation

Subjects: Medicine, Research & Experimental
Contributor: Muhammed Enes Gunduz, Bilal Bucak, Zafer Keser

Activity-based therapies are the key component of stroke neurorehabilitation. The principle of these therapies is to provide structuralized activities with adequate quantity and quality to induce plasticity for recovery. However, there are many challenges in clinical and research settings, including a lack of standardization, limited dose and intensity, and variability of responders. While the therapies with favorable plasticity use high intensity in animal studies with a range of 300–800 repetitions, achieving similar intensity in clinical settings has been challenging.

Keywords: stroke ; neurorehabilitation ; telerehabilitation ; robotics ; recovery

1. Introduction

Stroke is one of the leading causes of long-term disability worldwide. Stroke rehabilitation therapies aim to enhance favorable neuroplasticity. With the advances in technology, the stroke recovery field is rapidly evolving and various promising novel treatment approaches and technological advances are becoming part of the therapeutic armamentarium to improve post-stroke recovery in both the post-acute and chronic phases.

2. Constraint Induced Movement Therapy

Constraint-Induced Movement Therapy (CIMT) is an effective and popular rehabilitation approach primarily designed to improve the functional use of an affected limb in stroke patients. This therapy involves an intense functionally oriented task practice of the paretic extremity along with restraint of the less-impaired extremity for most waking hours [1]. The main two principles of CIMT are (i) constraint of forced use of the less-affected limb with a splint or mitt, preventing its use during 90% of the day and therefore promoting more frequent and intensive use of the more impaired limb; (ii) intensive training of more affected limb with task-oriented, structured, and repetitive activities for up to 6 h a day for two weeks.

The history of constraint-induced therapy theory dates back to the early 1900s when the phenomena of motor disability due to disuse was described in monkeys with pyramidal tract lesions by Franz and colleagues [2]. Subsequently, they provided the first documented evidence that these monkeys, forced to use their hemiparetic extremity by immobilizing the better limb, had increased and faster recovery. It was hypothesized that the deafferentation leads to inactivity and behavioral changes of not using the affected limb; “learned nonuse” could be overcome by behavioral strategies such as CIMT [3]. The current evidence is from the multicentered, randomized, single-blinded EXCITE trial, the first National Institute of Health (NIH)-funded stroke neurorehabilitation trial, and the only randomized-controlled Phase III trial that has shown efficacy in stroke recovery [4]. EXCITE trial showed significant and clinically relevant improvement in upper extremity motor function in patients with first stroke within the previous 3–9 months as a result of 10 days of CIMT therapy. These clinical improvements persisted for at least one year after the intervention. Although this therapy was designed to improve upper extremity weakness, further studies in the lower extremity suggested improvement in motor functions and balance-related motor function [5]. The current evidence supports the use of CIMT in stroke patients, particularly in upper extremity motor recovery.

Besides the theory of overcoming “learned nonuse”, plasticity plays an important role in CIMT outcomes. Several studies showed cortical reorganization after CIMT-based interventions by changes in the size and excitability of regions representing the affected limb [6][7]. Researchers evaluated the motor cortex changes with TMS motor mapping and showed an increase in the size of hand muscles only in the ipsilesional hemisphere after CIMT treatment, as well as changes in excitability corresponding to recovery [8]. Given these changes in inter and intra-cortical excitability, further investigations of CIMT in combination with non-invasive brain stimulation techniques are underway (NCT03826030). Further studies are needed to develop biomarkers to identify the best responders and to guide concomitant interventions to optimize the rehabilitation of stroke patients.

3. Robot-Assisted Therapies

Robot-assisted therapies (RAT) are another novel modality in which patients are provided upper or lower limb therapy by robotic devices rather than conventional hands-on therapy. RAT can provide a high-intensity standardized therapy, which is thought to be important in motor cortex reorganization and promoting recovery. RAT aims to increase the capacity of motor control of the paretic arm or leg, muscle strength, and upper limb capacity, and thus promote basic activities of daily living.

As a proof-of-concept study, Takahashi and colleagues conducted a 3 week-long upper limb RAT in 13 patients with stroke. They showed that RAT produced a significant motor gain in patients with moderate post-stroke motor deficits [9]. In a larger-scale, multicenter, randomized, and controlled trial, Lo and colleagues compared RAT, intensive comparison therapy, and usual care in chronic stroke patients with moderate-to-severe upper-limb impairments [10]. They showed that RAT increased motor function in 36 weeks compared to standard therapy. However, RAT was not superior to intensive therapy, which suggested that RAT was as good as intensive behavioral therapy. Similarly, Rodgers and colleagues showed that compared with usual care, RAT did not lead to better motor recovery in patients with stroke-related moderate to severe upper limb dysfunction [11]. At this point, RAT is safe and induces positive effects in motor recovery after stroke, but its superiority to usual intense therapy is yet to be proven [12]. Overall, repetition and intensity are the key factors for favorable motor recovery, and RAT is a promising alternative to conventional therapies to achieve these goals.

4. Telerehabilitation

Telerehabilitation is a method of delivering rehabilitation services remotely using communication methods. This therapy aims to address the main challenges of providing higher doses of rehabilitation therapies, such as cost-related issues, traveling difficulties, limited access to high-quality rehabilitation centers/providers, poor compliance, and dose limitations of in-clinic therapy sessions. Furthermore, telerehabilitation’s principles of high intensity, easy access, and gamification of tasks help to promote a higher quality of therapy by creating more challenging, motivating, and variable goal-oriented tasks in more relevant environments with the supervision and feedback of therapists. A randomized, multicentered, non-inferiority trial showed comparable efficacy of home-based telerehabilitation to traditional in-clinic rehabilitation, with excellent adherence and higher arm movement repetition (average 1031 repetitions per day) [13].

Most studies enrolled patients with chronic stroke patients, but a recent study assessing the optimal time for motor recovery showed that the task-specific motor therapies were most effective within the first 2–3 months, suggesting enhanced neural plasticity in earlier stages after stroke [14]. In clinical practice, the early initiation of rehabilitation is challenging due to limited, fragmented, and often delayed transition care from initial hospitalization to in-facility rehabilitation and/or to home settings. Telerehabilitation may address these challenges of transition and improve earlier access to rehabilitation with better continuity of care. A recent feasibility study supports that telerehabilitation is feasible, safe, and possibly efficacious in providing therapy to early stroke patients [15]. Further controlled studies are needed to expand the use of telerehabilitation.

References

1. Kwakkel, G.; Veerbeek, J.M.; Van Wegen, E.E.H.; Wolf, S.L. Constraint-induced movement therapy after stroke. Lancet Neurol. 2015, 14, 224–234.
2. Ogden, R.; Franz, S.I. On cerebral motor control: The recovery from experimentally produced hemiplegia. Psychobiology 1917, 1, 33–49.
3. Fritz, S.L.; Butts, R.J.; Wolf, S.L. Constraint-induced movement therapy: From history to plasticity. Expert Rev. Neurother. 2012, 12, 191–198.
4. Wolf, S.L.; Winstein, C.J.; Miller, J.P.; Taub, E.; Uswatte, G.; Morris, D.; Giuliani, C.; Light, K.E.; Nichols-Larsen, D. Effect of Constraint-Induced Movement Therapy on Upper Extremity Function 3 to 9 Months After Stroke: The EXCITE Randomized Clinical Trial. JAMA 2006, 296, 2095–2104.
5. Tedla, J.S.; Gular, K.; Reddy, R.S.; Ferreira, A.d.S.; Rodrigues, E.C.; Kakaraparthi, V.N.; Gyer, G.; Sangadala, D.R.; Qasheesh, M.; Kovela, R.K.; et al. Effectiveness of constraint-induced movement therapy (cimt) on balance and functional mobility in the stroke population: A systematic review and meta-analysis. Healthcare 2022, 10, 495.
6. Liepert, J.; Miltner, W.; Bauder, H.; Sommer, M.; Dettmers, C.; Taub, E.; Weiller, C. Motor cortex plasticity during constraint-induced movement therapy in stroke patients. Neurosci. Lett. 1998, 250, 5–8.

7. Wittenberg, G.F.; Chen, R.; Ishii, K.; Bushara, K.O.; Taub, E.; Gerber, L.H.; Hallett, M.; Cohen, L.G. Constraint-Induced Therapy in Stroke: Magnetic-Stimulation Motor Maps and Cerebral Activation. Neurorehabilit. Neural Repair 2003, 17, 48–57.
8. Sawaki, L.; Butler, A.J.; Leng, X.; Wassenaar, P.A.; Mohammad, Y.M.; Blanton, S.; Sathian, K.; Nichols-Larsen, D.S.; Wolf, S.L.; Good, D.C.; et al. Constraint-Induced Movement Therapy Results in Increased Motor Map Area in Subjects 3 to 9 Months After Stroke. Neurorehabilit. Neural Repair 2008, 22, 505–513.
9. Takahashi, C.D.; Der-Yeghiaian, L.; Le, V.; Motiwala, R.R.; Cramer, S.C. Robot-based hand motor therapy after stroke. Brain 2014, 131, 425–437.
10. Lo, A.C.; Guarino, P.D.; Richards, L.G.; Haselkorn, J.K.; Wittenberg, G.F.; Federman, D.G.; Ringer, R.J.; Wagner, T.H.; Krebs, H.I.; Volpe, B.T.; et al. Robot-Assisted Therapy for Long-Term Upper-Limb Impairment after Stroke. N. Engl. J. Med. 2010, 362, 1772–1783.
11. Rodgers, H.; Bosomworth, H.; Krebs, H.I.; van Wijck, F.; Howel, D.; Wilson, N.; Aird, L.; Alvarado, N.; Andole, S.; Cohen, D.L.; et al. Robot assisted training for the upper limb after stroke (RATULS): A multicentre randomised controlled trial. Lancet 2019, 394, 51–62.
12. Veerbeek, J.M.; Langbroek-Amersfoort, A.C.; van Wegen, E.; Meskers, C.; Kwakkel, G. Effects of Robot-Assisted Therapy for the Upper Limb After Stroke: A Systematic Review and Meta-analysis. Neurorehabilit. Neural Repair 2017, 31, 107–121.
13. Cramer, S.C.; Dodakian, L.; Le, V.; See, J.; Augsburger, R.; McKenzie, A.; Zhou, R.J.; Chiu, N.L.; Heckhausen, J.; Cassidy, J.M.; et al. Efficacy of Home-Based Telerehabilitation vs In-Clinic Therapy for Adults After Stroke: A Randomized Clinical Trial. JAMA Neurol. 2019, 76, 1079–1087.
14. Dromerick, A.W.; Geed, S.; Barth, J.; Brady, K.; Giannetti, M.L.; Mitchell, A.; Edwardson, M.A.; Tan, M.T.; Zhou, Y.; Newport, E.L.; et al. Critical Period After Stroke Study (CPASS): A phase II clinical trial testing an optimal time for motor recovery after stroke in humans. Proc. Natl. Acad. Sci. USA 2021, 118, e2026676118.
15. Edwards, D.; Kumar, S.; Brinkman, L.; Ferreira, I.C.; Esquenazi, A.; Nguyen, T.; Su, M.; Stein, S.; May, J.; Hendrix, A.; et al. Telerehabilitation Initiated Early in Post-Stroke Recovery: A Feasibility Study. Neurorehabilit. Neural Repair 2023, 37, 131–141.