OLLE HÖÖK LECTURESHIP 2019: THE CHANGING WORLD OF STROKE REHABILITATION

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The paper presents a summary of the Olle Höök lecture, which was presented at the Baltic and North Sea Conference on Physical and Rehabilitation Medicine in Oslo, Sweden, in October 2019. The paper aims to provide a worldwide picture of stroke, developments in this field, and the evolution of stroke rehabilitation. It sets out the background to, evidence for, and content of the comprehensive stroke unit. The paper also describes some rehabilitation techniques based on neurophysiology, the use of robotics, and the evidence level for interventions. Organization of the stroke care chain and different aspects of rehabilitation during its trajectory are described. However, the need for rehabilitation is often not met, due to restricted and unevenly distributed resources. With increasing knowledge of neurophysiology and evidence from meta-analyses, the content of stroke rehabilitation will continue to evolve.

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STROKE WORLDWIDE

Research into the global burden of disease shows that the number of stroke cases is increasing (1) and that the incidence risk of having a stroke is 1 in 4 (1 in 2 in China, and 1 in 3 in some Eastern European countries). This global increase is due to the increasing number of cases in less developed parts of the world. Socioeconomic status is associated with stroke incidence (2); poverty leads to stroke and stroke leads to poverty (3). In the high-income countries, the incidence of stroke is decreasing (1). However, improved acute care has been shown to result in higher survival rates and increased disability adjusted life years (DALYs) (4). One reason for improved acute care is the provision of stroke units (5) with reperfusion therapy (6, 7) (Fig. 1).

![Fig. 1. Angiogram showing a clot blocking blood circulation. Pre- (left-hand image) and post- (right-hand image) reperfusion.](image)
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Disability (5), and that these gains were also seen up to 10 years after the acute incidence (21).

Training Based on Neurophysiological Theories

Stroke damages the brain, with the resulting impairment being related to the localization of the damaged area. Most motor and sensory functions are more localized than are cognitive functions, such as perception, attention, memory and language, which are more distributed in interactive and overlapping networks.

Motor control theory is based on the interaction of the individual’s resources (perception, cognition and action), the nature of the task (stability, mobility, manipulation) and the characteristics of the environment (22). The theory is that there are systems in which higher levels in the nervous system activate lower levels, while the lower levels activate synergies (muscles that act as a unit). It is thought that the person gains motor control through searching for an optimal solution for performing a task. On the basis of this theory, current stroke rehabilitation is individualized, task-specific and goal-oriented (Fig. 3).

Discovery of the central gait pattern (23) and, subsequently, the possibility of regaining function through training (24), provided a basis for the idea of providing support for people to enable them to take more steps while walking on a treadmill (25). Studies in Canada (26) and Germany (27), and a multicentre RCT in Sweden (28), however, have divergent results. Meta-analyses, performed by Cochrane (latest update 2017; www.medicaljournals.se/jrm

Development of Stroke Units

The 1970s saw the beginning of increasing interest in stroke care. An early report from Sweden dealt with the need for stroke rehabilitation (13), highlighting the needs of individuals of working age. The study showed that only approximately 30–40% of those who survived 6 years after stroke returned to work. There were reports of more intensive care stroke units (14, 15), as well as comprehensive units in which the rehabilitation team was important (16, 17), and of subsequent randomized controlled trials (RCTs) (18–20). The results showed that the stroke unit saved lives and reduced disability (5), and that these gains were also seen up to 10 years after the acute incidence (21).
The changing world of stroke rehabilitation

(29)), which included 56 trials with 3,105 participants, showed that the likelihood of being independent walkers after using treadmill, was no different from those not receiving treadmill training. However, walking speed and walking endurance may improve slightly in the short term and the energy cost may be reduced (30), which could make this an alternative gait training modality.

The idea that the brain can change, i.e. plasticity, was first suggested in the 1980s. Brain plasticity is a broad term for the ability of the brain to change and adapt as a result of environmental pressure, experiences and challenges, including brain damage. An early publication in this area discussed the possible impact of this in stroke rehabilitation (31). However, the implications for rehabilitation did not really take off until later. Nudo & Friel (32) Nudo & Milliken (33) found increased cortical representation of the hand in a monkey with stroke, and the changes that occurred when the monkey had to feed himself with the paretic limb. This led to a wave of studies on constraint-induced movement therapy (CIMT) (34–36). CIMT involves the use of a splint (or similar), which is applied to the intact hand for 90% of the day in order to force use of the paretic hand, combined with ‘shaping’ (including verbal feedback) by which the tasks are made progressively more difficult (37). Finally, a large multicentre RCT (38) with a strict training procedure, showed an effect of CIMT on upper extremity function, not only on impairment level, but also in activities of daily living (ADL) (Fig. 4). Modification of this intervention has also shown improvements in motor impairment and motor function; however, this did not result in improved function (reduced disability).

Mirror neurones were discovered in the mid-1980s; first in macaque monkeys and subsequently in humans (40, 41). Mirror neurones are involved in the process of humans understanding the meanings of others while observing their actions; for example, when a person smiles and gets a smile in return. This has implications for stroke rehabilitation; it was shown that when a person watches a hand movement the neurones are activated in the same way as when they actually perform the action (42). This mimicking in the brain is useful when the therapist shows a patient how to accomplish a movement, such as lifting the arm. Looking at the action in a mirror also results in the same activation of neurones as when watching the movement directly. Thus, when a person with stroke uses the mirror to observe a movement they are performing with their better hand, the brain interprets the image as if it is observing the impaired hand (Fig. 5). A Dutch RCT study (43) showed that, in a group of subacute stroke patients, mirror therapy as an add-on to a conventional rehabilitation programme led to improved function in the impaired limb immediately after 4 weeks of treatment, as well as at the 6-month follow-up. A Cochrane review (44) has shown the efficacy of mirror therapy in improving upper extremity function and ADL. Mirror therapy is easy to perform, and can be carried out by patients on their own, or with family, and is not dependent solely on professionals.

The brain is organized such that the cortical sensory and motor representation of the hand exerts inhibitory influences on the homonymous representation in the opposite hemisphere. This inhibition from the opposite hemisphere is thought to contribute to skilled motor performance. After a stroke, the surrounding intact tissue has an inhibitory effect on the damaged area. In order to increase the activity of the injured area, different neurophysiological strategies have been tried. The 2 most-studied approaches are transcranial magnetic

Fig. 4. Washing the window using the impaired left hand, with a restraining orthosis on the right hand.

Fig. 5. Use of a mirror box. The subject performs movements with their right (unaffected) hand, while the left (impaired) hand is in the box (out of sight). They observe the movements of their right hand in the mirror.
stimulation, TMS (45) and transcranial direct current stimulation (tDCS) (46). In the clinic, 2 approaches for changing the hemispheric dominance have been applied. One approach is to reduce cortical activity on the intact side by applying low-frequency rTMS. Another approach is to enhance activity in the damaged hemisphere. This can be achieved by high-frequency rTMS or anodal tDCS. Anodal tDCS is less focused, but can be applied while performing rehabilitation. There has also been a trial in which the focus was to increase the sensory input by electrical stimulation of peripheral nerves in the impaired upper extremity (47). In theory, the combination of peripheral nerve stimulation with tDCS while performing an activity should enhance the effects of the different components.

Robots are of possible use in stroke rehabilitation. There are 2 main types of rehabilitation robots.

The first is an assistive robot that substitutes for lost movement. An example of this is a wheelchair-mounted robotic, controlled via a switch or other input device or a powered wheelchair. These devices are sometimes used for persons with locked-in syndrome after a brainstem stroke, who may still have very weak muscle function around the eyes or in a finger or toe.

The second type is a therapy robot. Therapy robots are tools for the therapist that allows the patient to practice with the aid of the robot. There are differences in the construction of these robotic devices. The robots can be divided into exoskeleton and end-effector types, according to their method of supporting and pulling the limb.

Exo-skeleton robots are wearable mobile machines powered by a system of electric motors, pneumatics, levers, hydraulics, or a combination of these. Structurally, exoskeleton robots can be divided into upper limb exoskeleton robots, lower limb exoskeleton robots, whole-body exoskeleton robots, and all kinds of joint correction or restorative training skeletal robots. The limb is enclosed by the robot, which results in the limb movement being performed with the help of the exoskeleton. The level of input provided by the robot to execute the movement can be altered. Most exoskeletal robots in clinical use are for the lower limb. Examples of these devices are the Lokomat®, which requires walking on a treadmill, and the newer device, HAL®, which allows movement on the floor (Fig. 6).

The end-effector rehabilitation robot system consists of ordinary connecting rod and series robot mechanism. Here the patient is connected only to the end of the robot. There are end-effector robots in clinical use for both lower and upper extremity training. MIT-Manus® is an example of upper extremity end-effector training robot. G-EO® gait trainer is a device for the lower limb, where only the feet are fixated in the working state, the robot drives the movement of the upper limbs by connecting with the patient’s arm to achieve the rehabilitation training.

There have been a number of small positive studies with the different modalities for both upper and lower limbs. However, the results of meta-analyses are not as convincing.

Electromechanical arm and hand training in combination with other occupational therapy or physical therapy for impaired arm and hand mobility after stroke has the following effects (48):

• some positive effect on the ability of the arm and hand compared with manual arm training after completion of treatment (strong scientific evidence);
• some positive effect on the muscle strength of the arm and hand compared with manual arm training after completion of treatment (strong scientific evidence);
• some positive effect on activity (ADL) compared with manual arm training after completed treatment (strong scientific evidence);

There is no scientific evidence to assess the effect on pain, muscle tone, joint mobility, quality of movement, participation, or quality of life.

Electromechanical walking training in combination with other physiotherapy in case of impaired walking ability after stroke has the following effects (49):

• some positive effect on the need for walking support (reduced level of dependence) compared with treatment with other walking training after completion of treatment. The results were better for patients who could not walk at the start of training and for those in
the acute and subacute phase (within 3 months after stroke) (*limited scientific evidence*). No difference in effect was seen on the need for walking support compared with treatment with other walking training at follow-up 3–6 months after treatment (*limited scientific evidence*);

- no difference in effect on walking speed after completed treatment compared with other walking training (*limited scientific evidence*), or at follow-up 3–6 months after treatment (*moderately strong scientific evidence*);
- no difference in effect on walking quality (step length) after completion of treatment compared with other walking training (*limited scientific evidence*);
- no difference in effect on activity (movement ability) after completion of treatment compared with other walking exercise (*limited scientific basis*);
- no difference in effect on activities in daily life (ADL) after completed treatment compared with other walking training (*limited scientific evidence*);
- no difference in effect on quality of life after treatment, or at follow-up 3 months after treatment compared with other walking training (*limited scientific evidence*).

## ORGANIZATIONAL ASPECTS OF STROKE CARE

**The burden of stroke in Europe**

The Stroke Alliance for Europe (SAFE) is an organization of different patient organizations from all over Europe. Together with King’s College, London, they launched the Burden of Stroke in Europe in 2017. The report, based on governmental statistics, shows large disparities between and within countries along the entire stroke care pathway. For many countries, there is very little information on the rehabilitation therapies that stroke survivors receive, especially once they have left hospital. Quality control of rehabilitation services is scare. Rehabilitation services are usually unevenly distributed and vary in quality. Specialist rehabilitation may be available only in large urban areas. In many countries, occupational therapy and psychological support are either very limited or not available. Capacity is lacking in rehabilitation centres, as well in the communities, which leads to long delays in starting rehabilitation. Reports from the Swedish quality registries “Riksstroke” and “WebRehab”, show variation in services within Sweden.

The European Stroke Organisation (ESO) and SAFE made a joint effort to launch the European Stroke Action Plan (ESAP). The aim of the ESAP is to produce a roadmap and define goals for the treatment of stroke in Europe through to 2030. The ESAP includes 7 domains: primary prevention; organization of stroke services; management of acute stroke; secondary prevention; rehabilitation; evaluation of stroke outcome and quality assessment; and life after stroke.

The ESAP includes an overview of state of the art in the union and tries to identify the areas where rehabilitation is lacking.

The goals defined by ESAP are (50):

- to guarantee that at least 90% of the population have access to early rehabilitation within the stroke unit;
- to increase the availability of early supported discharge;
- to offer physical fitness programmes in the community;
- to provide individuals with a documented plan for community rehabilitation and self-management support for all patients with stroke who have with residual difficulties on discharge from hospital;
- to ensure that reviews of rehabilitation and other needs are carried out annually, and not only at 3–6 months post-discharge.

**Stroke units**

A stroke unit is a geographically identifiable unit in a hospital, which is devoted entirely (or almost entirely) to stroke care. The stroke unit is staffed by a multidisciplinary team with specialist knowledge of stroke care, and consists of the components described below.

The stroke unit contains 3 elements (51):

- early assessment and treatment;
- early measures, such as physiological measures (temperature, control of blood glucose level), early mobilization (to reduce the risk of pressure sores, better pulmonary ventilation and better overall circulation) and skilled nursing;
- it is staffed by a multidisciplinary team, which is responsible for the rehabilitation process as well as a planned discharge. The multidisciplinary team consists of physician(s), nurse(s), assistant nurse(s), physiotherapists(s), occupational therapist(s), social worker(s) and speech therapist, and has access to a dietician and a psychologist, preferably with a neuropsychological profile. The team meets at least once a week.

The stroke unit has established a programme for interventions to meet common problems among patients with stroke and for recording quality of care. It provides detailed information and educates patients and next-of-kin during the hospital stay. The comprehensive stroke unit has been shown to have a major impact on outcome after stroke. It has no side-effects and is beneficial for all types of stroke, stroke severity
and ages of patients. In addition, cognitively impaired stroke patients benefit from stroke unit care.

**Early supported discharge**

Early supported discharge (ESD) (52) is an innovative approach to rehabilitation, in which services are provided at home by a mobile rehabilitation team, and should be regarded as a part of the stroke treatment pathway. Multidisciplinary, specialist stroke ESD teams should plan and co-ordinate discharge from hospital and provide rehabilitation in the community (53). The target audience is mainly patients with mild or moderate stroke symptoms, which includes approximately 30% of the stroke population in most settings. Meta-analyses (52) show that reduces the length of hospital stay and reduces the odds of dying due to stroke or being dependent after stroke by 20%. However, another study evaluated the real-world aspects (ecological validity) of ESD (54) and the results were similar, with significantly shorter lengths of hospital stay and reported significantly higher levels of satisfaction with services received (54). The carers also experienced the ESD as positive (Fig. 7).

**Slow-stream rehabilitation**

Approximately 50–70% of stroke patients have a moderate to severe stroke. They also need access to stroke rehabilitation, either during a prolonged stay in hospital or with adequate rehabilitation to address their needs in the community. With continued recovery, there is an increase in stamina, and the intensity of training may increase. Stroke survivors are often physically deconditioned, with muscle weakness in both the affected and unaffected sides, and reduced cardiorespiratory fitness. Physical fitness training after stroke has many benefits (55). It reduces disability, improves walking ability, and may improve other stroke-related deficits, such as cognition, mood and fatigue. Patients with aphasia and better stamina can receive high-intensity speech training over a long period. This type of training has been shown to improve functional communication (56). ADL training, provided in the home-setting after discharge until 1 year after stroke, has also been shown to have a beneficial effect (57).

**Back into life**

The ultimate goal for rehabilitation is for the person who needs rehabilitation, to be living a life again with quality. The World Stroke Organization (WSO) has stated a priority to identify and evaluate the best ways to address and improve life after stroke (58). Patient organizations have launched the Global Stroke Bill of Rights (59), in which the importance of longer-term support is highlighted.

Reports from stroke survivors show that they experience unmet needs in terms of communication, social relationships, loneliness, fatigue and finances (60), as well as lack of rehabilitation (61). It is estimated that approximately 25% of strokes occur in people of working age (62), 18–65 is what has been applied in most studies whose needs may also include support to return to work (63–65).

**CONCLUSION**

The burden of stroke, both for society and for individuals, is high. The consequences for individuals vary, depending on the type of stroke, its severity, and location, and on the person’s life situation. The need for rehabilitation is often not met, due to restricted resources and their uneven distribution. This means that the rehabilitation delivered needs to be adapted to the individual, as well as to the society in which they live. Increasing knowledge of neurophysiology and evidence from meta-analyses will lead to continuing changes to rehabilitation in practice. With continued willingness to change, stroke rehabilitation providers can continue to make a difference and improve the lives of stroke survivors.

**REFERENCES**

1. Global Burden of Disease Collaborators – Feigin VL, Nguyen G, Cercy K, Johnson CO, Alam T, et al. Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. N Engl J Med 2018; 379: 2429–2437.
2. Avan A, Digaleh H, Di Napoli M, Stranges S, Behrouz R, Shojaeianbabaie G, et al. Socioeconomic status and stroke incidence, prevalence, mortality, and worldwide burden: an ecological analysis from the Global Burden of Disease Study 2017. BMC Med 2019; 17: 191.
3. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring,
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surveillance, and modelling. Lancet Neurol 2009; 8: 345–354.

4. Kassebaum NJ, Arora M, Barber RM, Bhutta ZA, Brown J, Carter A, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388: 1603–1658.

5. Stroke Unit Trialists’ Collaboration. Organised inpatient (stroke unit) care for stroke. Cochrane Database Syst Rev 2013; 9: CD000197.

6. Wardlaw JM, Murray V, Berge E, del Zoppo GJ. Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev 2014; 7: CD002013.

7. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2017; 389: 1723–1731.

8. Langhorne P, Legg L. Evidence behind stroke rehabilitation. J Neurol Neurosurg Psychiatry 2003; 74 (suppl 4): iv18–iv21.

9. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ 2015; 350: h1258.

10. Ali M, Eng JJ, Bernhardt J, Sunnahrhen KS, Brady M. More outcomes than trials: a call for consistent data collection across stroke rehabilitation trials. Int J Stroke 2013; 8: 18–24.

11. Kwakkel G, Van Wegen E, Burridge J, Winsten C, Van Dokkum L, Alt Murphy M, et al. Standardized measurement of quality of upper limb movement after stroke: consensus-based core recommendations from the Second Stroke Recovery and Rehabilitation Roundtable. Neurorehabil Neural Repair 2019; 33: 951–958.

12. Fugl-Meyer AR, Jaasko L, Leyman I, Olsson S, Stegland S. The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. Scand J Rehabil Med 1975; 7: 13–31.

13. Fugl-Meyer AR, Jaasko L, Norlin V. The post-stroke hemiplegic patient. II. Incidence, mortality, and vocational return in Gothenburg, Sweden with a review of the literature. Scand J Rehabil Med 1975; 7: 73–83.

14. Kennedy FB, Pozen TJ, Gabelman EH, Tuthill JE, Zaentz SD. Stroke intensive care – an appraisal. American Heart Journal 1970; 80: 188–196.

15. Norris J, Hachinski V. Intensive care management of stroke patients. Stroke 1976; 7: 573–577.

16. Von Arbin M, Britton M, De Faire U, Helmers C, Miah K, Murray V. A study of stroke patients treated in a non-intensive stroke unit or in general medical wards. Acta Med Scand 1980; 208: 81–85.

17. Von Arbin M, Britton M, De Faire U, Helmers C, Miah K, Murray V, et al. A stroke unit in a medical department: organization and the first 100 patients. Acta Med Scand 1980; 208: 81–85.

18. Indredavik B, Bakke F, Solberg R, Rokseth R, Haavel LH. Holme I. Benefit of a stroke unit: a randomized controlled trial. Stroke 1991; 22: 1026–1031.

19. Juby L, Lincoln N, Berman P. The effect of a stroke rehabilitation unit on functional and psychological outcome: a randomised controlled trial. Cerebrovascular Diseases 1996; 6: 106–110.

20. Fagerberg Br, Claesson L, Gosman-Hedström G, Blomstrand C. Effect of acute stroke unit care integrated with care continuum versus conventional treatment: a randomized 1-year study of elderly patients: the Goteborg 70+ Stroke Study. Stroke 2000; 31: 2578–2584.

21. Indredavik B, Bakke F, Sjördahl SA, Rokseth R, Haavel LH. Stroke unit treatment 10-year follow-up. Stroke 1999; 30: 1524–1527.

22. Shumway-Cook A, Woollacott MH. Motor control: translating research into clinical practice. 3rd edn. Baltimore, MD: Lippincott Williams & Wilkins; 2007.

23. Grillner S, Zangger F. The effect of dorsal root transection on the efferent motor pattern in the cat’s hindlimb during locomotion. Acta Physiol Scand 1984; 120: 393–405.

24. Barbeau H, Rossignol S. Recovery of locomotion after chronic spinalization in the adult cat. Brain Res 1987; 412: 84–95.

25. Norman KE, Pepin A, Ladouceur M, Barbeau H. A treadmill apparatus and harness support for evaluation and rehabilitation of gait. Arch Phys Med Rehabil 1995; 76: 772–778.

26. Visintin M, Barbeau H, Korner-Bitensky N, Mayo NE. A new approach to retrain gait in stroke patients through body weight support and treadmill stimulation. Stroke 1998; 29: 1122–1128.

27. Hesse S, Bertelt C, Jahnke MT, Schaaffrin A, Baake P, Ma­ lezic M, et al. Treadmill training with partial body weight support compared with physiotherapy in nonambulatory hemiparetic patients. Stroke 1995; 26: 976–981.

28. Nilsson L, Carlsson J, Danielsson A, Fugl-Meyer A, Hellstrom K, Kristensen L, et al. Walking training of patients with hemiparesis at an early stage after stroke: a comparison of walking training on a treadmill with body weight support and walking training on the ground. Clin Rehabil 2001; 15: 515–527.

29. Mehrholz J, Thores S, Elnser B. Treadmill training and body weight support for walking after stroke. Cochrane Database Syst Rev 2017; 8: CD002840.

30. Danielsson A, Sunnahrhen KS. Oxygen consumption during treadmill walking with and without body weight support in patients with hemiparesis after stroke and in healthy subjects. Arch Phys Med Rehabil 2000; 81: 953–957.

31. Bach-y-Rita P. Brain plasticity as a basis of the development of rehabilitation procedures for hemiplegia. Scand J Rehabil Med 1981; 13: 73–83.

32. Nudo RJ, Friel KM. Cortical plasticity after stroke: implications for rehabilitation. Rev Neurol (Paris) 1999; 155: 713–717.

33. Nudo RJ, Milliken GW. Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. J Neurophysiol 1996; 75: 2144–2149.

34. Taub E, Miller NE, Novack TA, Cook EW, Fleming W, Ne­ pomuceno C, et al. Technique to improve chronic motor deficit after stroke. Arch Phys Med Rehabil 1993; 74: 347–354.

35. Brogårdh C, Sjölund BH. Constraint-induced movement therapy in patients with stroke: a pilot study on effects of small group training and of extended mitt use. Clin Rehabil 2003; 17: 721–727.

36. Hammer AM, Lindmark B. Effects of forced use on arm function in the subacute phase after stroke: a randomized, clinical pilot study. Phys Ther 2009; 89: 526–539.

37. Taub E, Crago JE, Burgio LD, Grooms TE, Cook III EW, DeLuca SC, et al. An operant approach to rehabilitation medicine: overcoming learned nonuse by shaping. J Exp Anal Behav 1994; 61: 281–293.

38. Wolf SL, Thompson PA, Winston CJ, Miller JP, Blanton SR, Nichols-Larsen DS, et al. The EXCITE stroke trial: com­ paring early and delayed constraint-induced movement therapy. Stroke 2010; 41: 2309–2315.

39. Corbetta D, Sirtoni V, Castellini G, Moja L, Gatti R. Con­ straint-induced movement therapy for upper extremities in people with stroke. Cochrane Database Syst Rev 2015; 10: CD004433.

40. Gallesse V, Goldman A. Mirror neurons and the simulation theory of mind-reading. Trends Cogn Sci 1998; 2: 403–408.

41. Iacoboni M, Molnar-Szakacs I, Gallesse V, Buccino G, Mazzio­ otta JC, Rizzolatti G. Grasping the intentions of others with one’s own mirror neuron system. PLoS Biol 2005; 3:e79.

42. Buccino G, Solodkin A, Small SL. Functions of the mirror
neuron system: implications for neurorehabilitation. Cogn Behav Neurol 2006; 19: 55–63.
43. Yavuzer G, Selles R, Sezer N, Sutbeyaz S, Bussmann JB, Koseoglu F, et al. Mirror therapy improves hand function in subacute stroke: a randomized controlled trial. Arch Phys Med Rehabil 2008; 89: 393–398.
44. Thiere H, Mehrholz J, Pohl M, Behrens J, Dohle C. Mirror therapy for improving motor function after stroke. Cochrane Database Syst Rev 2012; 3: CD008449.
45. Ward NS, Cohen LG. Mechanisms underlying recovery of motor function after stroke. Arch Neurol 2004; 61: 1844–1848.
46. Hummel FC, Cohen LG. Non-invasive brain stimulation: a new strategy to improve neurorehabilitation after stroke? Lancet Neurol 2006; 5: 708–712.
47. Sawaki L, Wu CW-H, Kaelin-Lang A, Cohen LG. Effects of somatosensory stimulation on use-dependent plasticity in chronic stroke. Stroke 2006; 37: 246–247.
48. Mehrholz J, Pohl M, Platz T, Kugler J, Elsner B. Electromechanical and robot-assisted arm training for improving activities of daily living, arm function, and arm muscle strength after stroke. Cochrane Database Syst Rev 2018; 9: CD006876.
49. Norrving B, Barrick J, Davalos A, Dichgans M, Cordonnier C, Guekht A, et al. Action Plan for Stroke in Europe 2018–2030. Eur Stroke J 2018; 3: 309-336.
50. Langhorne P, Pollock A. What are the components of effective stroke unit care? Age Ageing 2002; 31: 365–371.
51. Langhorne P, Baylan S, Trialists ESD. Early supported discharge services for people with acute stroke. Cochrane Database Syst Rev 2017; 5: CD006185.
52. Daniel K, Wolfe C, Busch M, McKEvitt C. What are the social consequences of stroke for working-aged adults? A systematic review. Stroke 2009; 40: e431–e440.
53. Palstam A, Tornbom M, Sunnerhagen KS. Experiences of returning to work and maintaining work 7 to 8 years after a stroke: a qualitative interview study in Sweden. BMJ Open 2018; 8: e021182.
54. Tornbom K, Lundalv J, Sunnerhagen KS. Long-term participation 7–8 years after stroke: experiences of people in working-age. PLoS One 2019; 14: e0213447.
55. Gard G, Persah-Rasmussen H, Brogårdh C, Nilsson Å, Lindgren I. Need for structured healthcare organization and support for return to work after stroke in Sweden: experiences of stroke survivors. J Rehabil Med 2019; 51: 741–748.