

Evaluating the use of robotic and virtual reality rehabilitation technologies to improve function in stroke survivors: A narrative review

William E Clark¹ , Manoj Sivan^{1,2} and Rory J O'Connor^{1,2,3}

Abstract

This review evaluates the effectiveness of robotic and virtual reality technologies used for neurological rehabilitation in stroke survivors. It examines each rehabilitation technology in turn before considering combinations of these technologies and the complexities of rehabilitation outcome assessment. There is high-quality evidence that upper-limb robotic rehabilitation technologies improve movement, strength and activities of daily living, whilst the evidence for robotic lower-limb rehabilitation is currently not as convincing. Virtual reality technologies also improve activities of daily living. Whilst the benefit of these technologies over dose-controlled conventional rehabilitation is likely to be small, there is a role for both technologies as part of a broader rehabilitation programme, where they may help to increase the intensity and amount of therapy delivered. Combining robotic and virtual reality technologies in a rehabilitation programme may further improve rehabilitation outcomes and we would advocate randomised controlled trials of these technologies in combination.

Keywords

Stroke, brain injury, spinal cord injury, neurorehabilitation, therapy, assistive technology, activities of daily living

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Introduction

Rehabilitation plays a vital role in improving the independence and quality of life (QOL) of people with acquired neurological conditions. The effectiveness of current multidisciplinary rehabilitation strategies is well established for people with acquired neurological conditions.^{1,2} However, many individuals are still left with residual disability that affects their ability to function in daily life.³ There is great interest in exploring novel rehabilitation technologies to augment conventional therapies to reduce neurological disability and improve function.

Acquired neurological conditions are the commonest cause of severe disability acquired during adulthood. Stroke is the most common of these, affecting 16 million people a year globally.^{4,5} The number of stroke survivors living in the UK is expected to more than double by 2035, as the estimated cost to the UK economy rises from £26 billion a year to £75 billion,⁶

making this a major challenge for the future. Stroke related lower-limb impairment impacts on the ‘mobility’ domain of QOL, and upper-limb impairment on all other QOL domains.⁷ Hence, rehabilitation of stroke survivors is of vital importance.

One of the major limitations of conventional rehabilitation programmes is an inadequate dose of rehabilitation therapy, in terms of repetition and intensity.

¹Academic Department of Rehabilitation Medicine, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Faculty of Medicine and Health, University of Leeds, Leeds, UK

²National Demonstration Centre for Rehabilitation Medicine, Leeds Teaching Hospitals NHS Trust, Leeds, UK

³National Institute of Health Research Devices for Dignity MedTech Co-operative, Royal Hallamshire Hospital, Glossop Road, Sheffield, UK

Corresponding author:

Manoj Sivan, Academic Department of Rehabilitation Medicine, University of Leeds, D Floor, Martin Wing, Leeds General Infirmary, Leeds LS1 3EX, UK.
Email: m.sivan@leeds.ac.uk



Patients often receive insufficient rehabilitation therapy after an acquired neurological condition.⁸ The current evidence suggests that there is a high practice threshold required to achieve significant upper-limb functional improvements.⁹ This threshold is achievable in humans¹⁰ to deliver the repetition and intensity that are thought to be important in experience-dependent plasticity.¹¹ Pollock et al. found moderate quality evidence of benefit from a high dose of task practice but not for a low dose.¹² There is hope that new approaches to rehabilitation could increase the therapy dose.

The use of novel rehabilitation technologies to deliver these increased doses is a rapidly growing field. Rehabilitation technology development has been identified as a priority area for research by the Medical Rehabilitation Research Coordinating committee (USA).⁸ There are a wide range of technologies with applications in rehabilitation including robotic and virtual reality technologies, assistive devices, neuroprostheses and even smartphone applications.⁸ Rehabilitation technologies are defined as 'those whose primary purpose is to maintain or improve an individual's functioning and independence, to facilitate participation and to enhance overall well-being'.¹³ Rehabilitation technologies therefore overlap partially with robotics but also encompass non-robotic technologies, e.g. environmental control systems and communication devices. This review focuses on the application of robotic and virtual reality technologies in stroke survivors.

Robotic technologies

A robot is 'a machine capable of carrying out a complex series of actions automatically'.¹⁴ Robotic technologies in rehabilitation are an established and rapidly growing field. Robotic technologies in rehabilitation encourage motor re-learning with the goal of reducing impairment.¹⁵ Robotic technologies offer numerous potential advantages over conventional therapies, chief among these being the ability to provide high-intensity repetitive training.

A Cochrane systematic review¹⁶ found high-quality evidence of a benefit of upper-limb robotics (e.g. MIME, Bi-Manu-Track and ARMin) on activities of daily living ADL, arm function and arm muscle strength, although the effect size is small and heterogeneity among studies substantial. These findings are consistent with Ferreira et al., whose recent systematic review found a benefit of upper-limb robotics compared to conventional therapy on motor control and strength, but not on other measures of body function or structure; ADL outcomes were not analysed.¹⁷ Another recent systematic review by Veerbeek et al. also found a benefit of upper-limb robotics (when compared to conventional therapy) on motor control and strength

but no benefit on ADL.¹⁸ This may be explained by the inclusion of more studies with over twice the number of participants in the Mehrholz et al. Cochrane review¹⁶ ADL analysis in comparison to the Veerbeek et al. analysis,¹⁸ as evidenced by a similar standardised mean difference value but a wider confidence interval in the Veerbeek review. However, a subgroup analysis for dose by Veerbeek et al. found a statistically significant benefit of robotics on ADLs for non-dose-matched trials but not for dose-matched trials¹⁸; unfortunately, there was no sensitivity analysis on dose matching in the Cochrane review¹⁶ to explore the impact on their findings. Rehabilitation dose is known to be very important; indeed, sub-group analysis by Ferreira et al. demonstrated an impact of the number of treatment sessions and treatment volume on the effects seen.¹⁷ We therefore conclude that upper-limb robotics improve ADLs at least as much as conventional therapy, but there is currently insufficient evidence of superiority.

A systematic review of robotics for lower-limb rehabilitation, including the Lokomat and Gait Trainer devices, demonstrated that the use of electro-mechanical-assisted gait-training devices in combination with physiotherapy increases the chance of walking independently after stroke.¹⁹ However, the devices were not shown to improve walking velocity or distance walked in 6 min. The greatest benefits in independence in walking and walking speed were achieved by participants who were non-ambulatory at the start of the study and in those for whom the interventions were applied early post-stroke.

The evidence so far suggests that it is unlikely that robotic systems will provide additional benefit over conventional rehabilitation methods with exactly equivalent amount and intensity of therapy.²⁰ However, even if that is true, there is still a place for robotic systems, as in most settings, it is simply not feasible to provide such a high dose of intensive conventional rehabilitation therapy due to a lack of resources, especially a lack of therapist time. There might be concern amongst some therapists that robotic developments are a threat to their jobs; however, this is not the case, as these robotic systems still need setup, programming and monitoring. Instead, these systems will enable therapists to use their time more efficiently by supervising several individuals simultaneously to achieve better rehabilitation outcomes, effectively maximising the benefit of the limited therapist resource.²¹

Concerns about the costs of robotic devices must also be put into perspective. Whilst devices are undoubtedly costly at the present time, one needs to consider the cost savings of therapist time, where patients use robotic systems independently, as well as wider economic benefits related to productivity gains. Furthermore, with such a proliferation of devices, it is

likely that competition and mass-production will eventually drive prices down. There are also some low-cost robotic devices in early stages of research.²² A formal up-to-date cost-effectiveness analysis is lacking; however, work from 2011 suggested that the cost-effectiveness of robotic devices was comparable to that of conventional therapy.²³

Virtual reality technologies

Virtual reality (VR) involves using interactive simulations produced by computer technology to allow users to engage in environments that closely resemble the real-world. VR can be used for simulated independent practice at higher doses than that could be achieved through conventional therapy.¹² These technologies therefore share some of the benefits of robotics in terms of increasing training intensity and repetitions, and reducing therapist time. The typical portrayal in the lay media of VR is usually that of a so-called ‘immersive’ VR, with a head-mounted screen.²⁴ However, low immersion systems involving a simple flat screen are much more commonplace. Indeed, commercially available video gaming systems have been adapted for use in VR rehabilitation.²⁵

The provision of visual and often multi-sensory feedback is a key attribute of VR technologies. Individuals who have survived neurological injuries such as a stroke often have sensory impairments, including in proprioception, and therefore have lost some of the normal feedback associated with a typical motor action.¹² It is recognised that feedback plays an important role in skill acquisition²⁶ and is an essential element in experience-dependent plasticity.²⁷ In motor learning, it is important to receive feedback not just on the end results – ‘success or failure’ – but on movement performance²⁸; this is possible with the use of VR technologies.

VR can also help with patient engagement and motivation.²⁹ Psychological problems are common after stroke and SCI,^{30,31} and strategies that focus on patient engagement are important for successful rehabilitation.⁸ The level of engagement affects the degree of active participation which in turn can improve outcomes. Mekki et al. demonstrated that when individuals were given both feedback on their walking speed and competition against virtual opponents, there was increased muscle activity.³² Laver et al. in their review of VR technologies recommended that future studies evaluate the impact of VR on patient motivation and engagement.³³

There is growing interest in VR technologies, with 35 new trials published in just a two-year period.³³ The most up-to-date Cochrane review found a significant benefit to upper-limb function with a moderate

effect size (standardised mean difference 0.49, 95% confidence interval 0.21–0.77) when VR was used as an adjunct to usual care but not when compared to dose-controlled conventional therapy.³³ However, there was a small benefit in ADLs with VR technology, which increased to a moderate benefit when therapy was not dose-controlled. Thus, whilst VR may not be superior to conventional rehabilitation therapy, it could be a useful adjunct to increase therapy duration and intensity.

Combination technologies

It is important to remember that rehabilitation is a multi-disciplinary and multi-modal endeavour and not a ‘one size fits all’ intervention. A combination of interventions may be better suited to treat the multifactorial nature of the disability associated with neurological conditions, such as motor and sensory impairments, cognitive problems and psychological issues. Veerbeek et al. recommend that robotic therapy is seen not as a ‘standalone therapy’, but is integrated into a comprehensive rehabilitation programme.¹⁷

The combination of VR and robotic technology is particularly interesting as it can theoretically activate more of the neural circuits involved in motor learning, and hence promoting neuroplasticity.^{34,35} A number of controlled trials have investigated the combination of VR and robotic technologies in upper-limb rehabilitation. Thielbar et al. investigated the use of a robot-assisted finger training system linked to the movements of a virtual hand and found a significant improvement in upper-limb activity and task performance compared to controls.³⁶ Byl et al. examined a robotic orthosis in a virtual training environment and found no between-group differences.³⁷ Unfortunately, not only did both studies have very few participants but both used a control group of physical therapy only, which makes it impossible to determine if any benefits identified are related to the combination technology or simply one of its components, e.g. the robotics. Klamroth-Marganska et al. looked at the effects of the exoskeleton robot ARMin, which provides intensive task-specific training in a virtual environment, as compared to conventional therapy and found a small benefit in the Fugl – Meyer upper-extremity scale which was not clinically significant.³⁸ Whilst this trial had a moderate sample size, it again compared the combination technology to physical therapy only. There are currently no randomised controlled trials (RCTs) of dual VR-robotic technology combinations for upper-limb rehabilitation with a single technology control group.

Early work by Mirelman et al. with participants with lower-limb impairments found that in individuals given combination VR and robotic therapy, compared to

robot therapy alone, there was a significant increase in walking speed and distance.³⁹ Furthermore, individuals reported less fatigue in the sessions, required shorter rest time and fewer therapist cues, despite the number of repetitions being the same. Uçar et al. examined the effectiveness of the Lokomat device, a treadmill and lower-limb robotic exoskeleton combination together with a virtual reality screen display, as compared to conventional therapy.⁴⁰ They found a significant improvement in the Timed Up and Go test and the Ten Metre Walk test in the intervention group as compared to the control group.

It is important to be clear about what is not true combination technology. Many trials of upper-limb robotics have included some form of visual feedback via a computer screen. Kutner et al. showed a series of LEDs on a screen and participants had to extend their hand up to the target LED.⁴¹ Kahn et al. used a screen to display the target angles for arm 'yaw and pitch' along with the actual 'yaw and pitch' angles of the participant's arm.⁴² Masiero et al. used the screen to show a virtual arm with arrows indicating the direction that participants should move their arm.⁴³ The common theme in all these cases is that, whilst technology is used to provide simple visual feedback, participants are not engaging in environments that closely resemble the real world, and hence this does not meet the criteria for virtual reality technology.

Outcome assessment

Assessment of rehabilitation outcomes is complex, due to in part to the personalised nature of rehabilitation, as well as the need to assess outcomes across the International Classification of Function, Disability and Health (ICF) domains.¹² Whilst we need to ensure we are measuring the correct markers in our research,⁸ determining what patients want remains ill-defined.⁴⁴ There is certainly no consensus among academics on what the best outcome measures are – a recent systematic review of upper-limb outcome measures in stroke rehabilitation found 48 different outcome measures used in these studies with only 15 outcome measures used in more than 5% of the studies.⁴⁵ Sivan et al. looked specifically at upper-limb outcome measures for robotic rehabilitation and found that whilst most studies have measured outcomes at the impairment level, this does not necessarily translate into measurement of limitation of activity or restriction of participation.⁴⁶ They proposed a systematic framework for selecting measures based on time since stroke and extent of arm weakness. Some authors, however, argue against activity and participation measures, as these can be improved with compensatory mechanisms and as such the actual motor impairment is not being

assessed.⁹ Geroin et al. found no consensus on lower-limb robotic rehabilitation outcomes, with 45 outcome measures in use, many of which have poor psychometric properties.⁴⁷

Psychometric evaluations of cognitive outcome measures are less common, despite the fact that cognitive impairment is common as a result of both age⁸ and neurological conditions such as stroke,⁴⁸ and that cognitive impairment affects an individual's ability to function in daily life.⁴⁹ Many trials have excluded patients with cognitive impairments, which is disappointing given the potential for VR technologies in particular to improve cognition.³³ Moreover, very few trials have assessed QOL or cost-effectiveness, although evaluation of both is essential, for a new rehabilitation intervention to be adopted in a publicly-funded health care system.⁴⁴ Robust evidence is required to be able to justify to healthcare commissioners why they should fund new rehabilitation technologies. A recent Cochrane review made a recommendation that future trials should include measures of ADL, QOL and cost-effectiveness.¹⁹

Discussion

There is high-quality evidence that upper-limb robotic technology improves muscle strength, motor function and ADLs. There is evidence from subgroup analyses that greater numbers of treatment sessions and greater treatment volume are related to motor outcomes.¹⁸ This is consistent with the findings of Pollock et al., who suggested a greater benefit for higher dose therapy.¹² Robotic lower-limb rehabilitation increased the odds of individuals walking independently but did not affect walking velocity or the distance walked in 6 min. We would urge caution in the interpretation of the independent walking findings, as this analysis was significantly flawed, with the majority of studies seeing no change in walking independence between the start and end of the study.

Upper-limb VR rehabilitation compared to conventional therapy improves ADLs but not upper-limb motor function. Whilst the ADL benefit is small when VR is compared to dose-controlled conventional therapy, this increases to a moderate benefit when not dose controlled. This suggests a potential role for VR as an adjunct to increase total therapy time and therefore rehabilitation benefit.

Robotic technology when combined with VR may offer some benefits in patients with lower-limb impairments by increasing walking speed and distance, although this is based on the findings of a single small trial. The studies which looked at combined robotic and VR rehabilitation of the upper-limb show mixed results, with one small trial finding a treatment benefit,

another small trial no benefit and a third larger trial a small treatment benefit which is not clinically relevant. Interpretation in each of these studies is hampered by the lack of a single technology control group. Whilst the literature on combination technologies is currently limited, this is a promising area of research worthy of further investigation. It can often be difficult to determine from reading studies whether the reported ‘virtual environment’ used meets the criteria for virtual reality technology. Therefore, we would encourage authors to provide enough information on their intervention for this judgement to be made.

This literature review has examined the effectiveness of robotic and VR technologies on neurological rehabilitation. One limitation of this review is the failure to examine other forms of technologies with applications in rehabilitation. Secondly, although the intention of this review is not to limit itself by neurological diagnosis, the majority of the published literature concerns stroke survivors, which tends to be representative of the neurological rehabilitation literature as a whole.

This review has examined the effectiveness of rehabilitation technologies on stroke survivors only; hence, generalisability to patients with other neurological conditions may be limited. We would encourage research on other patient groups to confirm applicability of the findings in stroke survivors to a wider population. Another limitation is that whilst there are a wealth of studies of robotic-enhanced rehabilitation, there is great variability between studies in terms of participants’ characteristics, rehabilitation regime, therapy duration and intensity. Most are also small in size. Some consistency between studies would help; a starting point would be agreement on the use of outcome measures.

In summary, there is high-quality evidence that upper-limb robotic technology is as effective as dose-controlled conventional therapy at improving ADLs, motor function and strength; the evidence for robotic-enhanced lower-limb rehabilitation is currently not as convincing. There is a small benefit in ADLs with VR technologies as compared to dose-controlled conventional therapy; however, no significant difference for upper-limb function, gait speed or balance. Nevertheless, both technologies can be beneficial as part of a broader rehabilitation programme and may help to improve the intensity and amount of rehabilitation delivered. There is a need for RCTs of combined VR and robotic technologies, although we would also advocate the exploration of other technology combinations. RCTs should assess a range of outcomes corresponding to the ICF framework but should endeavour to include measures of ADL, cognition, QOL and cost-effectiveness.

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WEC researched the literature and wrote the first draft of the article. All authors reviewed and edited the article and approved the final version of the article.

ORCID iD

William E Clark  <https://orcid.org/0000-0001-5376-0175>

References

1. Veerbeek JM, van Wegen E, van Peppen R, et al. What is the evidence for physical therapy poststroke? A systematic review and meta-analysis. *PLoS One* 2014; 9: e87987.
2. Pollock A, Baer G, Campbell P, et al. Physical rehabilitation approaches for recovery of function, balance and walking after stroke. *Cochrane Database Syst Rev* 2014; 4: CD001920.
3. Yang Y, Shi Y, Zhang N, et al. The disability rate of 5-year post-stroke and its correlation factors: a national survey in China. *PLoS One* 2016; 11: e0165341.
4. Murray CJ and Lopez AD. Mortality by cause for eight regions of the world: global burden of disease study. *Lancet* 1997; 349: 1269–1276.
5. World Health Organization. *Neurological disorders: public health challenges*. Geneva: WHO Press, 2006.
6. Patel A, Berdunov V, King D, et al. *Executive summary Part 2: societal cost of Stroke in the next 20 years and potential returns from increased spending on research*. London: Stroke Association, 2017.
7. Franceschini M, La Porta F, Agosti M, et al. Is health-related-quality of life of stroke patients influenced by neurological impairments at one year after stroke? *Eur J Phys Rehabil Med* 2010; 46: 389–399.
8. Frontera WR, Bean JF, Damiano D, et al. Rehabilitation Research at the National Institutes of Health: moving the field forward (Executive Summary). *Am J Occup Ther* 2017; 97: 393–403.
9. Krakauer JW, Carmichael ST, Corbett D, et al. Getting neurorehabilitation right – what can we learn from animal models? *Neurorehabil Neural Repair* 2012; 26: 923–931.

10. Birkenmeier RL, Prager EM and Lang CE. Translating animal doses of task-specific training to people with chronic stroke in 1-hour therapy sessions: a proof-of-concept study. *Neurorehabil Neural Repair* 2010; 24: 620–635.
11. Subramanian SK, Massie CL, Malcolm MP, et al. Does provision of extrinsic feedback result in improved motor learning in the upper limb poststroke? A systematic review of the evidence. *Neurorehabil Neural Repair* 2010; 24: 113–124.
12. Pollock A, Farmer SE, Brady MC, et al. Interventions for improving upper limb function after stroke. *Cochrane Database Syst Rev* 2014; 11: CD010820.
13. World Health Organization. Assistive devices and technologies, www.who.int/disabilities/technology/en/ (2018, accessed 8 November 2018).
14. Oxford Dictionaries. Definition of robot in English, <https://en.oxforddictionaries.com/definition/robot> (2018, accessed 8 November 2018).
15. Fassoli SE, Krebs HI and Hogan N. Robotic technology and stroke rehabilitation: translating research into practice. *Top Stroke Rehabil* 2004; 11: 11–19.
16. Mehrholz J, Pohl M, Platz T, et al. 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.
17. Ferreira FMRM, Chaves MEA, Oliveira VC, et al. Effectiveness of robot therapy on body function and structure in people with limited upper limb function: a systematic review and meta-analysis. *PLoS One* 2018; 13: e0200330.
18. Veerbeek JM, Langbroek-Amersfoort AC, van Wegen EEH, et al. Effects of robot-assisted therapy for the upper limb after stroke. *Neurorehabil Neural Repair* 2017; 31: 107–121.
19. Mehrholz J, Thomas S, Werner C, et al. Electromechanical-assisted training for walking after stroke. *Cochrane Database Syst Rev* 2017; 5: CD006185.
20. Kwakkel G, van Wegen EE and Meskers CM. Invited commentary on comparison of robotics, functional electrical stimulation, and motor learning methods for treatment of persistent upper extremity dysfunction after stroke: a randomized controlled trial. *Arch Phys Med Rehabil* 2015; 96: 991–993.
21. Lo K, Stephenson M and Lockwood C. Effectiveness of robotic assisted rehabilitation for mobility and functional ability in adult stroke patients: a systematic review protocol. *JBI Database System Rev Implement Rep* 2017; 15: 39–48.
22. Sivan M, Gallagher J, Makower S, et al. Home-based computer assisted arm rehabilitation (hCAAR) robotic device for upper limb exercise after stroke: results of a feasibility study in home setting. *J Neuroeng Rehabil* 2014; 11: 163.
23. Wagner TH, Lo AC, Peduzzi P, et al. An economic analysis of robot-assisted therapy for long-term upper-limb impairment after stroke. *Stroke* 2011; 42: 2630–2632.
24. Gaggioli A, Keshner E, Weiss PL, et al. *Advanced technologies in rehabilitation*. United States: IOS Press, 2009.
25. Levac D, Espy D, Fox E, et al. “Kinect-ing” with clinicians: a knowledge translation resource to support decision making about video game use in rehabilitation. *Phys Ther* 2015; 95: 426–440.
26. Muratori LM, Lamberg EM, Quinn L, et al. Applying principles of motor learning and control to upper extremity rehabilitation. *J Hand Ther* 2013; 26: 94–102.
27. Kleim JA and Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *J Speech Lang Hear Res* 2008; 51: S225–S239.
28. Cirstea MC and Levin MF. Improvement of arm movement patterns and endpoint control depends on type of feedback during practice in stroke survivors. *Neurorehabil Neural Repair* 2007; 21: 398–411.
29. Lewis GN and Rosie JA. Virtual reality games for movement rehabilitation in neurological conditions: how do we meet the needs and expectations of the users? *Disabil Rehabil* 2012; 34: 1880–1886.
30. Kneebone II and Lincoln NB. Psychological problems after stroke and their management: state of knowledge. *Neurosci Med* 2012; 3: 83–89.
31. Post MWM and van Leeuwen CMC. Psychosocial issues in spinal cord injury: a review. *Spinal Cord* 2012; 50: 382–389.
32. Mekki M, Delgado AD, Fry A, et al. Robotic rehabilitation and spinal cord injury: a narrative review. *Neurotherapeutics* 2018; 15: 604–617.
33. Laver KE, Lange B, George S, et al. Virtual reality for stroke rehabilitation. *Cochrane Database Syst Rev* 2017; 11: CD008349.
34. Saleh S, Bagee H, Qiu Q, et al. Mechanisms of neural reorganization in chronic stroke subjects after virtual reality training. *Conf Proc IEEE Eng Med Biol Soc* 2011; 2011: 8118–8121.
35. Comani S, Velluto L, Schinaia L, et al. Monitoring neuro-motor recovery from stroke with high-resolution EEG, robotics and virtual reality: a proof of concept. *IEEE Trans Neural Syst Rehabil Eng* 2015; 23: 1106–1116.
36. Thielbar KO, Lord TJ, Fischer HC, et al. Training finger individuation with a mechatronic-virtual reality system leads to improved fine motor control post-stroke. *J Neuroeng Rehabil* 2014; 11: 171.
37. Byl NN, Abrams GM, Pitsch E, et al. Chronic stroke survivors achieve comparable outcomes following virtual task specific repetitive training guided by a wearable robotic orthosis (UL-EXO7) and actual task specific repetitive training guided by a physical therapist. *J Hand Ther* 2013; 26: 343–352.
38. Klamroth-Marganska V, Blanco J, et al. Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomised trial. *Lancet Neurol* 2014; 13: 159–166.
39. Mirelman A, Bonato P and Deutsch JE. Effects of training with a robot-virtual reality system compared with a robot alone on the gait of individuals after stroke. *Stroke* 2008; 40: 169–174.

40. Uçar DE, Paker N and Buqdayci D. Lokomat: a therapeutic chance for patients with chronic hemiplegia. *NeuroRehabilitation* 2014; 34: 447–453.
41. Kutner NG, Zhang R, Butler AJ, et al. Quality-of-life change associated with robotic-assisted therapy to improve hand motor function in patients with subacute stroke: a randomized clinical trial. *Phys Ther* 2010; 90: 493–504.
42. Kahn L, Zygman M, Rymer W, et al. Robot assisted reaching exercise promotes arm recovery in chronic hemiparetic stroke: a randomized controlled pilot study. *J NeuroEng Rehabil* 2006; 3: 12.
43. Masiero S, Celia A, Rosati G, et al. Robotic-assisted rehabilitation of the upper limb after acute stroke. *Arch Phys Med Rehabil* 2007; 88: 142–149.
44. Cumberland Consensus Working Group, Cheeran B, Cohen L, et al. The future of restorative neurosciences in stroke: driving the translational research pipeline from basic science to rehabilitation of people after stroke. *Neurorehabil Neural Repair* 2009; 23: 97–107.
45. Santisteban L, Térémetz M, Bleton JP, et al. Upper limb outcome measures used in stroke rehabilitation studies: a systematic literature review. *PLoS One* 2016; 11: e0154792.
46. Sivan M, O'Connor RJ, Makower S, et al. Systematic review of outcome measures used in the evaluation of robot-assisted upper limb exercise in stroke. *J Rehabil Med* 2011; 43: 181–189.
47. Geroin C, Mazzoleni S, Smania N, et al. Systematic review of outcome measures of walking training using electromechanical and robotic devices in patients with stroke. *J Rehabil Med* 2013; 45: 987–996.
48. Sun J, Tan L and Yu J. Post-stroke cognitive impairment: epidemiology, mechanisms and management. *Ann Transl Med* 2014; 2: 80.
49. Dassonville P, Nash S, Servajean V, et al. Cognitive impairments and impact on activities of daily living after minor stroke. *Ann Phys Rehabil Med* 2016; 59: e71.