Chapter 12
Effect of Rehabilitation Robot Training on Cognitive Function in Stroke Patients: A Systematic Review and Meta-analysis

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Abstract Objective: Post-stroke cognitive impairment is one of the major dysfunctions after stroke, which can lead to a variety of negative health outcomes. This study aims to evaluate the effects of rehabilitation robotic therapy in post-stroke cognitive impairment patients. Methods: As of December 2022, PubMed, Embase, Web of Science, Cochrane Library, and China National Knowledge Infrastructure were searched through electronic databases. Eligibility criteria RCTs evaluate RCTs of rehabilitation robots on treatment events in patients with cognitive impairment after stroke, compared to control groups. Results: Eight studies were included (n = 431). When combined with routine cognitive training efficacy, rehabilitation robot intervention observably reduced MOCA scores, MBI scores, and FMA scores. Furthermore, the FIM scores and MMSE scores were also better than the control groups. Rehabilitation robot training can improve the cognitive function of stroke patients and is an effective means of stroke rehabilitation.

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12.1 Introduction

Post-stroke cognitive impairment is a clinical syndrome characterized by cognitive impairment that occurs after stroke and lasts for 3–6 months. It is one of the major functional disorders after stroke. Statistically, three quarters of stroke survivors show cognitive impairment, with an incidence of up to 80% [1]. Cognitive dysfunction includes executive force, memory, visual-spatial, and emotional defects associated with depressive/anxiety issues. Post-stroke cognitive impairment makes patients unable to well cooperate with rehabilitation training, hinders the progress of functional recovery, affects the ability of daily life activities, reduces the living quality and survival time of patients, significantly adds the pressure of family and social and economic burden of, and has a negative impact on rehabilitation strategies.

Traditional rehabilitation therapy only carries out routine cognitive training, which consumes a considerable amount of manpower and material resources, and the training process is relatively simple and lacks interest. It relies on the skills and professional knowledge of therapists, and has few active participation of patients, which makes the effect of rehabilitation training not ideal. Currently, increasing evidence highlights the possible impact of robotic rehabilitation on functional recovery in neurology patients. At present, the rehabilitation robot has been gradually applied in clinical rehabilitation, studies have shown that rehabilitation robots can combine task orientation and virtual reality technology, with high intensity, high repetition, and rich environment stimulation characteristics, and can provide personalized auxiliary support, to ensure that the patients in the right way to complete the task needed to keep power, is an important supplement of cognitive rehabilitation training. Previous meta-analysis studies have involved only rehabilitation robots being useful in improving motor function and daily living ability, but no clear study suggests its role in enhancing cognitive skills. Therefore, we strictly included the experiment by standardized screening and demonstrated the conclusion by comparing the scores of five aspects. This article aimed to assess the impact of rehabilitation robot therapy in post-stroke cognitive impairment patients by meta-analysis.

12.2 Methods

In accordance with the comments contained in the Cochrane Interventions System Review Manual, we performed detailed operational definition instructions before starting the search [2], as shown in Fig. 12.1.

Study	Participant characteristics (N, diagnosis, average age, % male)	Setting	Intervention initiation (post-stroke cognitive impairment)	Intervention and control description	Frequency and duration	Outcome measures
SU Lili et al CHINA	n=65 (33 intervention) subacute stroke with cognitive impairment Age range 60-71 years Male 46.7%	Wenzhou Medical University, the First Affiliated Hospital	3weeks-6weeks	Intervention:Upper limb rehabilitation robot training Control:routine cognitive training	Frequency: 1×per day Session length:20 min Duration: 4weeks	Baseline and at 4weeks: ▸ MOCA ▸ MMSE ▸ FMA-UE ▸ MBI
Zhao Defu et al CHINA	n=59 (39 intervention) mild to moderate cognitive impairment after stroke Age range 40-87 years Male 49.2%	unclear	unclear	Intervention:rTMS therapy and upper limb robot virtual scenario training Control:conventional cognitive training and therapy	Frequency: 1×per day Session length:20 min Duration: 20days	Baseline and at 6weeks: ▸ MOCA ▸ MBI
Alfredo Manuli et al Italy	n=60 (30 intervention) mild to moderate cognitive impairment after stroke Age range 32-55 years Male 55.6%	unclear	>6 months	Intervention: Robotic Rehabilitation Control: conventional physical and cognitive therapy	Frequency: 5×per week Session length: 60 min Duration: 8weeks	Baseline and at 16weeks: ▸ FAB BDI FIM COGN MOT TOT MOCA TOT MH TMT VS WEIGL
Irene Aprile et al Italy	n=100(51intervention) post-stroke anxiety neurosis Age range 35-85 years Male unclear	unclear	>6months	Intervention:three robots (Motore, Amadeo, and Diego) and one sensor-based device(Pablo) Control: routine cognitive training	Frequency: 5×per week Session length: 45 min Duration:6 weeks	Baseline and at 4weeks: ▸ several cognitive tests ▸ Fugl - Meyer ▸ Motricity ▸ Index MBI
Sahel Taravati et al Italy	n=37(17intervention) Stroke hemiplegia Age range 33-68 years Male 75.7 %	unclear	4-30months	Intervention: robotic rehabilitation Control: conventional rehabilitation	Frequency: 5×per week Session length: 30-45 min Duration: 4weeks	Baseline and at 8weeks: ▸ MAS ▸ FIM ▸ NEADL ▸ FMA ▸ SS-QOL ▸ MoCA ▸ CES-D
Gi-Wook KIM et al Korea	n=30(15 intervention) chronic stroke patients with hemi plegia Age range 20-85 years Male73.3 %	Department of Rehabilitation Medicine of Chonbuk University Hospital	>6months	Intervention:performed upper extremity training with the Neuro-X® Control:conventional rehabilitation	Frequency:3×per week Session length: 40 min Duration:6 weeks	Baseline and at 4weeks: ▸ FMA ▸ HFT ▸ MAS ▸ K-MMSE
Derya Zengin Metli et al Turkey	n=35 (20 intervention) Stroke patients Age range 51-67 years Male 60%	Ankara Physical Medicine and Rehabilitation Training and Research Hospital	6 - 24 weeks	Intervention: robotic rehabilitation Control:conventional rehabilitation program	Frequency:3×per week Session length:30 min Duration:5 weeks	Baseline and at weeks: ▸ MMT ▸ MI ▸ FMA ▸ FIM ▸ SF-36
SU Lili et al CHINA	n= 60(30intervention) Stroke and hemiplegia were complicated with cognitive dysfunction Age range 61-70 years Male 46.7%	Department of Rehabilitation Medicine, the First Affiliated Hospital of Wenzhou Medical University	unclear	Intervention:Virtual scene task-oriented training of the upper limb robot Control:routine cognitive training	Frequency: 5×per week Session length:40 min Duration: 4weeks	Baseline and at 4weeks: ▸ MOCA ▸ MMSE ▸ MBI

Fig. 12.1 Summary characteristics of studies

12.2.1 Selection Criteria

We included studies evaluating adults (>18 years old) with mild to moderate cognitive impairment after stroke (ischemic or hemorrhagic) according to the WHO definition. Randomized controlled trials involving only evaluating the outcome of rehabilitation robotic interventions and compared with conventional cognitive training and routine rehabilitation training interventions. Different experiments adopt different rehabilitation training systems, but all of them can combine task orientation with virtual reality technology, have the characteristics of high intensity, high repetition, and rich environmental stimulation, and can achieve the purpose of training patients' cognitive function. Only studies reporting the MBI, MoCA, FMA, FIM, and MMSE were included.

12.2.2 Search Strategy

As of December 2022, the electronic databases are retrieved. Combine the selected medical topic titles with free-text terms such as robotics (e.g., remote operation, telerobotics, soft robotics) and stroke (e.g., cerebrovascular accident, cerebral infarction) to create a final search strategy. This can be used in other databases by using the appropriate Boolean operators and search symbols. And the Chinese translation is also used in the Chinese database. Our study does not extend to the grey literature field.

12.2.3 Study Selection and Data Extraction

The authors independently extracted the data into a predesigned spreadsheet including the study background and timeframe, the participants' demographics, the intervention of their descriptors, and outcome measures. Collect data required for meta-analysis including relevant SD and mean difference between baseline and postintervention to assess outcomes. Differences in data extraction or study selection were discussed by two reviewers and commented on and judged by a third reviewer.

12.2.4 Quality Assessment

The reviewers estimated the risk of error in all research that accorded with the selection standard by identifying the bias attributable to randomization, attrition bias, blinding, and reporting through the checklist. The overall high risk was for research with a high risk of bias under different fields, while the moderate risk was for studies with ambiguous information in any domain. Low risk criteria in each domain apply to studies. Grade measures (recommendation, evaluation, progress, and assessment levels) methods were also used for assessing the quality of each outcome and measuring evidence for the tabulated data (MoCA, MBI, FIM, MMSE, and FMA). The initial "high quality" rating of the RCT fell by one level due to serious concern (or a very serious problem on two levels), involving the risk of bias, indirect, inconsistency, or publication bias associated with associated evidence for each result.

12.2.5 Data Analysis

The study characteristics were qualitatively integrated. The mean difference and SD of mean difference were used in the meta-analysis of continuous variables (MoCA, MBI, FIM, MMSE, FMA). Not all research has stated the numerical values of SDs before and after using the robots. Under these circumstances, the direct contact study's authors requested missing data and, if not, we estimated the missing values by an indirect approach. We deal with heterogeneity by using a random effects model caused by the expected population (post-stroke cognitive impairment) and robotic interventions.

12.3 Results

Based on the search strategy of this research, 1325 articles were identified after removing duplicates; 16 full-text articles (Fig. 12.2) were retrieved from them. After exclusion, they were systematically reviewed and meta-analyzed in eight retained RCTs involving a total of 431 patients. Relatively low risk of bias in four research, two research moderate, and one research relatively high (Fig. 12.3). The ratings of the quality of evidence scores for each meta-analysis result ranged from medium to very low.

12.4 Quantitative Synthesis (Meta-analysis)

12.4.1 MBI Score

MBI data from three studies [3–5], including 184 patients (intervention n = 102, showed that rehabilitation robots improved MBI scores more significantly (MD = 19.93, 95%, CI = 17.94 to 21.91, $P < 0.00001$, $I^2 = 99\%$, Fig. 12.4). We found that heterogeneity comes from Zhao (2020) through a susceptivity analysis. Heterogeneity was significantly lowered when this research was eliminated (MD = 8.67, 95%, CI = 6.13 to 11.21, $P < 0.00001$, $I^2 = 0\%$).

12.4.2 FMA Score

Two RCTs measured the FMA scores, representing 72 patients (n = 37), as compared to the control groups [6, 7]. From the summary data of these two studies, rehabilitation robots significantly reduced the FMA scores (MD = 3.04, 95%, CI = 1.42 to 4.66, $P = 0.0002$, $I^2 = 0\%$, Fig. 12.5).

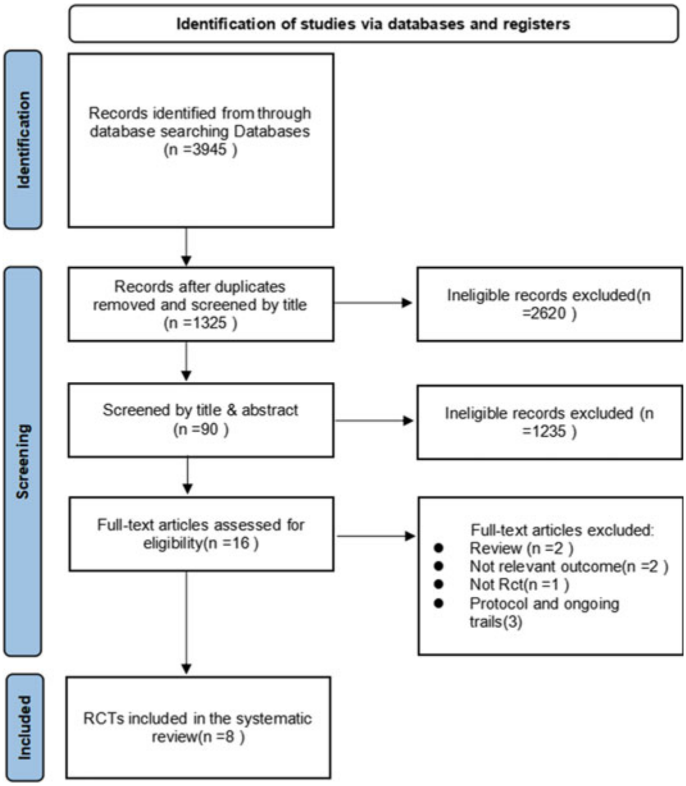

Fig. 12.2 Flow chart for research selection process

12.4.3 MOCA Score

The MOCA data came from five studies [3–5, 7, 8], including 281 patients (intervention n = 149), the intervention group significantly improved the MOCA scores when compared with the conventional cognitive training groups (MD = 5.86, 95%, CI = 5.60 to 6.11, and $P < 0.00001$, $I^2 = 99\%$, Fig. 6a). We found that heterogeneity comes from Zhao (2020) and Alfredo (2020) through a susceptivity analysis. Therefore, the heterogeneity was recalibrated and found to be reduced (MD = 2.27, 95%, CI = 1.77 to 2.77, $P < 0.00001$, $I^2 = 0\%$).

12.4.4 MMSE Score

Rehabilitation robots were associated with improved MMSE scores (MD = 3.07, 95%, CI = 2.63 to 3.51, $P < 0.00001$, $I^2 = 0\%$, Fig. 6b), involving two randomized

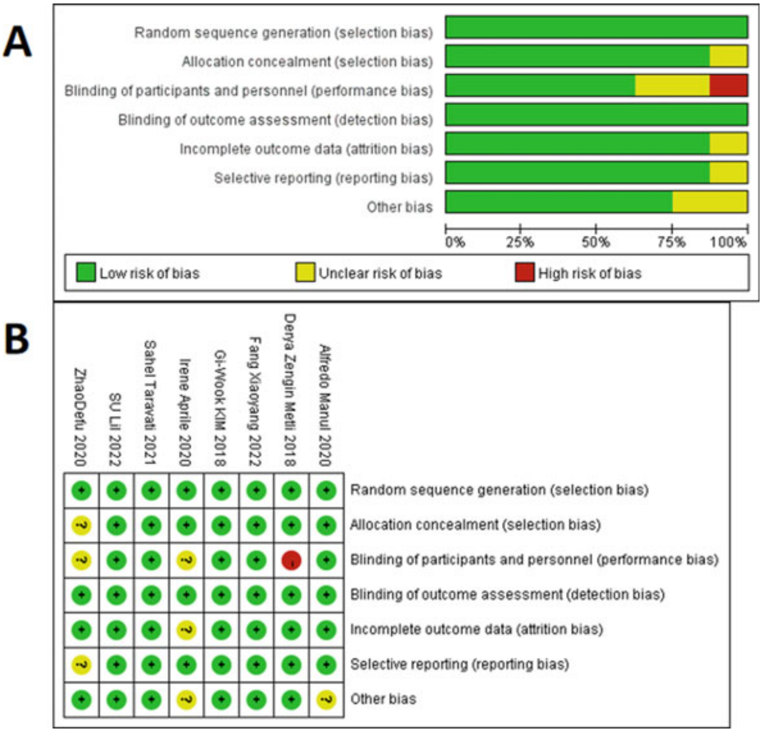

Fig. 12.3 **a** Risk of bias: review writers' estimates of the involved research on the percentage of items in each risk of bias; **b** Risk of bias summary: inspect the writers' estimates on the items expressed in each risk of bias in the involved research

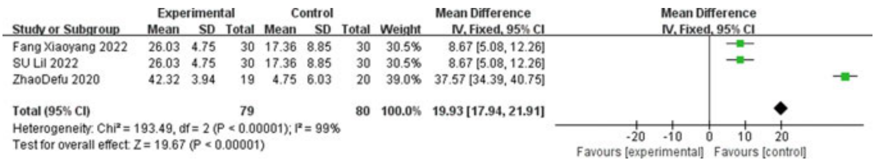

Fig. 12.4 Forest plot of MBI scores induced by rehabilitation robots and control intervention

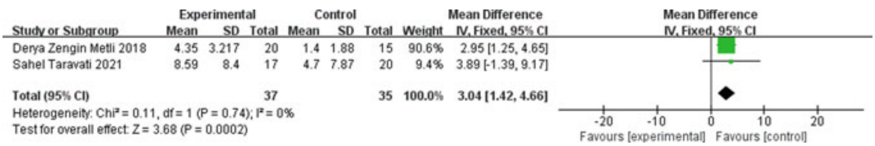

Fig. 12.5 Forest plot of FMA score induced by rehabilitation robots and control intervention

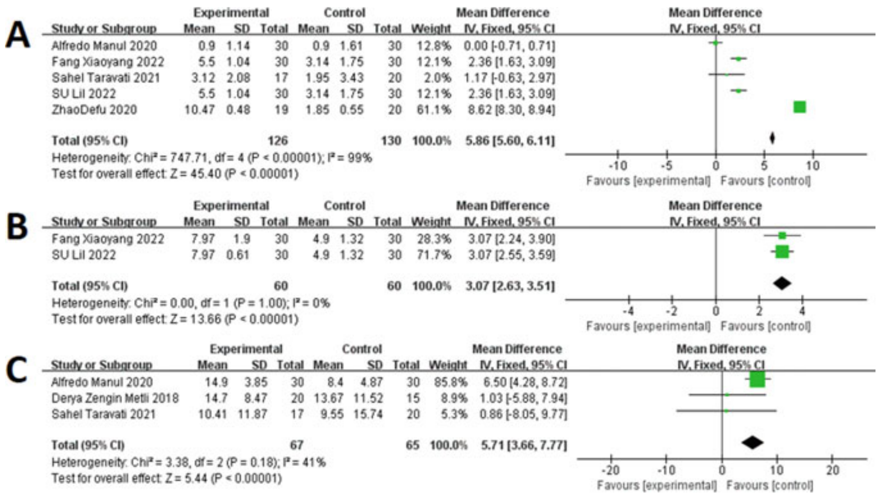

Fig. 12.6 Forest plot of **a** MOCA scores, **b** MMSE scores, **c** FIM induced by rehabilitation robots and control intervention

controlled trials including 125 patients (n = 63) [3, 5]. Because very few studies were included, it was impossible to find a source of heterogeneity.

12.4.5 FIM Score

Three RCTs represented 132 patients (intervention n = 67), in comparison with the control group [6–8]. Summary data from these three experiments showed better treatment outcomes in rehabilitation robot groups (MD = 5.71, 95%, CI = 3.66 to 7.77, $P < 0.00001$, $I^2 = 41\%$, Fig. 12.6c).

12.4.6 Adverse Events

Only one patient in the eight RCTs had an adverse event, developed scalp tingling at the start of the treatment, which disappeared after 1 day of rest, and continued participation in therapy.

12.5 Discussion

Post-stroke cognitive impairment is one of the major dysfunctions after stroke [9]. The advantage of this study is the introduction of multiple outcome scores, including five aspects: MOCA, MBI, FIM, MMSE, and FMA, which can show practical improvements in subfields including attention, memory, and executive function, making the findings more comprehensive and credible. We addressed studies with less heterogeneity by using fixed-effects models and sensitivity analyses. The MOCA, MBI, FIM, MMSE, and FMA scores in the rehabilitation robot groups were all dramatically improved compared with the conventional cognitive training groups. At the same time, after the intervention, the scores of both groups were dramatically improved compared with those before the intervention. It suggests that routine homework training, whether combined with conventional cognitive training or rehabilitation robot training, can improve the cognitive function of stroke patients and improve their ability to live in their daily activities. However, the training effect of rehabilitation robot training combined with conventional operation therapy is more significant. This result did not significantly differ in cognitive function in patients with different cultural levels. The results are identical to the conclusions of several scholars [6, 10]. Cognitive impairment is mainly manifested as structural and visual-spatial function, memory, execution force, timing and orientation force, attention disorder, etc., and patients can have one or more symptoms. Patients with cognitive dysfunction are often difficult to pay attention to, training is missing the point, unable to well understand and implement the goals and treatment plans set by the therapist, and unable to apply the sports skills learned to daily life. The virtual scene training of the rehabilitation robot makes the patients get rid of the boredom of the routine operation treatment, mobilizes the enthusiasm of the patients, and makes the patients more actively participate in the daily training. It can give patients rich sound and light dynamic stimulation, attract patients' attention, and the computer system can also compare the patient training effect immediately [11]. Through repetitive training, it can effectively enhance sensory and motor information input, improve attention, increase patients' training interest and enthusiasm, accelerate the recovery of damaged brain function and, promote the recovery of cognitive function. It can effectively promote the improvement of attention in the cognitive function of PSCI patients, so as to improve their cognitive function and promote the improvement of ADL.

In the past few years, robotic therapy has aimed to improve exercise performance and ADL, although cognitive disorder is usually overlooked or its treatment is independent of exercise injuries [12]. Cognitive therapy is critical in subjects with frequent concurrent cognitive and exercise disorders, such as stroke patients. Indeed, as observed in several studies [13], the limited shift in limb motor improvement of limb mobility, such as ADL, may be because of a lack of attention to coexisting cognitive impairment. Aprile et al. (2020) show that rehabilitation robot training has made tremendous strides in multiple domains of cognitive dysfunction after stroke [14]. In addition, the visual feedback, auditory feedback, situational feedback, and reward and punishment feedback generated during the training process of the rehabilitation robot form a rich environmental stimulus. Abundant environmental stimuli can activate gene expression associated with cellular remodeling, promote axonal elongation and the establishment of new synaptic connections, and increase neuroplasticity. Dendritic spines are an important region for synaptic remodeling. Studies in rats show that enriched environmental stimuli can increase the number of dendritic spines and synapses, increase the number of neuronal stem cells and neuroblasts in rats, and promote the migration of proliferating cells to the area of cerebral infarction. Rich environmental stimulation can promote the regeneration of neurons and processes in rats, accelerate the remodeling of neural network, transfer functional brain regions, and promote the reorganization of brain function.

Furthermore, our study currently has the following limitations. First, the study time is not long, and its long-term efficacy needs to be improved in subsequent studies. For future studies, studies planning more participants and long-term follow-up to draw conclusions are probably appropriate. Second, the virtual scene training is not immersive, and the training effect is not ideal. If further improvement can be achieved, it is not only more conducive to functional improvement, but also has a better patient training experience. Furthermore, future experiments should improve the standardized reporting of robot-assisted rehabilitation, encourage randomized controlled trials to follow the STRICTA guidelines, and rigorously design large-scale RCTs to fully meet the standard for reporting interventions included in the guidelines for clinical trials of rehabilitation robots.

12.6 Conclusion

Based on our study, rehabilitation robot training can improve the cognitive function of stroke patients and promote the improvement of daily living ability, which is an effective means of stroke rehabilitation.

References

1. Lo, J.W., et al.: Profile of and risk factors for poststroke cognitive impairment in diverse ethnoregional groups. Neurology **93**(24), e2257–e2271 (2019)
2. Moher, D., Liberati, A., Tetzlaff, J., Altman, D.: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. **6**(7), e1000097 (2009)
3. Su, L.L., et al.: Effects of upper limb robot-assisted training on cognition and upper limb motor function for subacute stroke patients. Chin. J. Rehabil. Theory Pract. **28**(05), 508–514 (2022)
4. Zhao, D.F., et al.: Repetitive transcranial magnetic stimulation combined with upper limb robot virtual scenario training for stroke patients with cognitive impairment. Chin. J. Rehabil. **35**(06), 295–298 (2020)
5. Lili, S., et al.: Virtual situational task-oriented training of upper limb robot for stroke study the influence of cognitive function in patients. Chin. J. Rehabil. **37**(02), 101–104 (2022)

6. Zengin-Metli, D., et al.: Effects of robot assistive upper extremity rehabilitation on motor and cognitive recovery, the quality of life, and activities of daily living in stroke patients. J. Back Musculoskelet. Rehabil. **31**(6), 1059–1064 (2018)
7. Taravati, S., et al.: Evaluation of an upper limb robotic rehabilitation program on motor functions, quality of life, cognition, and emotional status in patients with stroke: a randomized controlled study. Neurol. Sci. **43**(2), 1177–1188 (2022)
8. Manuli, A., Psy, M., Psy, D.L., Msc, A.C., Balletta, P.T., Luca, R.D., et al.: Can robotic gait rehabilitation plus virtual reality affect cognitive and behavioural outcomes in patients with chronic stroke? A randomized controlled trial involving three different protocols. J. Stroke Cerebrovasc. Dis. **29**(8), 104994 (2020)
9. Kim, G.W., Won, Y.H., Seo, J.H., Ko, M.H.: Effects of newly developed compact robot-aided upper extremity training system (Neuro-X®) in patients with stroke: a pilot study. J. Rehabil. Med. **50**(7), 607–612 (2018)
10. Mehrholz, J., 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. **9**(9), Cd006876 (2018)
11. McDowd, J.M., Filion, D.L., Pohl, P.S., Richards, L.G., Stiers, W., et al.: Attentional abilities and functional outcomes following stroke. J. Gerontol. Ser. B Psychol. Sci. Soc. Sci. **58**(1), P45–53 (2003)
12. Zinn, S., Dudley, T.K., Bosworth, H.B., Hoenig, H.M., Duncan, P.W., Horner, R.D.: The effect of poststroke cognitive impairment on rehabilitation process and functional outcome. Arch. Phys. Med. Rehabil. **85**(7), 1084–1090 (2004)
13. Hsieh, Y.W., Wu, C.Y., Lin, K.C., Yao, G., Wu, K.Y., Chang, Y.J.: Dose-response relationship of robot-assisted stroke motor rehabilitation: the impact of initial motor status. Stroke **43**(10), 2729–2734 (2012)
14. Aprile, I., et al.: Robotic rehabilitation: an opportunity to improve cognitive functions in subjects with stroke. An explorative study. Front. Neurol. **11**, 588285 (2020)