TYROSOLUTION – What's the evidence?

In the following, the evidence for the robotic-assisted and computer aided therapy devices AMADEO, DIEGO, PABLO, and TYMO is summarized. Together, the devices generate a comprehensive approach for upper extremity rehabilitation due to motor impairment following neurologic (e.g. stroke) and orthopedic disorders.

AMADEO - EFFECTS OF ROBOTIC HAND REHABILITATION (Pinter et al. 2013)

Rehabilitation of highly impaired finger and hand movements after stroke is challenging and often unsatisfactory. Therefore, the Amadeo was developed to improve rehabilitation of hand function by delivering intensive and repetitive movement sequences in an individualized way. The brain mechanisms underlying successful recovery of hand function after stroke are still not fully understood, although functional MRI (fMRI) studies underline the importance of neuronal plasticity.

We explored potential changes in brain activity in 7 patients with subacute to chronic stroke (69 ± 8 years) with moderate- to high-grade distal paresis of the upper limb after standardized robotic finger-hand rehabilitation training, in addition to conventional rehabilitation therapy for 3 weeks. Behavioral and fMRI assessments were carried out before and after training to characterize changes in brain activity and behavior.

15 sessions Amadeo therapy each lasting 20 minutes resulted in an average of 3600 grip movements. The Motricity Index (pre: 59.4, post: 67.2, $P < .05$) and grip force (pre: 7.26, post: 11.87, $P < .05$) of the paretic hand increased significantly after rehabilitation. On fMRI, active movement of the affected (left) hand resulted in contralesional (ie, ipsilateral) activation of the primary sensorimotor cortex prior to rehabilitation. After rehabilitation, activation appeared "normalized," including the ipsilesional primary sensorimotor cortex and supplementary motor area (SMA). No changes and no abnormalities of activation maps were seen during movement of the unaffected hand.

ROBOT-ASSISTED EXERCISE FOR HAND WEAKNESS AFTER STROKE (Stein et al. 2011)

The study was designed to test Amadeo therapy which is a promising robotic-assisted approach to enhance motor abilities of fingers and hand. 12 stroke patients with moderate to severe hemiparesis after stroke were included. Each participant received a total of 18 therapy sessions (1 hour device therapy daily, 3 days/week for 6 consecutive weeks). Each session included 20 min of "Continuous Passive Motion Plus" (CPMplus) mode, 20 min active therapy games, and 20 min CPMplus.

Significant improvements were seen in multiple measures of motor performance, including the Upper Extremity Fugl-Meyer Score, the Motor Activity Log, the Manual Ability Measure-36, and the Jebsen Hand Function Test ($p < 0.05$).

AMADEO THERAPY compared with CONVENTIONAL THERAPY techniques

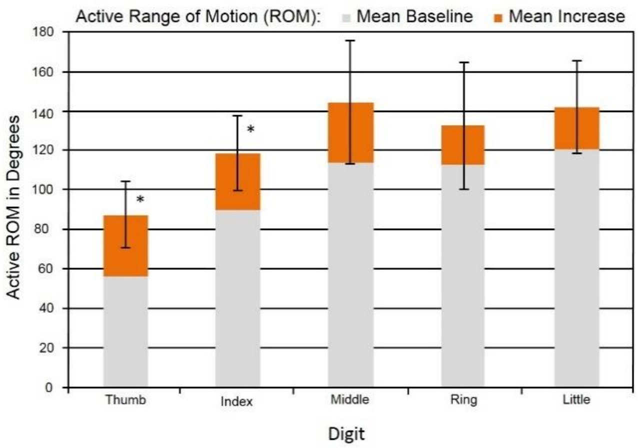


*FIGURE 1: Left: Robot-assisted therapy device Amadeo® from tyromotion. Right: 95% confidence intervals for the change in total active range of motion (ROM). *statistically significant (p < 0.05).*

CONVENTIONAL BOBATH THERAPY was compared to Amadeo therapy in a prospective randomized controlled blinded study from Helbok and colleagues (Medical University Innsbruck, Austria). The preliminary results for the outcome measures (Fugl-Meyer Score, Modified Ashworth Scale, finger ROM and Motor Activity Log) showed that both therapies improve motor-function of the hand.

JACOBSEN PROGRESSIVE MUSCLE RELAXATION TECHNIQUE was compared to add-on passive Amadeo training and add-on active Amadeo training. This study by Mayr and Saltuari (Hospital Hochzirl, Austria) randomly assigned 36 stroke patients into the three treatment groups that were evaluated over 10 weeks. From beginning to the end of the study, significant improvements were demonstrated for muscle strength in finger flexion for active Amadeo training group and for finger function measured by the Action Research Arm Test (ARAT) in both, active and passive Amadeo training groups ($p < 0.05$).

Robot-assisted hand rehabilitation was shown to be as effective as other methods when performing repetitive task practice in subacute stroke patients. In experiments in which the intensity of repetitive motions was equalized, both therapies were found to be of equal efficacy. However, ***robot-assisted repetitions were found to be simpler and easier to execute, and were found to be of greater intensity, compared to other therapies.*** *(Hwang et al. 2012)*

AMADEO – Therapy for all phases of stroke rehabilitation

ACUTE stroke patients (28.8 ± 8.1 days post stroke) were enrolled in a study by Sale and colleagues (2012). The positive effect of the robot-assisted approach in the early phase of recovery was demonstrated. Moreover, a reduction of sensorimotor impairment and a recovery on quality of life was found. Also the management of spasticity can be more effective if the rehabilitation treatment starts in the acute phase. A large clinical use of Amadeo originates from the good participation of the patients and absence of side effects.

SUBACUTE stroke patients (6.5 ± 5.3 month post stroke) participated in the prospective randomized controlled clinical trial of Hwang et al. (2012). All Patients underwent 4 weeks robotic rehabilitation program (20 sessions) without any other conventional occupational therapy during the study period. Investigating two groups at different intensities (full-term intervention vs. half-term intervention) resulted in a dose-dependent improvement in hand function.

CHRONIC stroke patients (> 6 month post stroke) were investigated by the study of Stein et al. (2011) that found robotic therapy for hand paresis after stroke to be safe and feasible.

AMADEO RCT - recovery of hand function by robot-assisted therapy in acute stroke

The randomized-controlled observer trial (RCT) by Sale and colleagues (2014) evaluates the effects of intensive robot-assisted hand therapy compared with intensive occupational therapy in the early recovery phases after stroke.

20 patients were randomized into two groups, the experimental group (EG) using the AMADEO or the control group (CG) receiving occupational therapy. All participants carried out 20 sessions, for 4 consecutive weeks (5 days/week).

Evidence of a significant improvement was shown by the Friedman test for the Fugl-Meyer Scale (EG: $P = 0.0039$, CG: $P <0.0001$), Box and Block Test (EG: $P =0.0185$, CG: $P = 0.0086$), Motricity Index (EG: $P < 0.0001$, CG: $P = 0.0303$) and Medical Research Council Scale for Muscle Strength (hand flexor and extensor muscles) (EG: $P < 0.0001$, CG: $P =0.001$).

These results provide further support to the generalized therapeutic impact of intensive robot-assisted treatment on hand recovery functions in individuals with acute stroke. The robotic rehabilitation treatment may contribute toward the recovery of hand motor function in acute stroke patients. The positive results obtained through the safe and reliable robotic rehabilitation treatment reinforce the recommendation to extend it to a larger clinical practice.

Study conclusions for AMADEO finger-hand therapy

- After rehabilitation, activation appeared "normalized" (Pinter 2013)
- All subjects tolerated the treatment well and no complaints were observed (Stein 2011)
- Improvements were found in multiple measures of motor performance (Stein 2011)
- Robotic therapy for hand paresis after stroke is safe and feasible (Stein 2011)

- Robot-assisted hand rehabilitation procedures should be considered a valuable tool for physicians (Hwang 2012)
- Four week robot-assisted intervention resulted in improved hand function that could be maintained for one month after the cessation of therapy (Hwang 2012)
- Management of spasticity is more effective if treatment starts during the acute phase (Sale 2012)
- This original rehabilitation treatment could contribute to increase the hand motor recovery in acute stroke patients (Sale 2012)
- The lack of side effects and good participation, with an absence of the dropout, may suggest a large clinical use (Sale 2012)
- The device supports the intensity, which is needed for the patient to exercise at their individual limit of performance, exactly (Sale 2012)
- Safe and reliable robotic rehabilitation treatment reinforce the recommendation to extend it to a larger clinical practice (Sale 2014)
- The clinical protocol is easy and reproducible, and allows the treatment of patients with moderate to severe upper limb paresis (Sale 2014)
- Results further support to the generalized therapeutic impact of intensive robot-assisted treatment on hand recovery functions in individuals with acute stroke (Sale 2014)

AMADEO – fundamental research studies generating a basis for innovative future applications

Moreover, fundamental research studies utilize the scientific I/O interface of the AMADEO to investigate promising future applications:

- Motor Imagery (MI) based Brain-Computer Interface (BCI) for neurologic rehabilitation. The MI is determined by classification of Electroencephalography (EEG) signals. According to the detected MI the AMADEO rehabilitation robot is moving the fingers of the affected hand. (Ortner 2013)
- Surface Electromyography (sEMG) driven robotic closed- hand therapy (Istenic 2014)
- Specified rhythmic auditory stimulation for robot-assisted hand function training in stroke therapy (Speth 2014)
- Transcranial Magnetic Stimulation (TMS) of the motor cortex and haptic feedback to the hand (AMADEO) were controlled by sensorimotor de-synchronization during motor-imagery and applied within a brain-machine interface (BMI). (Gharabaghi 2014)

DIEGO – Evidence from large scale database

THE COCHRANE COLLABORATION®

Evidence for robot-assisted arm training was demonstrated by the meta-analysis conducted from Mehrholz and colleagues (2012). The analysis included 19 trials (666 stroke patients) examining the effects of robot-assisted arm training. They found that patients who receive robot-assisted arm training after stroke are more likely to improve their activities of daily living, with an improvement of the paretic arm function.

DIEGO – Transfer of Clinical Guideline recommendations to clinical practice

Figure 2: Evidence based practice – Clinical guidelines for stroke rehabilitation.

Developed together with doctors and therapists, the arm rehabilitation robot DIEGO is inspired by the considerations on the clinical daily basis. Thereby, as result DIEGO integrates numerous interventions for arm motor rehabilitation for all phases of stroke rehabilitation. The potential clinical benefit of DIEGO therapy is obvious considering the compliance with the recommendations given by clinical guidelines, i.e. VA/DoD (2010) and DGNR (2012). The most important goal of the VA/DoD guideline (2010, p 6) is to provide a scientific evidence base for practice evaluations and interventions. The Clinical Practice Guideline for the Management of Stroke Rehabilitation was developed to assist facilities to implement processes of care that are evidence-based and designed to achieve maximum functionality and independence as well as improve patient and family quality of life. This guide helps clinicians determine best interventions and timing of care for their patients, better stratify stroke patients, reduce re-admissions, and optimize healthcare utilization. Clinical guidelines for stroke rehabilitation use an evidence rating system to attribute interventions with the corresponding strength of recommendation. Thereby, the highest grades of evidence are grade B, which is the recommendation that clinicians provide the intervention to eligible patients, and grade A which is a strong recommendation. This rating system is used by the Department of Veterans Affairs, Department of Defense, and the American Heart Association/ American Stroke Association (VA/DoD, 2010) as well as by the German Association for Neurorehabilitation (DGNR, 2012).

Intelligent Gravity Compensation (IGC) enables an "assist-as-needed" approach with DIEGO. IGC meets the demand of the VA/DoD guideline that recommend that UE functional recovery should consist of the practice of functional tasks, emphasizing progressive difficulty and repetition. Further, the DGNR (2012) guideline indicates active repetitive practicing for a task or movement that should be relearned. DIEGOs IGC provides a smooth arm weight support through the entire range of motion. This unique feature enable even severely affected patients to actively and repetitively practice physiologic movements and functional tasks with real objects. The level of support can be adjusted and adapted individually to provide progressive difficulty. Further, IGC promotes the key element of the modern "hands-off" concept as described by the DGNR (2012). Therein, priority is given to the goal orientated active movement of the patient him-/ herself and not to the facilitation of movement sequences by the therapists hands any more.

DIEGO offers the biggest spectrum of robot-assisted therapies for customized treatment. According to the VA/DoD recommendations (2010), the UE treatment should be tailored to the individual patient and consider the interventions that are most appropriate, engaging, accessible, and available. In addition, recommendations for UE also cover Constraint-induced movement therapy (CIMT) [evidence grade A], robot-assisted movement therapy as adjunct to conventional therapy in patients with deficits in arm function to improve motor skill at the joints tailored [evidence grade B], and bilateral practice to improve UE function [evidence grade B].

It is well known and also indicated by the DGNR guidelines (2012) that patients with severe paresis early after stroke come up with a "learned non-use" of the affected arm. Similar to CIMT, the unilateral use of DIEGOs IGC can increase the use of the affected arm. For movement therapy focusing on this so called "forced use" the clinical efficacy is well proven. Further, DIEGO is the most advanced robotic therapy device for bilateral and bilateral symmetric training that is also recommended by the DGNR (Platz and Roschka, 2011). In addition, virtual reality feedback is incorporated in the system.

BILATERAL ARM TRAINING – Why and who benefits? (Waller and Whitall, 2008)

IN GENERAL, bilateral as well as unilateral re-training appears necessary for those with stroke. Bilateral arm training has emerged as an approach that leads to positive outcomes in addressing upper extremity paresis after stroke. Also, bilateral arm training can improve unilateral paretic upper extremity functions after stroke. Given the importance of bilateral activities in daily life, there is a need to recognize, train and assess the important contribution of supportive role functions of the paretic arm used on its own and as part of complementary bilateral functional skills.

WHY? Examining motor control and neural mechanisms underlying arm function and neural recovery lead to the justifications for bilateral arm training.

Functional justification: A primary reason to perform bilateral arm training is that much of what we do every day involves the use of both arms and therefore, bilateral re-training is necessary. Basic self-care skills such as feeding, dressing, toileting as well as instrumental skills as cooking rely heavily on bilateral arm use. Re-training bilateral tasks is optimized by bilateral and not unilateral training (task-specificity or transfer of learning principle). The control of each arm separately is not equivalent to the control of both arms together because of different neuro motor control mechanisms.

Motor control justification: Bilateral skills can be addressed by complementary, symmetrical, and asymmetrical bilateral training approaches. During complementary bilateral tasks that are the most common type, the arms cooperate while each has a separate function. During bilateral symmetrical tasks of daily living, which are relatively few, the coupling mechanism is maximally active. Asymmetrical bilateral arm movements are fewer, e.g. arm swing while walking. However, the fact remains that strong coupling exists between the arms when they act together and this is unique and different to unilateral skills which compose the bilateral task.

WHO BENEFITS? Three different approaches of bilateral arm training where reviewed by Wallner and Whitall (2008): repetitive reaching with hand fixed, isolated muscle repetitive task training, and whole arm function training. They conclude that individuals at all levels of severity can benefit in some manner from bilateral arm training, but not all approaches are effective for all severity levels. Thereby, the level of impairment is a critical factor to consider when choosing a bilateral training approach, e.g. using the whole arm approach is not sensible for moderate to severely affected patients.

PABLO - VIRTUAL REALITY AS A METHOD FOR EVALUATION AND THERAPY (Nica et al., 2013)

The results of Nica and colleagues (2013) demonstrated that Pablo is a modern evaluation tool for hand pathology, deficits, dysfunctions, with objective measurement replacement of classic goniometry & dynamometry. Further, Pablo can be part of the classic rehabilitation program for these patients giving the opportunity to adapt the game parameters to the realistic functional patient status. Moreover, game therapy sessions can be performed by the patient himself & at home. The better muscular & neurocognitive patient feedback during interactive therapeutic modules lead to benefits as improved ROM, force, prehension, attention, motivation, coordination & dexterity (statistically significant improvements for the Pablo group , with 32% better results at the 9-hole peg board test). The authors conclude that PABLO can improve the results of the classic rehabilitation program and can be integrated in occupational therapy methods as a supplement.

PABLO – RESULTS OF A REHABILITATION PROGRAM AFTER HAND SURGERY (Brailescu et al., 2013)

Work-related accidents or domestic traumas of upper extremities have become more frequent in the modern industrial and technological society. Major traumatic lesions need surgery and unfortunately, the recovery period is a very long and strenuous process which can last years, with multiple re-interventions for adherences, nerve and tendon surgical approaches and rehabilitation programs before and after surgeries.

Use objective tools of assessment and statistics to explore the benefits of the rehabilitation program on the clinical, neurological, functional, socio-professional and psychological status of patients after hand surgery.

The study elaborated and followed a prospective study based on 54 cases with surgery for traumatic hand lesions, who followed three series of medical rehabilitation programs consisting of three weeks of daily PRM therapeutic protocol in the Clinic of the National Institute of Physical and Rehabilitation Medicine.

The results confirmed the international epidemiologic data, with a statistically significant improvement of all the local post-surgical conditions, better quality of life and functional independence.

A rehabilitation program proved to be an essential sequence after or between surgeries for traumatic hands, with benefits for the functional independence of patients.

The influence of PABLO therapy

on functional re-education: Comparison of the subgroups with/without PABLO showed significant differences between mean values ($p < 0.01$) for the second compared to the first and for the third versus first evaluation. Patients who worked 30 minutes with PABLO in addition to the classical rehabilitation program experienced better functional scores, meaning better improvement for performing usual activities at home. An increase of the FIM score by 4.3 points suggest a greater functional independence and better possibilities for familiar and social re-integration for the PABLO group.

on motor re-education: For each of the 10 types of grips/pinches tested, the PABLO group had a favorable evolution for all the studied parameters (fig.4). Referring to the Pablo device, respecting the "evidence-based medicine" evaluation criteria and the correct statistical analysis, Brailescu and colleagues (2013) indicate the Pablo device is an objective testing possibility for the range of motion and grasping strength that can be very useful in the clinical assessment and monitoring of patients with a post-traumatic hand. As a therapy, the results demonstrated that the Pablo game modules based on Virtual Reality concepts improved the motor and functional scores at a superior level compared to patients who did not work with Pablo, but this kind of occupational therapy must be seen as an adjuvant method to standard therapy and not as a substitute for it.

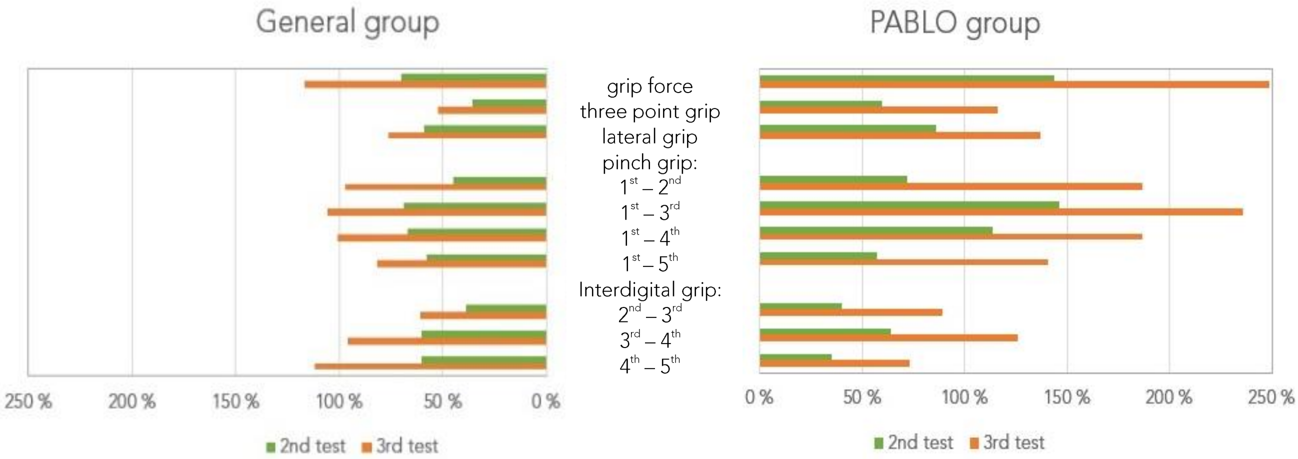


Figure 4: Evolution of 10 different grips and pinches based on the comparison between PABLO group and general group (averages). (Brailescu et al., 2013)

PABLO application study - visuomotor coordination in healthy, stroke, and Parkinson (Seitz et al. 2014)

Visuomotor performance can be improved by repetitive training on consecutive days. The aim of this study was to assess the training effect of visuomotor tracking in healthy subjects and hemiparetic patients with stroke and in moderately impaired patients with Parkinson's disease.

39 healthy right-handed subjects, 15 patients after acute cerebral artery stroke, and 15 patients with mid-stage Parkinson's disease were trained with the commercially available, multifunctional PABLO-device. This handhold device is equipped with force and acceleration sensors and connected to a personal computer for on-line data display and data storage. On three consecutive days the subjects were trained to navigate a target through obstacles in a virtual reality environment. Performance was assessed by modulation of force production and rotation of the hand in a visuomotor tracking paradigm using the PABLOR-device.

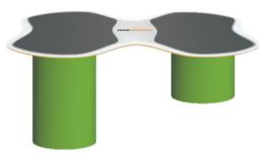
The main findings were that training of the right dominant hand improved visuomotor coordination of hand rotation movements in both hands in the healthy subjects ($p=0.0015$). Training of the right affected hand improved visuomotor coordination of hand rotation movements in either patient group ($p=0.026$). In contrast, training improved the visuomotor coordination of force tracking of the dominant hand only in the healthy subjects ($p<0.01$).

The visuomotor training scenario was effective to improve visually guided hand coordination within three days in the healthy controls and both patient groups. The improvement of hand rotation generalized to the non-trained hand in healthy subjects. The positive results reinforce a recommendation of the PABLO for larger clinical trials with longer training periods.

TYMO – TRAINING OF SIT-TO-STAND ABILITY and BALANCE

The RCP stroke guideline from the Royal College of Physicians states that any patient with significant impairment in maintaining their balance should receive progressive balance training.

Evidence for clinical effectiveness of force platform training with visual feedback for the TYMO application areas (sitting, sit-to-stand, standing, static and dynamic, and unstable surface, and circuit class therapy) using visual and auditory feedback can be found in various studies.



Training symmetry of weight distribution in sitting was investigated by Mudie et al. (2002), as postural symmetry is essential for normal balance. Stroke patients show predominantly weight bearing on one side (sitting & standing). It is possible to restore postural symmetry in sitting in the early stages of rehabilitation with a therapy creating awareness of body position. Force platform feedback was used to distribute body weight evenly and train the weight shift accordingly to the task requirements.

Weight-shift training on unstable surface in sitting position was investigated by Jung et al. (2014). The training group showed significant higher improvement than the control group with regard to trunk repository error (TRE), trunk impairment scale (TIS), and timed up and go (TUG) test. The authors conclude that weight-shift training is beneficial for improving trunk control and proprioception in patients with chronic hemiparetic stroke.

Sit-to-stand ability & standing balance can be improved by biofeedback (force) and repetitive task training. A systematic review on available evidence on interventions for motor recovery after stroke provides an overview by Langhorne and colleagues (2009). The key outcomes of this meta-analysis for sit-to-stand ability and standing balance are summarized in figure 5. Two interventions were identified using outcomes that reflected mobility during rising to stand. Biofeedback using a force plate was tested only in two small trials while repetitive task training showed significant improvement in sit-to-stand ability. Most trials observing standing balance used measures such as the Berg Balance Scale, weight distribution, or postural sway during sitting and standing.

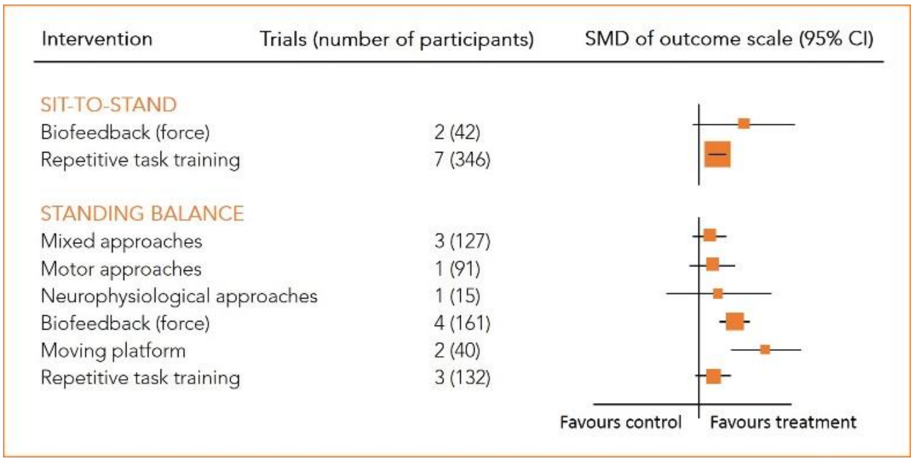


Figure 5: Interventions to improve sit-to-stand ability and standing balance after stroke. (Langhorne et al., 2009)

Effects of dynamic force platform training with visual feedback was on standing balance was investigated by the study of Srivastava et al. (2009). 45 chronic stroke patients participated in 20 sessions (20 min/day, 5 days/week for 4 weeks). Significant improvements in balance and functional outcome were found. Moreover, all subjects maintained improvements at 3 month follow up. The Berg Balance Scale (BBS) evaluated 14 sitting & standing activities (pre: 34.93 ±11.45, post: 46.85 ±8.39, 3 month follow-up: 48.44 ±8.76), Barthel Index (BI) as measures of discrete function of self-care & mobility (pre: 74.33 ±13.38, post: 83.88 ±7.10, 3 month follow-up: 92.94 ±6.75).

Effects of static standing balance training using force platform biofeedback on gait was investigated by Yavutzer et al. (2006) by a RCT. 41 patients late after stoke participated in the intervention in addition to the conventional inpatient rehab program. The authors conclude that balance training using force platform biofeedback was beneficial for postural control & weight bearing on paretic side while walking.

Supervised circuit class training focused on gait and mobility related functions and activities, in which patients train in various work stations can improve walking distance, balance, walking ability, and physical activity (Veerbeek 2014)

TYMO - SERIOUS GAMING FOR REHABILITATION NEEDS (Borghese et al. 2013)

In their study "Computational intelligence and game design for effective at-home stroke rehabilitation" Borghese and colleagues (2013) used the TYMO as tracking and feedback device following a hands-free approach engaging users at home. Computer games appear suited to guide rehabilitation due to their ability to engage users. However, the authors point out that commercial entertainment market videogames are not adequate for rehabilitation goals.

Principles for games designed for rehabilitation needs:

- adaptable game parameters to address each patients functional status
- monitoring the patients motion to avoid maladaptation
- feedback on performance & progression
- usable with all devices of the tyrosolution according to the patients pathology & rehabilitation goals

1D accuracy basic versions | 1D reaction | 2D motoric | 2D cognitive | Virtual Reality

REFERENCES

Brailescu CM, Scarlet R, Nica A, Lascar I. A study regarding the results of a rehabilitation program in patients with traumatic lesions of the hand after surgery. Palestrica of the third millennium – Civilisation and Sport; Vol. 14, no. 4, Oct-Dez 2013, 263-270.

Borghese NA, Pirovano M, Lanzi PL, Wüst S, de Bruin ED. Computational intelligence and game design for effective at-home stroke rehabilitation. Games for Health Journal. 2013 apr; 2(2): 81-88.

Gharabaghi A, Kaus D, Leão MT, Spüler M, Walter A, Bogdan M, Rosenstiel W, Naros G and Ziemann U. Coupling brain-machine interfaces with cortical stimulation for brain-state dependent stimulation: enhancing motor cortex excitability for neuro rehabilitation. Frontiers in Human Neuroscience, March2014, Vol.8: Article122.

Hwang CH, Seong JW, Son DS. (2012). Individual finger synchronized robot-assisted hand rehabilitation in subacute to chronic stroke: a prospective randomized clinical trial of efficacy. Clin Rehabil 2012; 26(8): 696–704.

Istenic R, Binder I, Turolla A. Surface EMG driven robotic hand rehabilitation. *Neurologie & Rehabilitation 6:2014.*

Jung K, Kim Y, Chung Y, Hwang S. Weight-Shift Training Improves Trunk Control, Proprioception, and Balance in Patients with Chronic Hemiparetic Stroke. Tohoku J Exp Med. 2014; 232(3):195-9.

Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. Lancet Neurol 2009; 8: 741-754.

Mehrholz J, Händrich A, Platz T, Kugler J, Pohl M. Electromechanical and robot-assisted arm training for improving generic activities of daily living, arm function, and arm muscle strength after stroke (Review). The Cochrane Library 2012, Issue 6.

Mudie MH, Winzeler-Mercay U, Radwan S, Lee L. Training symmetry of weight distribution after stroke: a randomized controlled pilot study comparing task-related reach, Bo bath and feedback training approaches. Clin Rehabil. 2002. 16:582.

Nica AS, Brailescu CM, Scarlet RG. Virtual reality as a method for evaluation and therapy after traumatic hand surgery. Stud Health Technol Inform 2013:191:48-52.

Ortner R, Ram D, Kollreider A, Pitsch H, Wojtowicz J, Edlinger G. Human-computer confluence for rehabilitation purposes after stroke. *15th International Conference on Human-Computer Interaction 2013.*

Pinter D, Pegritz S, Pargfrieder C, Reiter G, Wurm W, Gattringer T, Linderl-Madrutter R, Neuper C, Fazekas F, Grieshofer P, Enzinger C. Exploratory study on the effects of a robotic hand rehabilitation device on changes in grip strength and brain activity after stroke. Top Stroke Rehabil 2013; 20(4):308-316.

Platz T and Roschka S. Rehabilitative Therapie bei Armlähmungen nach Schlaganfall. Patientenversion der Leitlinie der Deutschen Gesellschaft für Neurorehabilitation (DGNR). 2011. Bad Honnef: Hippocampus. (Rehabilitation therapy for arm paresis following stroke. Patient version of the guideline of the German Neurorehabilitation Association 2011).

Royal College of Physicians, Intercollegiate Working Party for Stroke. National clinical guidelines for stroke, 4rd edition. London: Royal College of Physicians, 2012.

Sale P, Lombardi V, Franceschini M. Hand robotics rehabilitation: feasibility and preliminary results of a robotic treatment in patients with hemiparesis. Stroke Res Treat. 2012:820931.

Seitz, RJ., Kammerzell, A., Samartzi, M., Jander, S., Wojtecki, L., Verschure, P., Ram, D. (2014). Monitoring of visuomotor coordination in healthy subjects and patients with stroke and Parkinson's disease: An application study using the PABLO®-device. International Journal Neurorehabilitation 2014. 1:113.

Speth F, Wahl M. Evaluation of specified rhythmic auditory stimulation for robot-assisted hand function training in stroke therapy. *Neurologie & Rehabilitation 6:2014.*

Srivastava A, Taly AB, Gupta A, Kumar S, Murali T. Post-stroke balance training: Role of force platform with visual feedback technique. J Neurol Sci. 287 (2009) 89-93.

Stein J, Bishop L, Gillen G, Helbok R. Robot-assisted exercise for hand weakness after stroke: a pilot study. Am J Phys Med Rehabil. 2011 Nov; 90(11):887-894.

The Intercollegiate Working Party for Stroke, Royal College of Physicians. National clinical guidelines for stroke, 4rd edition. London: Royal College of Physicians, 2012.

The Management of Stroke Rehabilitation Working Group, Department of Veterans Affairs, Department of Defense, and the American Heart Association/ American Stroke Association. VA/DoD Clinical practice guideline for the management of stroke rehabilitation. Version 2.0. 2010.

Veerbeek JM, van Wegen E, van Peppen R, van der Wees PJ, Hendriks E, Rietberg M, Kwakkel G. What Is the Evidence for Physical Therapy Poststroke? A Systematic Review and Meta-Analysis. PLoS ONE 2014 9(2): e87987.

Waller S and Whitall J. Bilateral arm training: Why and who benefits? NeuroRehabilitation. 2008;23(1):29-41.

Yavuzer G, Eser F, Karakus D, Karaoglan B, Stam H. The effects of balance training on gait late after stroke: a randomized controlled trial. Clinical Rehabilitation 2006, 20, 960-969.