Document: Protocol

Official study title: Error augmentation for upper limb rehabilitation in stroke survivors

NCT identification number: pending

Document date: February 5, 2021

Error augmentation for upper limb rehabilitation in stroke survivors

Caroline Rajda,[1] Mindy F. Levin,[1] Sigal Berman,[2] Shelly Levy-Tzedek[3]
[1]School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Canada, [2]Department of IEM, Ben-Gurion University of the Negev
[3]Department of Physical Therapy, Ben-Gurion University of the Negev

Research Innovation – contribution beyond state of the art

Stroke is a leading cause of long-term sensorimotor disability with deficits in upper limb function persisting into the chronic stage in a large proportion of stroke survivors (Langhorne et al. 2009). This is partly due to the limited effectiveness of current upper limb rehabilitation interventions (Kwakkel et al. 2003). A stronger focus on training aligned with addressing the underlying causes of the motor control deficits rather than only on the behavioral output, is essential for significantly improving treatment efficiency.

Robotic augmented therapy can repetitively deliver patient-specific, high-dosage training. To-date, however, results of training approaches integrating robotics have not been highly successful (Maciejasz et al. 2014; Huang and Krakauer 2009). Robots have been used to administer high-dosage repetitive training, which leads to improvement in the trajectories practiced. While learned movement patterns may generalize across different movements made within the practiced regions (Conditt et al. 1997), whether such training leads to improvement in upper limb functional ability remains controversial. Upper limb motion is by nature variable and not pattern-specific due to the kinematic redundancy of the system. Therefore, repetitive practice of single motion paths may not be sufficient to improve generalized upper limb functional ability.

One way to increase the control of upper limb movement is through the use of a specialized robotic technique based on error augmentation (EA) (see Israely and Carmeli 2016 for recent review). In EA treatment, subjects are provided with feedback that enhances their motor errors and forces them to move into larger joint ranges. This is usually done by distorting visual feedback while additional haptic feedback can be provided using robotics. EA has resulted in positive effects for lower limb locomotor training, e.g., Kao et al. 2013; Tyrell et al. 2015). Recently, several researchers have implemented EA for upper limb training, but results have been disappointing in terms of functional improvement (e.g., Abdollahi et al. 2014; Molier et al. 2011). It is likely that the reason for the lack of functional effects is that the error enhancement is only applied in a generalized way, without consideration of the specific upper limb motor deficit of the patient; i.e., the training is not personalized to the patient's particular motor impairment.

In previous work, we have tested the effect of a patient-specific impairment-based training approach based on the threshold control theory (TCT) of motor control (Feldman 2015) in a tri-national randomized controlled trial (IDRC/CIHR/ISF 2015-20). According to TCT, voluntary movement is generated by regulating the spatial thresholds (STs) at which muscle activation begins. EMG emerges based on the interaction of the biomechanics of the system with the environment. The ability to regulate STs is reduced in patients with stroke, due to damage to descending neural pathways (Levin and Feldman 1994). The reduced capability leads to abnormal muscle activation patterns (i.e., excessive co-activation) as well as spasticity and weakness within well-defined spatial (angular) zones. The ***active control zone***, i.e., the angular zone in which voluntary movements can be made with typical muscle activation patterns, is reduced. Thus, in the previous trial

(Levin et al. 2018), the upper limb training was optimized to increase the patient's active control zone of the elbow joint by identifying and restricting reaching movements to that specific zone. Preliminary results suggest that this approach led to greater gains in upper limb function in the group who had individualized training compared to the group that did not.

Studies suggest that errors made during training improve later performance of the task. For example, in a study in which elderly subjects practiced rhythmic motion of the upper limb with and without visual feedback, greater errors made during treatment led to more movement improvement following training (Levy-Tzedek 2017). This result is consistent with the TCT as muscle activation is regulated by the difference between the actual limb position and referent limb position specified by the brain. The referent position also plays a role in the perception of the actual limb position, while the afferent component identifies the deflection of the limb from the referent limb position. Based on this combination, the system identifies the movement error, i.e., deviation of the limb from the target position. Movement correction is accomplished by properly adjusting the referent limb position.

The sensitivity of referent control may be enhanced by augmentation of the movement error, i.e., Joint Error Augmentation (JEA). Furthermore an improvement in referent limb control is likely to be associated with improvement in threshold (referent control) at the level of individual joints. Development of rehabilitation treatment protocols based on motor control theory, such as that underlying JEA, is a promising direction for robotic rehabilitation therapy.

Research Objectives:

Our goals are to investigate the effect of JEA on motor learning in healthy subjects and on upper limb rehabilitation in subjects with stroke.

Hypothesis 1: In both groups, JEA applied to the elbow joint range will lead to better learning of movement speed and precision of a reaching task compared to no JEA.
Hypothesis 2: In patients with stroke, JEA applied to the elbow joint range will lead to a greater increase in the patient's active control zone at the elbow compared to no JEA and thus in his/her ability to perform isolated voluntary movement of the elbow.

Research plan

In our preliminary proof of principle study, we developed and tested a passive robotic system in 21 healthy subjects (aged 26.2, SD 1.2 yrs). A passive robotic arm was developed for supporting and monitoring arm motion and combined with a simple virtual reality pick-and-place game (Sror et al. 2018). Software was developed for integrating input from the robotic arm and a Kinect camera. The software includes a pick-and-place VR game, game success feedback, and motion feedback with and without JEA. Individuals were assigned to a training group with or without EA and performed one 30 min training period. There was no difference between groups in terms of the success rate of hitting the targets. The group training with EA tended to work longer and be more motivated. The application was found to be acceptable to healthy individuals, to enhance motivation to exercise and not to cause fatigue or any adverse effects (Sror et al., 2018; 2019a; 2019b).

The next phases of the study are to investigate the effects on learning with JEA feedback in healthy subjects, and then to test the JEA feedback effect in patients with stroke.

In two separate studies, we will test 24 healthy subjects and 24 patients who have moderate-to-severe stroke (spasticity + some arm movement). Testing of the healthy subjects will be done in Canada and testing of patients will be done in two countries (Israel-Soroker Hospital, Beer-Sheva; Canada-Jewish Rehabilitation Hospital, Laval/Montreal). The motivation for testing the application in patients at two sites is to assess the feasibility of conducting a multi-site study using this technology.

In both studies: Subjects will be randomly allocated to two equal groups. One group (control) will receive regular feedback and the other group will receive JEA feedback (randomized with catch trials).

Subjects will perform ~30 min of target reaching with their non-dominant/affected arm, 3 times in one week, with a minimum of 1 day between sessions. Rest periods will be provided when needed to avoid subject fatigue. In the experimental group, target locations will be tailored to coincide with active control range limits determined at the beginning of each session. In the stroke group, workspace extensions will be added as active range increases (i.e., exercise progression) for patients receiving JEA feedback.

Session 1 (1 hour and 15 min) will include a Reaching Pre-Test of 10 trials to a fixed target (see below), reaching training and evaluation of perceived exertion. Session 2 (1 hour) will include the evaluation of the TSRT in the stroke group, reaching training and perceived exertion rating. Session 3 (2 hours) will be the same as Session 2 but the last 10 trials of Session 3 will be done to a fixed target (Post-Test). Following Session 3, there will be a pause of 1 hour after the training and then a Reaching Follow-up Test of 10 trials to a fixed target will be done. In addition, the stroke group will undergo a clinical evaluation including determination of the elbow flexor TSRT angle prior to Session 1 and another clinical evaluation following Session 3.

For Study 1, the **primary outcome measures** are change in the index of performance (IP), which is a measure of reaching efficiency (Takeda et al., 2019).

For Study 2, the **primary outcome measures** are the same as those for the healthy group as well as the area of the active control workspace based on the TSRT and spasticity. The **secondary outcome measures** are the change in the FMA-UL and patient effort according to the Borg scale.

Evaluations for Study 2:

Clinical evaluation sessions: Clinical assessments will be conducted by a blinded assessor before (Pre-test) and after (Post-test) the last training session. In the Pre and Post-test sessions, all of the following assessments will be done.

Arm motor impairment: **i)** *Voluntary arm motor ability and coordination* will be evaluated using the valid (Berglund and Fugl-Meyer 1986) and reliable Fugl-Meyer Arm Assessment (FMA; Fugl-Meyer et al. 1975) that measures reflexes, volitional movements and UL

coordination on a 66 point scale. FMA also evaluates sensation (light touch), kinaesthesia and passive range of motion on ordinal scales; **ii)** *spasticity* will be measured by the Modified Ashworth Scale (Bohannon and Smith 1987) on a scale of 0 to 4 : **iii)** TSRT The *threshold of the active control zone* of the elbow will be identified by determining the tonic stretch reflex threshold (TSRT) angle in elbow flexors using the Montreal Spasticity Measure (Calota et al. 2008). This methodology has been successfully implemented in our previous RCT (Levin et al. 2018). It consists of recording electromyographic signals from the elbow flexors and extensors with surface electrodes as well as the elbow angle using a goniometer, while the elbow is stretched from flexion to extension 20 times. Then, determination of the active control workspace will be done by passively moving the arm attached to the robot arm at a moderate speed throughout the horizontal workspace while monitoring elbow extensor and flexor EMG on an oscilloscope and respecting the identified elbow joint range limitation. Since, no EMG activity should be present at rest, the appearance of elbow flexor or extensor activation during passive manipulation of the arm through the horizontal shoulder/elbow workspace will indicate that the elbow has been moved beyond the TSRT angle. In this way, the TSRT angle will define the limits of the whole arm active control workspace. The area of the active control workspace will be computed from the x, y workspace recorded by the Kinect II camera using enhanced tracking and expressed as a percentage of the full biomechanical workspace defined by the limits of the passive shoulder horizontal/elbow area.

Fig. 1. Training position and set-up.

For both studies: Training protocol (Fig 1): As described above, the arm active control workspace will be measured by the Kinect II camera and reproduced in the VR workspace for each session. Objects to be reached will be displayed within this defined VR workspace for both groups. In this way, the training will be personalized to the range of active motion in each subject. Three 30 min training sessions will be done. At the end of each training session, the patient's perceived *sense of effort* will be evaluated with the valid and reliable 20 pt Borg Rating of Perceived Exertion Scale (Borg 1982).

The robotic system consists of an ergonomic double-joint horizontal manipulandum mounted on a rigid, movable support (Fig. 1). The subject sits in an armless chair with a high back support and trunk movement is restricted. The forearm is attached to the manipulandum with Velcro and the wrist and hand are free to move. Movements of the arm and manipulandum are used as input signals to move the arm avatar in the VR game. For the stroke group, the game (Fig. 2) is adapted to patient capabilities, based on her/his active control range for isolated elbow flexion and extension determined before each training session. The initial hand position is 10 cm sagittal to the patient's midline. Prior to

Session 1, a Pre-Test will be conducted in which subjects will reach 10 times to a fixed target placed at arm's length in the subject midline. The same protocol will be added to the end of Session 3 as a Post-Test and repeated 1 hour after Session 3 as the Follow-up Test.

Training Protocol: Objects to be reached are randomly presented within the virtual workspace every 2-10s. The subject is instructed to reach each object from the specified starting position as quickly and as accurately as possible in a session of at least 30 minutes (approximately 138 reaches, considering 3s/reach). To control training intensity, practice will be extended to the time needed to complete 138 reaches per session. During reaching, the motion of the whole arm is shown by an avatar, while vision of the subject's actual arm is blocked by a screen, to minimize visual-proprioceptive mismatch (Dietz 1992). For JEA trials, the avatar depiction includes a 10° elbow flexion error based on forward kinematic calculation. For implicit learning to occur, we will use a small (i.e., 10°) instead of a large error, to decrease direct perception of elbow position and conscious correction. Feedback in the form of task success of endpoint (hand) movement is presented at the end of each reaching trial to increase motivation and engagement (Guadagnoli and Lee 2004). The introduced error causes the subject to perceive their hand position as undershooting the target. The subject's task is to solve the problem of moving the arm further by learning to incorporate more elbow extension into the whole arm reaching task. Multiple solutions are needed in order to solve problems for targets located in different parts of the arm workspace. **Game difficulty** will be progressed according to the Challenge Point theory of motor learning (Guadagnoli and Lee 2004), which suggests that learning is enhanced by optimally challenging the individual through manipulation of task difficulty according to their motor skill level and cognitive capacity. Difficulty level will be increased by altering target locations (i.e., based on changes in active ranges for the JEA stroke group and by increments of 2 cm for the non-JEA group) and by decreasing the allowable movement time for each reach (increasing movement speed). Difficulty will be progressed when the participant reaches a 90% success rate. Low-cost motion tracking is used for clinical accessibility. **Motion tracking** is based on the Kinect II skeleton and an extended Kalman filter (Simon 2006) to improve accuracy (Fig. 3). A Kalman filter has two steps in each iteration. First, a prediction is made based on the current location and the motion model. The prediction is of both the state variables and their uncertainty. Then, the predictions are updated based on the current measurement using a weighted average, which incorporates the uncertainties of the measurements and the predicted states. The model assumes no shoulder motion, and motion along the same direction as in the previous step in the elbow and wrist. At each step, model predictions are combined with the measured locations, where weights are based on the Kalman gain calculated on the estimated state error. Due to the incorporation of rigid body relations,

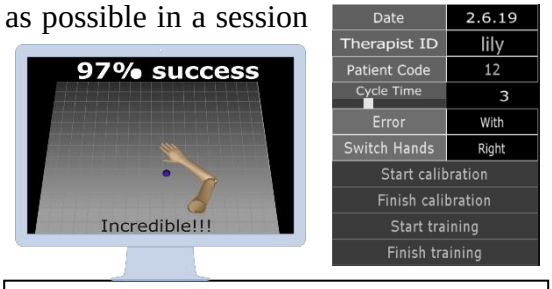

Fig. 2. Left: View of the subject's arm avatar and arm workspace for the VR training. Right: Therapist's control screen showing patient information and training parameters.

calculations of Kalman gains for elbow and wrist also account for shoulder and elbow error covariance respectively. Segment lengths are updated after each measurement step. Objects to be reached in VR are determined before training based on the subject's arm range of motion. The RANSAC algorithm (Fischler and Bolles 1981) is used to fit the recorded arm positions into the plane to reduce measurement errors.

Subjects and subject recruitment. Participants will be allocated by random numbers to either an *experimental group* that will receive JEA feedback (randomized with catch trials) or a *control group* that will receive no JEA feedback. ***Blinding:*** The sequence of allocation will be concealed from those assigning participants to groups until the moment of assignment, to prevent them from consciously or unconsciously influencing which participants are assigned to which groups. Participants will also be blinded to group allocation. Finally, evaluators will be blinded by concealing participant group allocation.

Patients will be recruited through well-established procedures at the JRH. Potential participants will be identified from chart or database review and sent a letter of information describing the study. If they are interested, they will be directed to contact the research assistant by phone or email who will schedule them for a screening interview. Healthy subjects will be recruited from the community with the help of information flyers posted on bulletin boards. Subjects will participate after signing informed consent forms approved by the Center for Interdisciplinary Research in Rehabilitation (CRIR) Ethics Committee. Handedness will be measured for both studies with the Edinburgh Handedness Inventory (Oldfield 1971) but for Study 2, both right- and left-handed subjects will be included since hemispheric dominance is not expected to influence results. For Study 1, healthy women and men will be included who 1) are between the ages of 18-75 yrs; 2) have normal or corrected-to-normal vision; and 3) are able to provide informed consent. For Study 2, women and men will be included who 1) sustained a first cortical/sub-cortical ischemic/hemorrhagic stroke <1 yr previously and are medically stable; 2) are aged 18-75 yrs to minimize confounding effects of age-related changes in muscular responses; 3) are no longer receiving treatment; 4) have arm paresis (Chedoke-McMaster Arm Scale of 2-6 /7; Gowland et al. 1993) but are able to perform voluntary elbow movement of at least 30° per direction; 5) have mild-moderate elbow flexor spasticity; and 6) are able to provide informed consent. Subjects will be excluded if they have/are: 1) other major neurological neuromuscular/orthopaedic/pain problems that may interfere with task performance; 2) major cognitive deficits (<26 on Montreal Cognitive Assessment; Nasreddine et al. 2005) or 3) depression (> 14 on Beck Depression Inventory II; Beck et al. 1988; 1996).

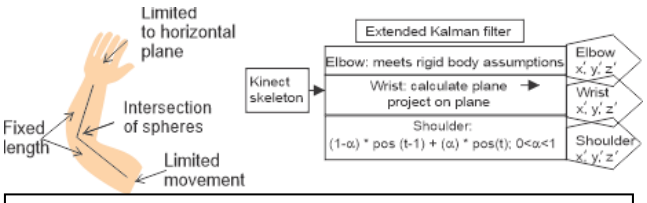

Fig. 3. UL model based on the Kinect II skeleton (left) and explanation of the extended Kalman filter (right) to improve motion tracking accuracy.

Data analysis

For Study 2, data from Canada will be combined with those from Israel for a total of 12 subjects per group.

To address Hypothesis 1, we will compare the change in the IP between the Pre-Test and the Post-Test as an indicator of motor improvement and the change from Post-Test to Follow-Up as an indicator of motor learning using paired t-tests after verifying for data normality.
To address Hypothesis 2, changes in the area of the active control workspace and clinica scores will be compared between groups using paired t-tests after verifying for data normality.

Knowledge translation
The preliminary results will primarily be used to inform the design of a full randomized controlled trial. However, preliminary results will be shared with clinicians at both sites and by oral or poster presentations at local, national or international meetings.

Participating researchers

Caroline Rajda is a 1st year Master's student in the Integrated Program of Neuroscience at McGill University. **Mindy Levin** is Professor in the School of Physical and Occupational Therapy in the Faculty of Medicine at McGill University. She has pioneered many innovations in the area of upper limb rehabilitation, including identification of underlying motor control deficits at the joint and interjoint level, measurement of spasticity, incorporation of VR training interventions and the distinction between compensation and recovery. **Sigal Berman** is an Associate Professor in the Department of Industrial Engineering and Management at Ben-Gurion University of the Negev. She leads the Telerobotics laboratory where robotic motion control, learning, and interaction methodologies are developed and assessed. Prof. Berman has applied advanced mathematical methods for modeling and analysis of arm motion in healthy subjects and in patients with stroke. **Shelly Levy-Tzedek** is a Senior Lecturer in the Department of Physiotherapy who has been studying human movement in health and in disease for over a decade, publishing in journals that are either specific to neurological rehabilitation, or appropriate for inter-disciplinary research (e.g., in Scientific Reports). Profs. Berman and Levin have been collaborating on stroke rehabilitation for close to a decade. They have jointly published papers in leading journals and conferences [e.g., 15-17] and have worked together in two funded research projects. Prof. Berman and Dr. Levy-Tzedek have collaborated on robotic rehabilitation, and have jointly supervised a student working on robotic mirror-game treatment [18].

Budget and matching funds: details and justification

The project is funded by an ABC (Agricultural, Biological and Cognitive Robotics) grant to Sigal Berman from Ben-Gurion University for the portion of the research done in Israel. Funds are allocated for supporting a scholarship or a graduate student. During the first year, most of the funds were allocated to the construction of the passive manipulator and purchase of equipment (i.e., computer, Montreal Spasticity Measure). Funds are allocated for subject compensation, publications and student travel to conferences.

Table 1. ABC budget Israeli team

Funding plan per fiscal year k US$	**Y - 1**	**Y - 2**	**Y - 3**	**Total**
Scholarship for graduate student	2	2	2	

Building manipulandum + computer for the system	11			
Spasticity measurement equipment		9.5		
Supplies, peripherals, software license, Kinect, etc.	1	0.5	2	
Human subject reimbursement		2	3	
Travel: To Canada (year 2) Hosting in IL (year 1+3)	1	1	2	
Student travel to conferences			3	
Publications			3	
Total k US$	15	15	15	45

Justification: Most of the budget in the first year is allocated to adapting the current robot/manipulandum and writing/implementing appropriate software for EA. Personnel costs are related to this activity in year 1 and to conducting the study in years 2 and 3. Human subject reimbursement ($25 x 14 sessions (3 test + 10 training) x 12 subjects = 4200). Funds are allocated to defray travel costs to Israel in year 1 and 3 and hosting costs in Canada in year 2 for PI and students, as well as to defray costs of publication and presentation in years 2 and 3.

Table 2. Matching budget Canadian team

Matching funding is provided by Mindy Levin from the Canada Research Chairs fund (until March 2019) and then the Distinguished James McGill Professor fund.

Funding plan per fiscal year k US$	**Y - 1**	**Y - 2**	**Y - 3**	**Total**
Personnel (Research assistant + engineer)	10			10
Personnel (Research assistant + student)		10	10	20
Adapting manipulandum, software + computer for the system	3			3
Supplies, peripherals, software license, Kinect, etc.				
Human subject reimbursement		2	2	4
Travel: To IL (year 1+3) Hosting in Canada (year 2)	2	1	2	5
Conference presentation and publications		2	1	3
Total k US$	15	15	15	45

References

F. Abdollahi, E. D. Case Lazarro, M. Listenberger, R. V. Kenyon, M. Kovic, R. A. Bogey, D. Hedeker, B. D. Jovanovic, J. L. Patton, 2014. Error augmentation enhancing arm recovery in individuals with chronic stroke: A randomized crossover design, Neurorehabilitation and Neural Repair, 28(2):120–128.

A. T. Beck, R. A. Steer, G. K. Brown, 1996, Beck Depression Inventory-Second Edition Manual. San Antonio (TX): The Psychological Corporation.

A. T. Beck, R. A. Steer, M. Garbin, 1988, Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. Clinical Psychology Review, 8:77-100.

K. Berglund, A. R. Fugl-Meyer, 1986, Upper extremity function in hemiplegia. A cross validation study of two assessment methods. Scandinavian Journal of Rehabilitation Medicine, 18:155–157.

R. W. Bohannon, A. B. Smith, 1987, Inter-rater reliability of a Modified Ashworth Scale of muscle spasticity. Physical Therapy, 2:206-208.

G. A. Borg, 1982. Psychophysical bases of perceived exertion. Medicine Science Sports and Exercise, 14(5):377–381. doi:10.1249/00005768-198205000-00012.

A. Calota, A. G. Feldman, M. F. Levin, 2008, Spasticity measurement based on tonic stretch reflex threshold in stroke using a portable device. Clinical Neurophysiology, 119(10):2329-2337, doi: 10.1016/j.clinph.2008.07.215.

M. A. Conditt, F. Gandolfo, F. A. Mussa-Ivaldi, 1997. The motor system does not learn the dynamics of the arm by rote memorization of past experience, Journal of Neurophysiology, 78(1):554-60.

V. Dietz, 1992, Human neuronal control of automatic functional movements: interaction between central programs and afferent input. Physiology Review, 72:23-69.

A. G. Feldman, 2015. Referent Control of Action and Perception. Challenging Conventional Theories in Behavioral Neuroscience, Springer: NY.

M. Fischler, R. Bolles, 1981, Random sample consensus: a paradigm for model fitting with application to image analysis and automated cartography. Com. of the ACM 24

A. R. Fugl-Meyer, L. Jääskö, I. Leyman, S. Olsson, S. Steglind, 1975. The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. Scandinavian Journal of Rehabilitation Medicine, 7(1):13-31.

C. Gowland, C. Huijbregts, A. McClung, A. McNern, 1993, Measuring clinically important change with the Chedoke-McMaster Stroke Assessment. Canadian Journal of Rehabilitation, 7:14-16.

M. A. Guadagnoli, T. D., 2004, Challenge point: A framework for conceptualizing the effects of various practice conditions in motor learning. Journal of Motor Behavior, 36:212-224.

V. S. Huang, J. W. Krakauer, 2009. Robotic neurorehabilitation: a computational motor learning perspective, Journal of NeuroEngineering and Rehabilitation, 6:5

S. Israely, E. Carmeli, 2016. Error augmentation as a possible technique for improving upper extremity motor performance after a stroke – a systematic review, Topics in Stroke Rehabilitation, 23(2):116-125.

P.-C. Kao, S. Srivastava, S. K. Agrawal, J. P. Scholz, 2013. Effect of robotic performance-based error-augmentation versus error-reduction training on the gait of healthy individuals, Gait & Posture, 37(1): 113–120.

G. Kwakkel, B. J. Kollen, J. van der Grond, A. J. H. Prevo, 2003. Probability of regaining dexterity in the flaccid upper limb: Impact of severity of paresis and time since onset in acute stroke. Stroke, 34:2181-2186.

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

M. F. Levin, M. C. Baniña, S. Frenkel-Toledo, S. Berman, N. Soroker, J. M Solomon, D. G. Liebermann, 2018, Personalized upper limb training combined with anodal-tDCS for sensorimotor recovery in spastic hemiparesis: study protocol for a randomized controlled trial, Trials, 19:7, https://doi.org/10.1186/s13063-017-2377-6

M. F. Levin, A. G. Feldman, 1994, The role of stretch reflex threshold regulation in normal and impaired motor control. Brain Research, 657(1-2):23-30.

S. Levy-Tzedek, (2017). Motor errors lead to enhanced performance in older adults. Scientific Reports, 7:3270.

P. Maciejasz, J. Eschweiler, K. Gerlach-Hahn, A. Jansen-Troy, S. Leonhardt, 2014. A survey on robotic devices for upper limb rehabilitation, Journal of NeuroEngineering and Rehabilitation, 11:3

B. I. Molier, G. B. Prange, T. Krabben, A. H. Stienen, H. van der Kooij, J. H. Buurke, M. J. Jannink, H. J. Hermens, 2011. Effect of position feedback during task-oriented upper-limb training after stroke: five-case pilot study, Journal of Rehabilitation Research and Development, 48(9):1109-1118.

Z. S. Nasreddine, N. A. Phillips, V. Bédirian V., 2005, The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. Journal of the American Geriatric Society, 53(4):695-699. doi:10.1111/j.1532-5415.2005.53221.x.

R. C. Oldfield, 1971, The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia, 9(1):97-113.

D. Simon, 2006, Optimal State Estimation. John Wiley & Sons, NJ, USA.

L. Sror, S. Levy-Tzedek, M. F. Levin, S. Berman, 2018. Low-cost virtual reality system with passive arm support for stroke rehabilitation, Workshop on Robots for assisted living, IEEE/RSJ International Conference on Intelligent Robots and Systems, Madrid, October 1-5.

L. Sror, S. Levy-Tzedek, I. Treger, M. Vered, M. F. Levin, S. Berman, 2019a. A virtual reality-based environment for error-augmented treatment in patients with stroke, The Israeli Industrial Engineering and Management Conference IE&M, Airport City, Israel, April, 1.

L. Sror, M. Vered, J. Treger, S. Levy-Tzedek, M. F. Levin, S. Berman, 2019b. A virtual reality-based training system for error-augmented treatment in patients with stroke (poster). International Conference on Virtual Rehabilitation, ICVR, July 22-24, 2019, Tel Aviv, Israel.

M. Takeda, T. Sato, H. Saito, H. Iwasaki, I, Nambu, Y. Wada, 2019. Explanation of Fitts's law in reaching movement based on human arm dynamics. Scientific Reports, 9:19804. doi: 10.1038/s41598-019-56016-7.

C. M. Tyrell E. Helm, D. S. Reisman, 2015. Locomotor adaptation is influenced by the interaction between perturbation and base line asymmetry after stroke, Journal of Biomechanics, 48:2849–2857.