Consideration-of-concept of EvolvRehab Body for upper limb virtual rehabilitation at home for people late after stroke

Ellis F, Hancock N, Kennedy N, Clark A, Wells, J, Chandler E, Payne D, Pomeroy VM

Fiona Ellis, PhD: School of Health Sciences, University of East Anglia, UK. ORCID: 0000-0003-2670-0104.

Nicola Hancock, PhD: School of Health Sciences, University of East Anglia, UK. ORCID: 0000-0003-4850-3152. Twitter: @NicolaJHancock.

Niamh C Kennedy, PhD: School of Psychology, University of Ulster, UK. ORCID: 0000-0001-7492-0828. Twitter: @dr_niamh

Allan Clark, PhD: Norwich Medical School, University of East Anglia UK. ORCID: 0000-0003-2965-8941

Jacob Wells, BSc: School of Health Sciences, University of East Anglia, UK.

Elizabeth Chandler, MSc: School of Health Sciences, University of East Anglia, UK. ORCID: 0000-0003-1405-0343

David Payne, BSc: School of Health Sciences, University of East Anglia, UK

Valerie M Pomeroy, PhD: School of Health Sciences, University of East Anglia, UK, and, National Institute of Health Research Brain Injury MedTech Cooperative, UK. ORCID: 0000-0003-4487-823X

Corresponding author: Professor Valerie M Pomeroy, Queen's Building, University of East Anglia, Norwich Research Park, Norwich, NR4 &TJ, UK; v.pomeroy@uea.ac.uk; 44(0)1603 591923.

Abstract: 247

Word Count: 3572

Number of tables: 5

Number of figures: 2

Consideration-of-concept of EvolvRehab-Body for upper limb virtual rehabilitation at home for people late after stroke

Abstract

Objective*:** EvolvRehab-Body is a non-immersive virtual rehabilitation system that could provide high-dose, exercise-based upper limb therapy after stroke. This consideration-of-concept study investigated: adherence rate to prescribed repetitions; viability of repeated measures in preparation for a dose-articulation study; and preliminary signal of potential benefit. ***Methods*:** pre-post and repeated measures with people at least six months after stroke. Twelve-week intervention: exercise-based therapy via EvolvRehab-Body. Pre-post-intervention measures: Wolf Motor Function Test (WMFT); hand grip force. Repeated-during-intervention measures: Motricity Index (MI) and Action Research Arm Test (ARAT). Analysis: adherence rate (%) to set repetitions; percentage of total possible measures collected; pre-to-post-intervention change estimated in relation to published minimally detectable changes of WMFT and hand grip force; and slope of plotted data for MI and ARAT (linear regression). ***Results*:** Eight of twelve participants completed the 12-week intervention phase. Adherence: 87.5% (1710 to 9377 repetitions performed). Viability repeated measures: 88 of 96 (91.7%) ARAT and MI scores collected. Preliminary signal of potential benefit was observed in five participants but not always for the same measures. Three participants improved WMFT-time (-7.9 to -27.2 seconds/item), four improved WMFT-function (0.2 to 1.1 points/item), and nobody changed grip force. Slope of plotted data over the 12-week intervention ranged from: -1.42 ($p=0.26$) to 1.36 ($p=0.24$) points-per-week for MI and -0.30 ($p=0.40$) to 1.71 ($p<0.001$) points-per-week for ARAT. ***Conclusion: Findings of good adherence rate in home settings and preliminary signal of benefit for some participants gives support to proceed to a dose-articulation study. These findings cannot inform clinical practice.

Contribution of the article

- Adherence to prescribed exercise plan was 87.5% (1710 to 9377 repetitions) performed over a 12-week intervention period
- A dose-articulation study of EvolvRehab-Body is now required
- Findings of this study cannot be used in clinical practice as this is early phase research

Keywords: Virtual Rehabilitation, Virtual Reality, User-led design, Stroke.

Introduction

Further improvements in motor recovery (reduction in motor impairment) after stroke could be achieved with higher doses of evidenced-based therapy [1,2]. Delivery of higher doses is often not realised in routine practice or efficacy trials [3,4] but could be achieved using virtual reality technology as an adjunct to in-person therapy [5–7] to reduce motor impairment [8].

Notably, meta-analysis indicates that VR systems specifically developed for stroke rehabilitation have greater benefit than commercially available systems designed for the general population such as the Wii device [7]. This may be because VR systems specifically designed for rehabilitation utilise more of the principles of stroke rehabilitation [2] than 'general population' systems [7]. In particular, the capacity to deliver evidenced-based rehabilitation that is meaningful, repetitive and with relevant feedback [9]. But of key importance is the need to use VR systems in peoples' homes where most rehabilitation takes place. Many VR systems are tested in laboratory environments, e.g., [10,11], and findings may not be transferable to home settings. For example, in laboratory environments there is precise control of lighting, exclusion of objects except for the participant from the field of view and expert assistance available for resolution of technical challenges. Essentially, home-based VR systems need: to be specifically developed for stroke rehabilitation; to provide evidenced based rehabilitation; provide relevant feedback; and to be useable by people with stroke in their own homes when expert assistance is not physically present.

These requirements for home-based VR rehabilitation systems are met by the non-immersive EvolvRehab-Body, a class 1 CE marked medical device that delivers upper limb exercise-based therapy (Evolve Rehabilitation Technologies, Spain; figure 1). The version of EvolvRehab-Body investigated in this study consisted of a laptop computer connected to a Microsoft Xbox Kinect V2 (Microsoft Corporation, USA) and a LEAP hand motion device

(LEAP motion inc, USA). Users' movements were detected by the Kinect and replicated, in real-time, by an on-screen avatar. The software consisted of assessments, exercises, and exergames that the developer reports were designed with advice from clinical therapists (see *https://evolvrehab.com/evolvrehab/evolvrehab_body/*). Personalised exercise-based rehabilitation prescriptions were creatable and updatable using a 'therapy editor' to ensure continued challenge in adherence to the principles of stroke rehabilitation [2].

The commercially available EvolvRehab-Body requires testing for clinical efficacy. But, before clinical efficacy of EvolvRehab-Body can be evaluated in a randomised controlled trial it is important to identify the optimal therapeutic dose [8,12] using pharmaceutical study designs for dose-articulation [13,14]. And then, even before dose-articulation can be conducted it is important to investigate consideration-of-concept [12,15] of EvolvRehab-Body for intended use in the homes of people with stroke. Investigation of consideration-of -concept of EvolvRehab-Body as the first step of research evaluation adheres to the stroke recovery trial development framework [12]. Stroke rehabilitation research also requires investigation of the relative contributions of motor recovery (reduction of motor impairment) and behavioural substitution (compensation for loss of neuromotor function) [16]. Consequently, it is important to measure motor impairment objectively with surface electromyography (sEMG) to identify appropriate muscle activation [17] in addition to clinical scales that are more subjective [18]. Therefore, as part of this consideration-of-concept study, it is important to assess the feasibility of using sEMG for people with stroke in their own homes.

The objectives of this study were to:

1. find if people with stroke adhere to 'prescribed' use of EvolvRehab-Body over a 12-week period.

2. assess the viability of making repeated measures of motor impairment and functional capacity during the intervention period to inform design of a subsequent dose-finding study.
3. provide preliminary information on the possibility that EvolvRehab-Body could, in a subsequent study, reduce motor impairment and increase functional capacity.
4. explore the feasibility of using surface electromyography (sEMG) for measures of muscle activity impairment in a subsequent dose-finding study based in the homes of people with stroke.

Materials and methods

Design and ethics

This study used a repeated measures design with a randomised duration (one to four weeks) of a baseline period. Outcome measures were made at the end of a 12-week intervention period (objectives 1-4). This design was used to explore whether a subsequent dose-articulation study would be able to use a randomisation to multiple baselines of different time durations, combined with, repeated measures during an intervention period.

Ethical approval was received from the UK National Research Ethics Service (ref 233548 18/LO/0562) who then placed a summary of the protocol on the Health Research Authority (HRA) website (https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/upper-limb-stroke-rehabilitation-via-the-virtualrehab-platform-v1/). Upon a later request from the HRA the study was registered on ClinicalTrials.gov (NCT04517812). All participants provided informed consent.

Participants

Participants were people with stroke recruited through their general practitioner practice and a convenience sample of ten adults with no neurological damage (healthy adults)

recruited through posters. People with stroke were adults (18+ years) six months or more after a stroke. All were able, with their more paretic upper limb to score at least 19/33 on the elbow/shoulder section of the Motricity Index [19] but unable to complete the Nine Hole Peg Test [20] in 50 seconds or less. This was to ensure that participants had ability to produce voluntary contraction of paretic muscle and had potential for improvement. Prior to the stroke, they could use the more paretic upper limb to pick up a cup and drink from it. They had space in their home for EvolvRehab-Body sensors to detect movement i.e., able to set up the Kinect 150-250cm in front of the participant on a flat stable surface 80-120cm above the floor without interference from vibration (e.g., speakers) or light (e.g., mirror reflection). All were able to follow instructions for this intervention (could play the 'boxing game' with their less paretic upper limb) and were fit to participate in the exercise-based intervention as assessed by a resting heart rate of no more than 90 beats-a-minute and a systolic blood pressure of 140mmHG or less.

Healthy adults (18+ years) reported that they had no clinical diagnosis of stroke, epilepsy or another neurological pathology. These participants acted as a preliminary reference group for the sEMG measures.

Procedure

The duration of the baseline period was allocated via a randomised sequence generated before the study began by a researcher independent of the study team. After a participant had completed baseline-one measures an administrator opened the next sealed opaque envelope in the numerical sequence to reveal the duration of the baseline period during which participants did not use EvolvRehab-Body. At the end of the baseline period the measures were repeated (baseline-two). Participants then used EvolvRehab-Body in their own homes during the 12-week intervention phase and undertook progress measures weekly. At the end of the intervention phase the outcome measures were conducted.

Healthy adults completed sEMG measures once in a movement analysis laboratory, to provide a preliminary estimate of reference values. They did not use EvolvRehab-Body.

Intervention

At the beginning of the intervention phase EvolvRehab-Body was set up in stroke participants' homes. Training was provided by the first author (Researcher) to ensure that participants could use EvolvRehab-Body. Participants were given the Researcher's contact details.

A personalised exercise programme was created for each participant by the Researcher in consultation with a member of the study team who was an academic registered physiotherapist. The personalised training programme consisted of a combination of the exercises and exergames that addressed participants' identified movement challenges. All participants were allocated the 'rowing' and the 'boxing' game as a standard element.

In the first week of the intervention period, participants were advised to use EvolvRehab-Body for 10-minutes on six days. Thereafter they were asked to undertake their training programme for up to one hour a day, six days a week. Adherence to prescription was recorded by EvolvRehab-Body (number of days used, exercises/exergames completed, number of repetitions performed). This information and participants' views were provided regularly to the study physiotherapist to enable appropriate adjustments to the prescription.

At the end of the first week, and each subsequent week, the Researcher visited the participant to ensure the participant had no problems using EvolvRehab Body, and undertake progress measures.

Outcome measures (baseline 1, baseline 2, outcome)

Ability to contract paretic upper limb muscles (motor impairment) was measured through hand grip force with the Jamar hand dynamometer (JLW Instruments, Chicago) placed in a purpose-made stand placed on a stable surface. A participant's paretic upper limb

was positioned on the surface with elbow at 90^0 and hand around the bars. Participants were instructed "squeeze as hard as you can" [3]. Three hand grips were performed with each upper limb. The mean of the three trials was used for analysis.

Functional capacity of the upper limb was measured using the Wolf Motor Function Test (WMFT) [21]. The 15-item test is scored as time (seconds) to complete each item (WMFT-time) with 'quality' of movement scored from 0 to 5 (WMFT-function).

Weekly progress measures

To minimise possibility of a learning effect from undertaking repeated outcome measures, different weekly progress measures were used. Motor impairment was measured with the Motricity Index upper limb section [22,23]. Upper limb functional capacity was measured with the Action Research Arm Test (ARAT) [24].

The probe measure used to test the feasibility of using sEMG (Trigno™, Delsys Inc) was the percentage of a standardised reach-grasp-retrieve task at which peak muscle activation occurred. Sensors were placed in accordance with the SENIAM guidelines (http://www.seniam.org) on the skin over the more and less affected: Deltoid, Biceps Brachii, and Triceps. A sensor was placed over Flexor Carpi Radials to collect accelerometer data that marked phases of the task. Details of the task and data processing are provided in Box 1 of the online supplement.

Analysis

To assess adherence to prescription (objective 1) the percentage of days that EvolvRehab-Body was used by a participant was calculated (duration [25]). Also calculated was the number of repetitions performed as a percentage of those prescribed. The number of repetitions performed by each participant each week was analysed using linear regression (Graph Pad Prism 9, GraphPad Software, San Diego) to summarise slope over time for each individual [26,27].

To assess viability of undertaking repeated measures (objective 2) the percentage of the total possible measures obtained during the intervention phase was calculated per measure.

To obtain initial information about possible benefits, signal of proof-of-concept, (objective 3) change of WMFT and grip force scores from baseline one and from baseline two were interpreted in relation to published minimal detectable change scores (MDC). The MDCs used were: 5.7s per item for WMFT-time [28,29], 0.2 points per item for WMFT-function [28,29], and 7.8Kg for grip force [30]. Also, to describe how progressive change over the intervention phase might occur in a subsequent study, the data for ARAT and MI were plotted (Graph Pad Prism 9). Then linear regression was used to provide preliminary estimates of (measurement) slope over the intervention period [26,27,31,32]. Statistical inference was not used to assess benefit or otherwise. However, a p-value of ≤ 0.05 was used to support visual interpretation of whether the slope for an individual could differ from zero. Potential stability of the slope was estimated with the R-squared value [31].

The feasibility of using sEMG to make measures of muscle activity in the homes of people with stroke (objective 4) was assessed in two ways. The number of weeks sEMG data was collected for each participant was calculated as a percentage of the 12 possible measures per upper limb. The number of weeks when data was of sufficient quality to derive a value for the probe measure was calculated as a percentage of the 12 possible measures per upper limb. Acceptable level of data collection was set as 75%.

Results

Participants and baseline

The characteristics of participants are provided in table 1 so only a summary is provided here. The ages of people with stroke (n=12) ranged from 56 to 93 years and time

since stroke ranged from 10 to 71 months. Healthy adults (n=10) had a mean (SD, range) age of 36.9 (13.5, 26 to 64) years.

There were four participants who did not complete the study. VR01 withdrew after baseline because of challenges with EvolvRehab-Body. A company representative eliminated the challenges before the next participant was recruited. VR03 became ill after baseline one and therefore withdrew. Two participants were withdrawn by the research team because of inability to contact after providing informed consent (VR08) and repeatedly declining measurement appointments (VR11).

The baseline period ranged from 29 to 75 days (table 2). None of the nine participants who completed both measures on both baselines were able to keep to the allocated length of time because of holidays and other commitments.

Adherence to prescribed use (objective 1)

Three of the eight participants who completed the intervention phase used EvolvRehab-Body on all 72 days of the intervention period (table 3). Indeed, two participants exceeded 72 days. Over the intervention period, participants performed between 1,710 and 9,377 repetitions of their prescribed exercises (Table 3). The adherence rates ranged from 46% to 121% (mean of 88%). One participant (VR06) requested that a large number of repetitions were set but only achieved a 46% adherence rate (9,377 of 20,517). Only one participant (VR04) showed a decrease in repetitions over time ($p=0.03$). All other participants increased number of repetitions over time (Table 3, supplementary Fig 1).

Viability of repeated measures in a subsequent dose-finding study (objective 2)

Eight participants completed the intervention phase. Four participants completed ARAT and MI measures on 10 weeks and four on all 12 weeks (supplementary Figs 2 and 3). Therefore, for the ARAT and MI scores 88 of the possible total of 96 (92%) were collected.

Initial information about possible benefits (objective 3)

Change from baseline to outcome (table 3)

Three of seven participants showed change of at least the MDC for WMFT-time. For WMFT-function four of the seven participants showed improvement of at least the MDC. However, no participant showed change of at least the MDC for grip force.

Progressive change over the 12-week intervention period

The actual values obtained for the MI and ARAT scores are provided in graphical form in the online supplement (supplementary figs, 2 and 3). Table 4 provides the synthesis of the slopes and stability of MI and ARAT scores over the 12-week intervention period.

For repeated measures of the ARAT the slope (p-value), ranged from -0.30 (p=0.397)) points per week for VR10 to 1.71 (p<0.0001) points per week for VR02 (table 4).

The slope of repeated MI scores ranged from -1.42 (p=0.262) points per week for VR09 to 1.36 (p=0.24)) points per week for VR07 (table 4).

Feasibility of sEMG to measure muscle activity (objective 4)

The number (percentage) of weeks sEMG data was collected for each participant is provided in Table 5. In summary, the sEMG data collected was 91% of that possible during the intervention phase. This was above the 75% acceptability level. Also provided in Table 5 is the number (percentage) of weeks when data was of sufficient quality to derive the probe measure of percentage of task when peak sEMG occurred. For the less affected upper limb 79% of the total possible measures were produced but only 35% for the more affected upper limb. This was because it was not always possible to identify the inflection points in the accelerometer signal for the more affected upper limb (figure 2).

The actual values collected from healthy volunteer participants (control) for percentage of task at which peak sEMG occurred are provided in supplemental Table 5. The data for stroke participants was plotted in the context of the mean control values ± 1SD for the healthy adults dominant and non-dominant upper limbs (supplementary figures 4-11).

These data are provided as supplementary files for completeness of reporting only. No inferences about efficacy of EvolvRehab-Body can be made from these data not least because the reference values are imprecise because of the small number of healthy adult participants.

Discussion

The findings of this study provide sufficient signal of potential benefit in some individuals. Thus, supporting continuing research into use of EvolvRehab-Body in the homes of people with stroke to enhance delivery of evidenced-based exercise-based therapy. The mean adherence rate of people with stroke to the prescribed exercise programme was 87.5% and they performed between 1,710 and 9,377 repetitions (objective 2). Repeated measures of motor impairment and functional capacity were found to be viable for use in a subsequent dose-finding study (objective 3) and preliminary information has been provided to support the possibility of benefit in a subsequent study (objective 4). Finally, collection of sEMG data is feasible in the homes of people with stroke and derivation of the probe measure is acceptable for the less affected upper limb (objective 5). However, derivation of the probe measure did not reach the acceptable level for the more affected upper limb because identification of the inflection points in the accelerometer signal was challenging (objective 5). These findings strengthen the potential for robust evaluation of the delivery of stroke rehabilitation via EvolvRehab Body, within the homes of people with stroke [33,34].

Interestingly, seven of eight stroke participants in this study increased the number of repetitions completed over a 12-week intervention phase. Notable is the number of repetitions of prescribed exercise that were performed by participants. This is higher than has been reported for routine therapy [3,4,35] and supports earlier findings that VR has the potential to increase intensity of therapy [32,36]. Whether this range of repetitions is the optimal therapeutic dose requires further study especially as it cannot been assumed that higher doses always produce better outcomes [37] although intensity is needed to drive

neoplastic changes [1]. Subsequent dose articulation studies need to be conducted to identify the optimum therapeutic dose using methodologies already developed for use in stroke rehabilitation research [13,37]. Then the optimum therapeutic dose needs to be evaluated for efficacy in a randomised controlled trial.

The study reported here is not the first investigation of use of a VR rehabilitation device in the homes of people in the chronic phase after stroke (for example [38–40]). However, these earlier studies have used shorter training durations of three weeks [38], four weeks [40] and six weeks [39]. It is notable that this study was able to deliver a 12-week intervention. Consequently, this study indicates that a subsequent dose-articulation study will be able to investigate the optimal duration of training for best effect.

Of key importance is that this study has shown that it is possible to collect sEMG data in the homes of people with stroke and derive a probe measure of muscle activity as required to quantify sensorimotor recovery [41]. Although earlier studies of VR systems have made measures of neuromotor function, they are often made in laboratory settings [10,11] and maybe on only a subset of participants [38]. However, the probe measure derived in this study, percentage of a reach-grasp-retrieve task at which peak sEMG occurred, does not appear suitable for the more affected upper limb. The movement patterns used by people with stroke meant that the inflection points in accelerometer data were not clearly discernible for the more paretic upper limb. Further work is required to identify an accurate means of detecting the onset and offset of task phases.

The limitations of this study are acknowledged. Measures were not undertaken by an assessor masked (blinded) to the study purpose, a control intervention was not used, and participants were aware of the intervention they undertook. In a clinical efficacy trial, all these omissions would increase risk of bias. However, this was a consideration-of-concept study and therefore not designed to provide evidence for use in clinical practice. Rather the

purpose was to find whether there was sufficient signal of potential benefit to continue research into EvolvRehab-Body and to explore whether a subsequent dose-articulation study would be able to use a randomisation to multiple baselines of different time durations, combined with, repeated measures during an intervention period. The findings of the present study cannot be used to inform clinical practice but will be useful for subsequent research.

Another potential limitation to this study was that Microsoft has withdrawn support for the Kinect V2. However, the developer has incorporated the new Microsoft Azure Kinect into EvolvRehab-Body. The Azure Kinect is: half the size of the old Kinect; can be plugged straight into a desktop or laptop computer; and uses state-of-the-art computer vision, speech models and artificial intelligence sensors. Thus, the updated EvolvRehab-Body meets participants' request from Workstream One for a lighter, more portable, design.

A key strength of this study is that it investigated proof-of-concept of EvolvRehab-Body which is an important step in the research pathway to dose-articulation studies and eventually adequately powered efficacy trials [12,15]. This study has provided important information to progress evaluation of EvolvRehab-Body with stroke participants with a mean age close to the UK average and a sample size similar to previous early phase studies of other VR systems [11] and larger than some others [10,32,34] . Importantly, this study also highlights the EvolvRehab-Body's potential for delivering stroke rehabilitation within the home setting where the majority of stroke rehabilitation takes place at an intensity level commensurate with driving beneficial neuroplasticity [1]. Especially as EvolvRehab-Body worked reliably on 95% of intervention days.

Conclusion

Findings of good adherence rate in home settings to the set exercise and preliminary signal of benefit for some participants gives signal of consideration-of-concept for EvolvRehab-Body to proceed to a dose-articulation study. No inferences about efficacy of EvolvRehab-Body

can be made from these data not least because the preliminary reference values are imprecise because of the small number of healthy adult participants.

Ethical approval

Ethical approval was provided by the National Research Ethics Services (ref 233548 18/LO/0562). All participants provided written informed consent.

References

[1] Nudo RJ. Recovery after brain injury: mechanisms and principles. Front Numan Neurosci 2013;7:1–14. https://doi.org/10.3389/fnhum.2013.00887.

[2] Kleim JA, Jones TA. Principles of Experience-Dependent Neural Plasticity: Implications for Rehabilitation After Brain Damage. J Speech, Lang Hear Res 2008;51:S225–39.

[3] Hunter SM, Johansen-Berg H, Ward N, Kennedy NC, Chandler E, Weir CJ, et al. Functional strength Training and movement performance therapy for upper limb recovery early poststroke—efficacy, neural correlates, predictive markers, and cost-effectiveness: FAST-INdiCATE Trial. Front Neurol 2018;8:1–24. https://doi.org/10.3389/fneur.2017.00733.

[4] Pomeroy VM, Rowe P, Clark A, Walker A, Kerr A, Chandler E, et al. A randomized controlled evaluation of the efficacy of an ankle-foot cast on walking recovery early after stroke: SWIFT Cast Trial. Neurorehabil Neural Repair 2016;30:40–8. https://doi.org/10.1177/1545968315583724.

[5] Levin MF. What is the potential of virtual reality for post-stroke sensorimotor rehabilitation? Expert Rev Neurother 2020;doi.org/10. https://doi.org/10.1080/14737175.2020.1727741.

[6] Nguyen AV, Ong YLA, Luo CX, Thuraisingam T, Rubino M, Levin MF, et al. Virtual reality exergaming as adjunctive therapy in a sub-acute stroke rehabilitation setting: facilitators and barriers. Disabil Rehabil Assist Technol 2019;14:317–24. https://doi.org/10.1080/17483107.2018.1447608.

[7] Maier M, Rubio Ballester B, Duff A, Duarte Oller E, Verschure PFMJ. Effect of Specific Over Nonspecific VR-Based Rehabilitation on Poststroke Motor Recovery: A Systematic Meta-analysis. Neurorehabil Neural Repair 2019;33:112–29. https://doi.org/10.1177/1545968318820169.

[8] Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. Cochrane Database Syst Rev 2017:Art. No.: CD008349. https://doi.org/10.1002/14651858.CD008349.pub4.

[9] Levin MF, Weiss PL, Keshner EA. Emergence of virtual reality as a tool for upper limb rehabilitation: incorporation of motor control and motor learning principles. Phys Ther 2015;95:415–25. https://doi.org/10.2522/ptj.20130579 [doi].

[10] Dhiman A, Solanki D, Bgasin A, Das A, Lahire U. An intelligent, adaptive performance-sensitive, and virtual reality-aided gaming platform for the upper limb. Comput Animat Virtual Worlds 2018;29:e1800. https://doi.org/10.1002/cav.

[11] Cameirão MS, Badia SBI, Oller ED, Verschure PFMJ. Neurorehabilitation using the virtual reality based Rehabilitation Gaming System: Methodology, design, psychometrics, usability and validation. J Neuroeng Rehabil 2010;7:48. https://doi.org/10.1186/1743-0003-7-48.

[12] Bernhardt J, Hayward KS, Dancause N, Lannin NA, Ward NS, Nudo RJ, et al. A stroke recovery trial development framework: Consensus-based core recommendations from the Second Stroke Recovery and Rehabilitation Roundtable. Int J Stroke 2019;14:792–802. https://doi.org/10.1177/1747493019879657.

[13] Colucci E, Clark A, Lang CE, Pomeroy VM. A rule-based, dose-finding design for use in stroke rehabilitation research: methodological development. Physiotherapy 2017;103:414–22. https://doi.org/10.1016/j.physio.2016.10.393.

[14] Hayward KS, Churilov L, Dalton EJ, Brodtmann A, Campbell BCV, Copland D, et al. Advancing stroke recovery through improved articulation of nonpharmacological intervention dose. Stroke 2021;52:761–9. https://doi.org/10.1161/STROKEAHA.120.032496.

[15] Dobkin BH. Progressive Staging of Pilot Studies to Improve Phase III Trials for Motor Interventions. Neurorehabil Neural Repair 2009;23:197–206.

[16] Bernhardt J, Hayward KS, Kwakkel G, Ward NS, Wolf SL, Borschmann K, et al. Agreed definitions and a shared vision for new standards in stroke recovery research : The Stroke Recovery and Rehabilitation Roundtable taskforce. Int J Stroke 2017;12:444–50. https://doi.org/10.1177/1747493017711816.

[17] Negro F, Hu X, Yao J. Editorial: Understanding altered muscle activation after central or peripheral neuromuscular injuries. Front Neurol Neurorehabilitation 2021;12:642207. https://doi.org/10.3389/fneur.2021.642207.

[18] Campanini I, Disselhorst-Klug C, Rymer WZ, Merletti R. Surface EMG in Clinical Assessment and Neurorehabilitation: Barriers Limiting Its Use. Front Neurol 2020;11:1–22. https://doi.org/10.3389/fneur.2020.00934.

[19] Demeurisse G, Demol O, Robaye E. Motor evaluation in vascular hemiplegia. Eur Neurol 1980;19:382–9.

[20] Oxford Grice K, Vogel K a, Le V, Mitchell A, Muniz S, Vollmer MA. Adult norms for a commercially available Nine Hole Peg Test for finger dexterity. Am J Occup Ther 2003;57:570–3.

[21] Wolf SL, Catlin PA, Ellis M, Archer AL, Morgan B, Piacentino A. Assessing Wolf

Motor Function Test as outcome measure for research in patients after stroke. Stroke 2001;32:1635–9.

[22] Cameron D, Bohannon RW. Criterion validity of lower extremity Motricity Index scores. Clin Rehabil 2000;14:208–11. https://doi.org/10.1191/026921500675786655.

[23] Fayazi M, Dehkordi SN, Dadgoo M, Salehi M. Test-retest reliability of Motricity Index strength assessments for lower extremity in post stroke hemiparesis. Med J Islam Repub Iran 2012;26:27–30.

[24] Yozbatiran N, Der-Yerghiaian L, Cramer S. A standardized approach to performing the Action Research Arm Test. Neurorehabil Neural Repair 2008;22:78–90.

[25] Hawley-Hague H, Horne M, Skelton DA, Todd C. Review of how we should define (and measure) adherence in studies examining older adults' participation in exercise classes. BMJ Open 2016;6. https://doi.org/10.1136/bmjopen-2016-011560.

[26] Frison LJ, Pocock SJ. Linearly divergent treatment effects in clinical trials with repeated measures: Efficient analysis using summary statistics'. Stat Med 1997;16:2855–72. https://doi.org/10.1002/(SICI)1097-0258(19971230)16:24<2855::AID-SIM749>3.0.CO;2-Y.

[27] Senn S, Stevens L, Chaturvedi N. Repeated measures in clinical trials: simple strategies for analysis using summary measures. Stat Med 2000;19:861–77.

[28] Lin K, Hsieh Y, Wu C, Chen C, Jang Y, Liu J. Minimal Detectable Change and Clinically Important Difference of the Wolf Motor Function Test in Stroke Patients. Neurorehabil Neural Repair 2009;23:429–34. https://doi.org/10.1177/1545968308331144.

[29] Fritz SL, Blanton S, Uswatte G, Taub E, Wolf SL. Minimal Detectable Change Scores for the Wolf Motor Function Test. Neurorehabil Neural Repair 2009;23:662–7. https://doi.org/10.1177/1545968309335975.

[30] Schreuders TAR, Roebroeck ME, Goumans J, Van Nieuwenhuijzen JF, Stijnen TH, Stam HJ. Measurement error in grip and pinch force measurements in patients with hand injuries. Phys Ther 2003;83:806–15. https://doi.org/10.1093/ptj/83.9.806.

[31] Lobo MA, Moeyart M, Cunha AB, Babik I. Single-case design, analysis, and quality assessment for intervention research. J Neurol Phys Ther 2017;41:187–97. https://doi.org/10.1016/j.physbeh.2017.03.040.

[32] Schuster-Amft C, Henneke A, Hartog-Keisker B, Holper L, Siekierka E, Chevrier E, et al. Intensive virtual reality-based training for upper limb motor function in chronic stroke: A feasibility study using a single case experimental design and fMRI. Disabil Rehabil Assist Technol 2015;10:385–92. https://doi.org/10.3109/17483107.2014.908963.

[33] Hung YX, Huang PC, Chen KT, Chu WC. What do stroke patients look for in game-based rehabilitation: A survey study. Medicine (Baltimore) 2016;95:1–10. https://doi.org/10.1097/MD.0000000000003032.

[34] Demers M, Chan Chun Kong D, Levin MF. Feasibility of incorporating functionally relevant virtual rehabilitation in sub-acute stroke care: perception of patients and clinicians. Disabil Rehabil Assist Technol 2019;14:361–7. https://doi.org/10.1080/17483107.2018.1449019.

[35] Broderick M, Almedom L, Burdet E, Burridge J, Bentley P. Self-directed exergaming for stroke upper limb impairment increases exercise dose compared to standard care. Neurorehabil Neural Repair 2021:pre-print. https://doi.org/10.1177/15459683211041313.

[36] Brunner I, Skouen JS, Hofstad H, Aßmuss J, Becker F, Pallesen H, et al. Is upper limb virtual reality training more intensive than conventional training for patients in the subacute phase after stroke? An analysis of treatment intensity and content. BMC

Neurol 2016;16:1–7. https://doi.org/10.1186/s12883-016-0740-y.

[37] Lang CE, Strube MJ, Bland MD, Waddell KJ, Cherry-Allen KM, Nudo RJ, et al. Dose-response of task-specific upper limb training in people at least 6 months post-stroke: a phase II, single-blind, randomized, controlled trial. Ann Neurol 2016;80:342–54.

[38] Ballester BR, Nirme J, Camacho I, Duarte E, Rodríguez S, Cuxart A, et al. Domiciliary VR-Based Therapy for Functional Recovery and Cortical Reorganization: Randomized Controlled Trial in Participants at the Chronic Stage Post Stroke. JMIR Serious Games 2017;5:e15. https://doi.org/10.2196/games.6773.

[39] Wittmann F, Held JP, Lambercy O, Starkey ML, Curt A, Höver R, et al. Self-directed arm therapy at home after stroke with a sensor-based virtual reality training system. J Neuroeng Rehabil 2016;13:1–10. https://doi.org/10.1186/s12984-016-0182-1.

[40] Piron L, Turolla A, Agostini M, Zucconi C, Cortese F, Zampolini M, et al. Exercises for paretic upper limb after stroke: A combined virtual-reality and telemedicine approach. J Rehabil Med 2009;41:1016–20. https://doi.org/10.2340/16501977-0459.

[41] Kwakkel G, Lannin N, Borschmann K, English C, Ali M, Churilov L, et al. Standardised measurement of sensorimotor recovery in stroke trials: consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable (SRRR). Int J Stroke 2017;12:451–61. https://doi.org/10.1177/1747493017711813.

Table 1. Participant characteristics

People with stroke (n = 12)*****	
Age in years: mean (SD), min-max	67.5 (12.6), 53-93
Sex: number (%) male	6 (50.0)
Months since stroke: median (IQR), min-max	20.0 (13.6-63.4), 10.0-70.6
More affected side: number (%) left	5 (41.6)
WMFT seconds/item more paretic: mean (SD), min-max	41.4 (31.9), 5.2-82.4
Grip force (Kg) more paretic (n = 10): mean (SD), min-max	4.3 (7.4), 0.0-25.0
Healthy adults (n = 10)	
Age in years: mean (SD), min-max	36.9 (13.5), 26-64

***** one participant withdrew before baseline

Table 2. Baseline length plus more affected Wolf Motor Function Test (WMFT) and Grip Force scores at baseline 1 (B1), baseline 2 (B2) and outcome (Out)

Participant	Days B1 to B2	Mean WMFT-time (seconds per item)			Mean WMFT-function (points per item)			Mean Grip Force (Kg)		
		B1	B2	Out	B1	B2	Out	B1	B2	Out
VR01	NA	10.8			2.3			#		
VR02	49	59.5	58.7	51.6$^{X, \S}$	2.1	2.1	2.2	0.0	0.0	0.0
VR03	NA	46.4			2.3			5.0		
VR04	30	21.8	13.1		2.9	3.1		0.1	#	
VR05	35	91.3	88.7	64.1$^{X, \S}$	1.4	1.3	1.1^{X,§}	1.5	2.2	0.4
VR06	30	13.6	6.3	8.0	3.3	3.3	3.4	25.0	31.3	26.7
VR07	75	42.8	53.1	40.9§	2.3	2.0	2.4§	2.7	3.0	5.0
VR09	36	74.5	69.8	69.7	1.5	1.7	1.7^{X}	0.5	1.0	2.0
VR10	37	7.7	7.5	3.8	3.9	3.3	4.4 ^{X,§}	3.0	3.6	5.0
VR11	37	82.4	83.0		1.1	1.2		2.0	1.3	
VR12	29	5.2	5.7	5.5	3.2	3.2	3.3	3.0	5.3	7.3

VR08 withdrew before baseline 1; VR01 and VR03 withdrew before baseline 2; and VR11 withdrew before intervention phase
= participant fatigued; ^{X} = change of MDC or more from baseline 1; § = change of MDC or more from baseline 2.

Table 3. Participants' adherence to 'prescription' of repetitions (reps) during the 12-week (72 day) intervention phase and number of days on which EvolvRehab-Body did not work

	Adherence to prescription (repetitions)				Number of repetitions performed each week														Days
	Number (%) of days platform used		Number reps prescribed	Number (%) reps performed		1	2	3	4	5	6	7	8	9	10	11	12	Trend over time: slope (p- value)[§]		did not work
VR02	75	(104)	2447	2478	(101)	40	195	294	316	266	228	223	152	170	196	140	258	0.5	(0.94)	n = 7
VR04	60	(83)	2573	2150	(84)	189	195	234	195	195	195	234	169	99	165	175	105	-7.4	**(0.03)**	n = 2
VR05	70	(97)	4205	3905	(93)	105	105	270	270	320	350	360	370	480	425	425	425	30.4	**(<0.01)**	n = 4
VR06	33	(46)	20517*	9377	(46)	577	714	476	906	618	927	927	618	927	927	618	1142	30.1	(0.07)	n = 2
VR07	56	(78)	5606	4404	(79)	225	365	312	425	255	352	448	272	287	415	498	550	17.3	**(0.03)**	n= 5
VR09	72	(100)	2618	1710	(65)	0	60	0	260	280	172	258	129	129	86	192	144	8.2	(0.33)	n = 2
VR10	47	(65)	2013	2442	(121)	228	289	251	164	123	82	164	164	184	244	244	305	2.4	(0.69)	n = 3
VR12	78	(108)	4146	4616	(111)	78	243	245	378	336	401	413	436	515	530	474	567	36.5	**(<0.01)**	n = 2

Note: VR08 withdrew before baseline 1; VR01 and VR03 withdrew before baseline 2; and VR11 withdrew before intervention phase

*** =** Participant requested a large number of repetitions; [§] = linear regression

Table 4. People with stroke: more paretic Action Research Arm (ARAT) and Motricity Index (MI) scores progressively over the 12-week intervention phase

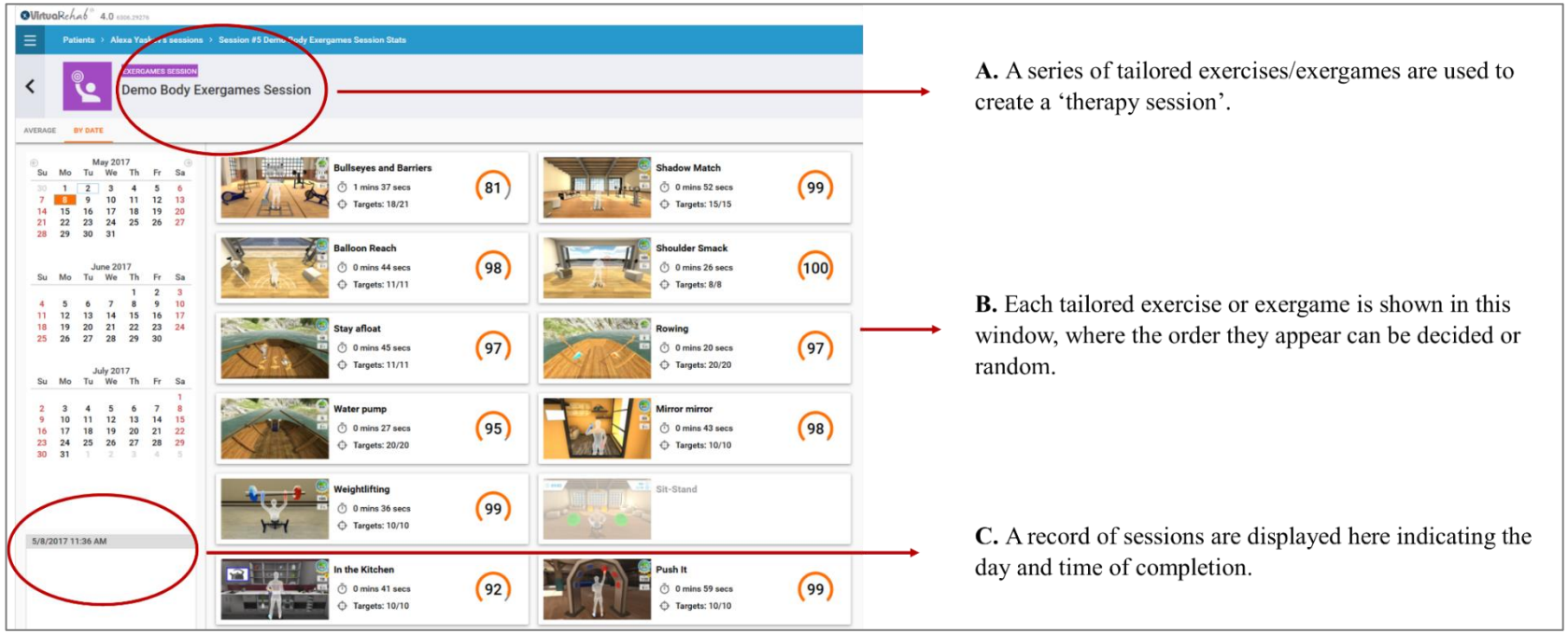
	Number of the 12 possible measures	Maximum possible score	Mean (SD[a]) score over the 12 weeks	Slope of scores over 12 weeks (p-value)[b, c]	Variation from slope (R-squared)
ARAT					
VR02	12	57	20.3 (6.9)	1.71 (**0.001**)	0.80
VR04	10		32.1 (3.5)	0.66 (**0.015**)	0.54
VR05	12		4.0 (0.4)	0.03 (0.459)	0.06
VR06	12		31.6 (3.6)	0.42 (0.164)	0.18
VR07	12		9.0 (2.6)	0.21 (0.358)	0.09
VR09	10		9.4 (2.1)	0.29 (0.200)	0.20
VR10	10		35.5 (3.9)	-0.30 (0.397)	0.09
VR12	10		36.5 (1.1)	0.07 (0.538)	0.05
MI					
VR02	12	100	69.8 (6.6)	-1.00 (0.065)	0.30
VR04	10		79.2 (6.1)	0.51 (0.358)	0.11
VR05	12		40.3 (7.2)	-0.57 (0.369)	0.08
VR06	12		80.3 (6.8)	-0.17 (0.776)	0.01
VR07	12		56.4 (7.6)	1.36 (**0.024**)	0.42
VR09	10		59.2 (11.6)	-1.42 (0.262)	0.15
VR10	10		77.0 (3.7)	-0.53 (0.098)	0.31
VR12	10		74.1 (4.4)	0.13 (0.781)	0.01

[a] Standard deviation; [b] Linear regression, slope with p-value; [c] Statistical inference not made about efficacy of EvolvRehab, but p-values used to support interpretation of change over time

Table 5. Number (%) of the total 12-week intervention phase that sEMG data was collected and the measure could be derived (percentage of task at which peak sEMG occurred).

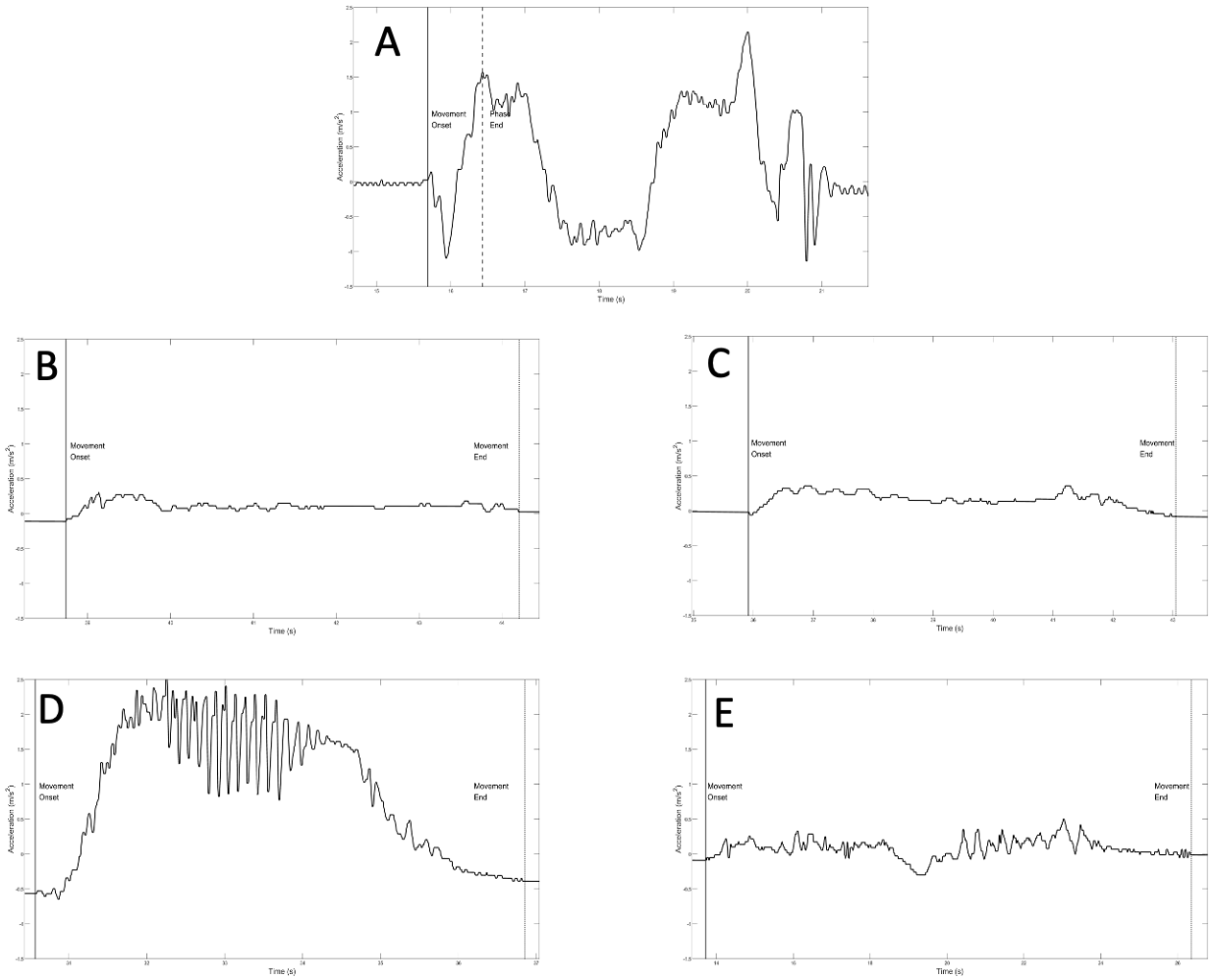
		Number (%) of total possible 12 weeks			
		sEMG data collected		Probe measure derived	
		Less affected	More affected	Less affected	More affected
VR02	Deltoid	12 (100%)	12 (100%)	10 (83%)	10 (83%)
	Biceps	12 (100%)	12 (100%)	11 (92%)	10 (83%)
	Triceps	12 (100%)	12 (100%)	8 (67%)	10 (83%)
VR04	Deltoid	10 (83%)	10 (83%)	6 (50%)	3 (25%)
	Biceps	10 (83%)	10 (83%)	6 (50%)	3 (25%)
	Triceps	10 (83%)	10 (83%)	6 (50%)	2 (17%)
VR05	Deltoid	12 (100%)	12 (100%)	8 (67%)	0 (0%)
	Biceps	12 (100%)	12 (100%)	9 (75%)	0 (0%)
	Triceps	12 (100%)	12 (100%)	10 (83%)	0 (0%)
VR06	Deltoid	10 (83%)	10 (83%)	8 (67%)	2 (17%)
	Biceps	10 (83%)	10 (83%)	8 (67%)	2 (17%)
	Triceps	10 (83%)	10 (83%)	8 (67%)	2 (17%)
VR07	Deltoid	11 (92%)	11 (92%)	9 (75%)	3 (25%)
	Biceps	11 (92%)	11 (92%)	8 (67%)	3 (25%)
	Triceps	11 (92%)	11 (92%)	7 (58%)	3 (25%)
VR09	Deltoid	10 (83%)	10 (83%)	9 (75%)	1 (8%)
	Biceps	10 (83%)	10 (83%)	9 (75%)	1 (8%)
	Triceps	10 (83%)	10 (83%)	9 (75%)	1 (8%)
VR10	Deltoid	11 (92%)	11 (92%)	10 (83%)	7 (58%)
	Biceps	11 (92%)	11 (92%)	10 (83%)	7 (58%)
	Triceps	11 (92%)	11 (92%)	8 (67%)	7 (58%)
VR12	Deltoid	11 (92%)	11 (92%)	11 (92%)	5 (42%)
	Biceps	11 (92%)	11 (92%)	11 (92%)	5 (42%)
	Triceps	11 (92%)	11 (92%)	11 (92%)	5 (42%)
	Totals	**261 (91%)**	**261 (91%)**	**228 (79%)**	**102 (35%)**

Fig 1. Illustration of EvolvRehab-Body



A =LEAP motion and arm bracket;
B = EvolvRehab in use;
C = space required

Fig 2. Illustrative examples of accelerometer signals obtained from less affected and more affected upper limbs of people with stroke performing the reach-grasp-retrieve task



Note: A = example obtained from less affected upper limb, B-E = examples obtained from more affected upper limb