

BMJ Open Hand-Arm Bimanual Intensive Therapy Including Lower Extremities (HABIT-ILE) in adults with chronic stroke: protocol of a randomised controlled trial

Daniela Ebner-Karestinos ^{1,2}, Estelle Gathy ¹, Astrid Carton de Tournai,¹ Enimie Herman,¹ Rodrigo Araneda ^{1,2}, Laurence Dricot ^{1,3}, Benoît Macq ^{1,4}, Yves Vandermeeren,^{1,5} Yannick Bleyenheuft ¹

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For numbered affiliations see end of article.

Correspondence to

Dr Yannick Bleyenheuft;
Yannick.bleyenheuft@uclouvain.be

ABSTRACT

Introduction Stroke causes multiple deficits including motor, sensitive and cognitive impairments, affecting also individual's social participation and independence in activities of daily living (ADL) impacting their quality of life. It has been widely recommended to use goal-oriented interventions with a high amount of task-specific repetitions. These interventions are generally focused only on the upper or lower extremities separately, despite the impairments are observed at the whole-body level and ADL are both frequently bimanual and may require moving around. This highlights the need for interventions targeting both upper and lower extremities. This protocol presents the first adaptation of Hand-Arm Bimanual Intensive Therapy Including Lower Extremities (HABIT-ILE) for adults with acquired hemiparesis.

Methods and analysis This randomised controlled trial will include 48 adults with chronic stroke, aged ≥40 years. This study will compare the effect of 50 hours of HABIT-ILE against usual motor activity and regular rehabilitation. HABIT-ILE will be provided in a 2-week, adult's day-camp setting, promoting functional tasks and structured activities. These tasks will continuously progress by increasing their difficulty. Assessed at baseline, 3 weeks after and at 3 months, the primary outcome will be the adults-assisting-hand-assessment stroke; secondary outcomes include behavioural assessments for hand strength and dexterity, a motor learning robotic medical device for quality of bimanual motor control, walking endurance, questionnaires of ADL, stroke impact on participation and self-determined patient-relevant goals, besides neuroimaging measures.

Ethics and dissemination This study has full ethical approval from the *Comité d'éthique Hospitalo-Facultaire/Université catholique de Louvain*, Brussels (reference number: 2013/01MAR/069) and the local medical Ethical Committee of the CHU UCL Namur-site Godinne. Recommendations of the ethical board and the Belgian law of 7 May 2004, concerning human experiments will be followed. Participants will sign a written informed consent ahead of participation. Findings will be published in peer-reviewed journals and conference presentations.

Trial registration number NCT04664673.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This protocol is a randomised controlled trial (RCT) aiming to determine the efficacy of an intensive intervention focused on upper and lower extremities in adults in the chronic phase of stroke.
- ⇒ Care providers and participants will be blind to allocation and the primary and behavioural motor outcomes of this RCT will be blindly assessed.
- ⇒ This study will quantify changes at functional, neuroimaging, kinematic and kinetic levels.
- ⇒ There is a risk of dropout due to the amount of assessments, assessment times and assessment locations.

INTRODUCTION

According to recent literature, stroke is the most common cause of motor disability in adults, with >101 million cases in Europe in 2019.¹ Sequelae can go from none or mild to severe difficulties, including motor, sensitive and cognitive impairments inducing different degrees of dependence for activities of daily living (ADL), diminished social participation and loss in quality of life.² The origin of the stroke can be either ischaemic (about 80%), resulting from an interruption of normal blood supply to cerebral tissues³ or haemorrhagic (about 20%), resulting from a cerebral vessel rupture.⁴ Haemorrhagic stroke generally induces larger deficits.⁴ Commonly, the rehabilitation process consists in different approaches including physical, occupational and speech therapy, as well as pharmacological and medical interventions.⁵ Concerning physical therapy, interventions vary in a wide range from strength and stretching programmes, walking rehabilitation, electrical stimulation and motor imagery to more specific therapies such as neurodevelopmental concepts, forced use, mirror therapy,

constraint-induced movement (CIMT) or bilateral arm training.^{5–7} Although duration, frequency or intensity of these interventions are heterogeneous, scientific evidence shows higher efficiency for intensive, highly repetitive, goal-oriented and task-specific training considering all phases poststroke.^{6,8} These characteristics are among the principles of motor skill learning,⁹ which the current evidence-based literature indicates as one of the key elements in tailoring neurorehabilitation.^{10,11}

Rehabilitation interventions designed for adult stroke survivors and based on the principles of motor learning exist for a while. The most popular is the CIMT, which involves intensity, task-oriented and task-specific activities focused only on the more affected upper extremity (UE).^{12,13} Significant improvements in strength and use of the UE have been demonstrated after 60 hours (10 days) of CIMT,¹⁴ with benefits maintained even 2 years after therapy.¹² Although efficient, the CIMT disregards the non-affected UE in its approach; actually, one of the key concepts of CIMT is to *prevent* the use of the non-affected UE. In contrast, bimanual or bilateral arm interventions aim to increase the coordination and bimanual use of UE, training with tasks of or similar to ADLs.^{15,16} A recent systematic review reported that bilateral arm training is probably more beneficial than conventional intervention to improve motor impairments of the UE in adults having a mild hemiparesis, particularly in the chronic phase of stroke.¹⁷ Moreover, the positive results of bilateral interventions were increased when higher doses were applied, that is, ≥ 7 hours per week or a total treatment time of ≥ 30 hours. Interestingly, the incorporation of functional tasks in the training programme seems to facilitate both motor and functional recovery.¹⁷ Despite the encouraging results of bimanual interventions, some features of ADLs are still missing in these therapies such as the intersegmental—UE and lower extremity (LE) coordination—components of the actions performed, for example, when manipulation is performed during locomotion or while standing, or when a stable sitting balance is needed.

For some years now, Hand-Arm Bimanual Intensive Therapy Including Lower Extremities (HABIT-ILE)¹⁸ has been one of the few neurorehabilitation interventions targeting UE and LE. HABIT-ILE applies motor skill learning concepts in intensive training; it requires a constant stimulation of both UE and LE as well as postural control through different activities performed continuously, with a progressive increase in difficulty, for several hours each day over a 2-week period. Its efficacy has been proved in children with congenital brain lesions from 1 to 18 years old,^{19–21} with improvements across the three domains of the International Classification of Functioning, Disability and Health,²² notably on motor function of UE and LE as well as neuroplastic changes.^{23,24} HABIT-ILE has never been tested on adults with acquired brain lesions.

Aims and hypotheses

This study aims to investigate, in adults with chronic stroke, the feasibility and effectiveness of HABIT-ILE versus usual motor activity including conventional outpatient rehabilitation. We hypothesise a positive effect of HABIT-ILE with improvements in body function impairments, activity limitation and restriction on participation, compared with regular rehabilitation of the control group. We designed a randomised controlled trial (RCT) to test our hypothesis immediately after 2 weeks of therapy and 3 months later. The effect of HABIT-ILE specifically on motor learning and neuroplasticity will also be tested at the same time periods. Results rated by participants, in case of questionnaires, and by experts in the case of tests, will be correlated with neuroplastic changes.

METHODS AND ANALYSIS

Research design, setting and timeline

This RCT will be a two parallel-group, care provider and main outcomes assessor blinded, with a 1:1 allocation ratio (figure 1). The Consolidated Standards of Reporting Trials (CONSORT) statements for non-pharmaceutical and pragmatic trials²⁵ will be used for the study. The Standard Protocol Items: Recommendations for Interventional Trials guidelines²⁶ were observed for this protocol. The study will be conducted at the Institute of Neuroscience and at Saint-Luc University Hospital of the UCLouvain in Brussels and at the Stroke Unit of the University Hospital CHU UCL Namur-Site Godinne in Yvoir, all in Belgium. The expected overall study duration is approximately 36 months, from December 2020 to December 2023.

Patient and public involvement

The development of the study design and methods did not involve adults with stroke. However, participants will have to determine their individualised functional goals, on which they will be trained throughout HABIT-ILE. After the intervention, the participants will receive a report of their progress and will be encouraged to communicate them with their close relatives and caregivers. Participants' perspectives on the intervention will be asked at the end of the study for tuning future interventions.

Participants, inclusion and exclusion criteria

Forty-eight adults with stroke in the chronic phase (> 6 months), aged 40–90 years, with a functional level allowing to walk independently with/without walking device and to perform active movement against gravity of any joint of the affected UE, who meet the criteria, will be considered. Potential participants will be recruited through the University Hospital CHU UCL Namur-Site Godinne, the Rehabilitation Unit of Saint-Luc University Hospital, through the national Belgian Stroke Council network and spontaneous applications via our lab's social media website, phone calls or mails from potential participants and their relatives who are not followed in any of

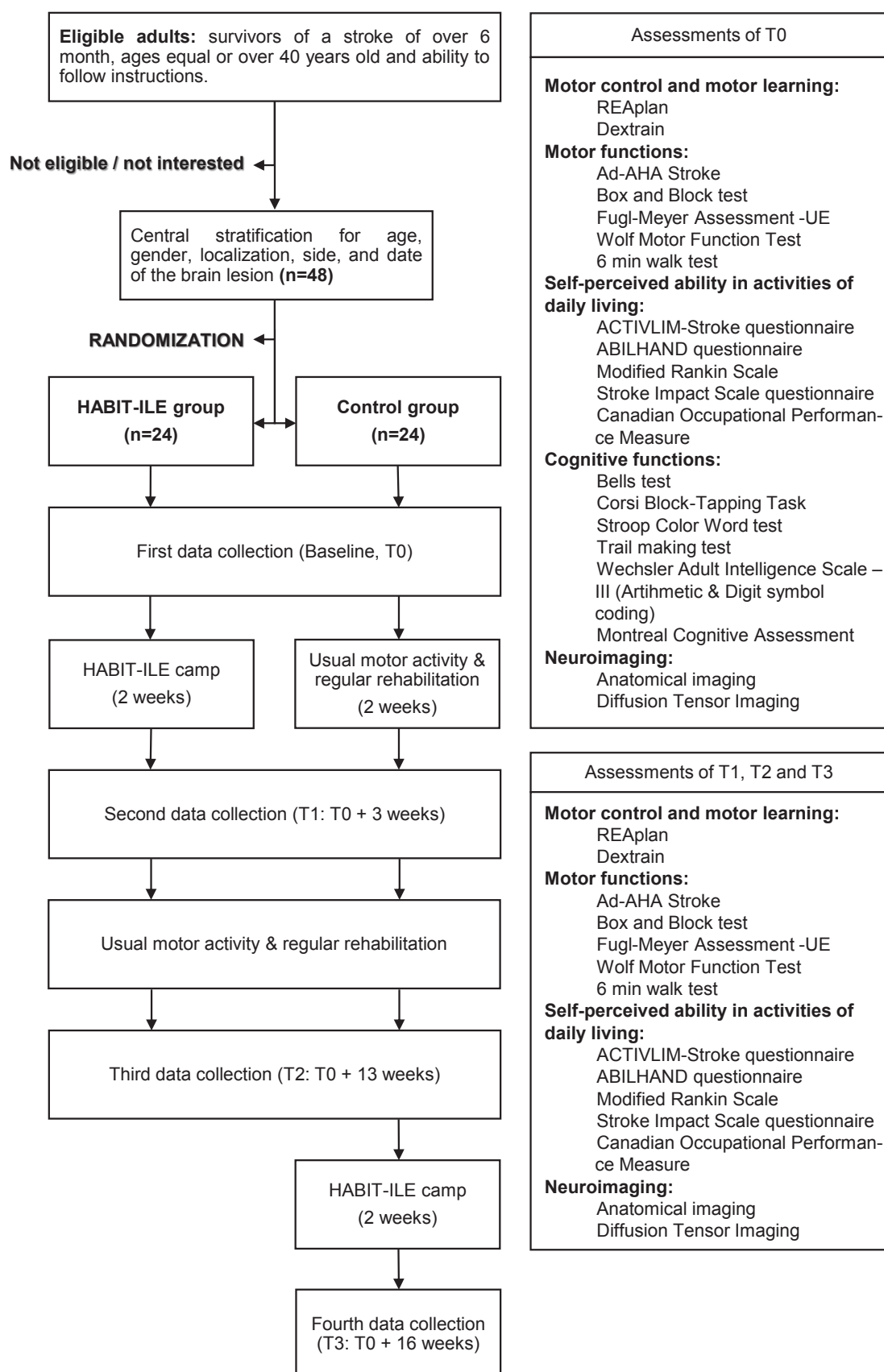


Figure 1 Consolidated Standards of Reporting Trials flow chart. Ad-AHA Stroke, Adult Assisting Hand Assessment Stroke; HABIT-ILE, Hand-Arm Bimanual Intensive Therapy Including Lower Extremities; UE, upper extremities.

the centres above mentioned. To assure study protocol understanding, compliance/fidelity and avoid drop-outs, potential participants will be contacted by one of the authors several times before inclusion (email, phone and/or in person). Moreover, this author will contact them by phone the days before every assessment visit to remind/reconfirm the appointment and check for any inconvenience about their presence.

Participants will be considered for eligibility if they present a diagnosis of hemiparesis secondary to a stroke of over 6 months of evolution (chronic phase), are able to understand and follow instructions and willing to complete all necessary assessments. Potential participants will be excluded if they present alcohol or drug abuse, if they are pregnant, present a major cognitive impairment interfering with the study (eg, psychiatric conditions), severe aphasia interfering with assessments or treatment, uncontrolled health issues (eg, cardiac or renal failure, uncontrolled epilepsy), any of the usual contraindications to magnetic resonance imagery such as metal implants or pacemaker or are unable or unwilling to provide by themselves written consent for their participation.

Sample size

Since this is the first time HABIT-ILE will be proposed to adults with stroke, the sample size was calculated regarding motor changes observed in a previous study of HABIT-ILE in school-aged children with congenital brain lesions.²¹ Based on the results of the Assisting Hand Assessment changes, a similar effect size is expected here. Thus, we hypothesise an incremental improvement of 1 SD between the intervention group and the control group (between-group difference=6, SD=5). With an $\alpha=0.05$ and a $1-\beta=0.9$, a sample size of 16 participants should be included in each group (32 total). Considering potential dropouts and data loss in assessments, 24 participants per group (48 in total) will be included.

Randomisation process

A blocked randomisation, stratified by localisation, side and date of the brain lesion, as well as age and gender of the participant, will be carried out before the baseline assessment and after collection of informed consent. Using an online computer-based pseudo-random number generator allocation system (www.randomizer.org²⁷), participants will be allocated to either the control or the intervention group.

Study interventions

Control group: regular care

Those participants allocated to the control group will continue with their customary or usual treatment performed in the participant's customary facility (hospital or private practice), next to their place of residence. By regular, usual care or conventional therapy, we mean the routine clinical rehabilitation (typically outpatient physical or occupational therapy) that people pursue regularly in the chronic phase of stroke. Specific information on

the content and dosage of regular care will be collected in the assessment log sheet for content comparison purposes (see 'Data collection and data management' section).

Intervention group: HABIT-ILE

HABIT-ILE¹⁸⁻²¹ is a motor skill learning-based therapy developed for children with unilateral and bilateral cerebral palsy. It is delivered as a day camp setting (commuting every day to receive the intervention) at a rented facility near the Institute of Neuroscience in Brussels, in a group of 12 participants at the same time but with individualised intervention. Structured activities are proposed during which an increase in motor difficulty is induced according to the participant progress. Likewise, it includes functional tasks requiring simultaneously the use of both hands and postural and/or locomotor activities.

For this protocol, we have considered the group age in order to adapt the intervention, based on the know-how gathered with children and young adults with cerebral palsy.¹⁸⁻²¹ The activities proposed during HABIT-ILE will be presented as playful activities (designed for adults) and the whole environment will allow to perform them in a recreational way. As described elsewhere,¹⁸ the activities performed will be defined by a group of experienced HABIT-ILE supervisors, based on the participants' abilities assessed at baseline. As well, functional goals (such as getting dressed, tying shoelaces, climbing stairs) will be defined at baseline conjointly by the participants and the supervisors. During HABIT-ILE, all activities are regularly reviewed regarding difficulty, to ensure a constant challenge in motor control of UE and LE, as well as posture. As mentioned, participants will begin with activities fitting their level according to their individual baseline degree of ability. Therefore, activities may range, for UE, from using the affected UE as a passive stabiliser (eg, weighting down paper during writing/drawing), evolving to an active, skilled manipulator (eg, construction with Lego bricks); for posture and LE, activities may evolve from sitting in a bench or therapeutic ball to riding a bike. When a new challenging activity for UE will be introduced, the posture and LE will be solicited in a non-challenging situation. Afterwards, the activity being mastered will be performed soliciting a more challenging postural/LE control.

Up to 12 participants will benefit from HABIT-ILE at the same time. In the same space, playful activities will be performed individually. Despite that, some activities may be performed between two participants or, at the end of the day, as a group activity including all participants, encouraging emulation and support between them. Each participant will benefit from one to two therapists (occupational/physical therapists or students in these fields) as interventionists. A team of certified HABIT-ILE experts (DE-K, RA) and the developer of the intervention (YB) will oversee all activities, ensuring the therapy content. Furthermore, to assure fidelity to the HABIT-ILE procedure, interventionists will be trained before the camp by the expert team and will be asked to provide only HABIT-ILE. Also, all activities will be regularly reviewed

during a daily meeting, discussing with the interventionist the corresponding evolution of the activities to be performed. Structured motor activities will be performed for at least 80% of the total time of intervention. The optimal dose for intensive interventions in adults with stroke is not established, ranging for significant results from a total of 10–86 hours for isolated UE or LE interventions, and over the course of 2–8 weeks.^{6 17 28 29} As HABIT-ILE is an intervention targeting the whole body, and considering the possible fatigability of participants and their age,³⁰ for this first study we established a therapy time of 5 hours per day, with a rest period at midday, completing a total of 50 hours over 10 weekdays.

Data collection and data management

At each assessment session, all information concerning data collection will be registered in the ‘assessment log sheet’, including patient code, date of assessment, test procedure and the context during the data acquisition. This information will also be collected and managed on the Research Electronic Data Capture (REDCap)^{31 32} register hosted at the UCLouvain. In the REDCap register, a codebook will be created indicating detailed information on each variable (name, possible values, label for each type of data, units, among others) and appropriate metadata will be created and associated with each file.

Data will be collected and created sequentially at each assessment time. Adults in the intervention group will be assessed three times: immediately before (T0) and after participating to the 2 weeks intensive intervention HABIT-ILE (T0+3 weeks) and at 3 months of follow-up (T0+13 weeks). Adults in the control group will be assessed at the same three time points, although they will benefit of HABIT-ILE only after the T0+13 weeks assessment (ie, after pursuing their regular care and rehabilitation). In addition, these participants will be assessed a fourth and last time after the 2-week intervention (T0+16 weeks) as postintervention assessment, in order to observe the pre-post effect in all participants. At each time point, participants will be assessed regarding neuroimaging, motor function, motor control and ADLs using the tools described below in the Outcomes.

Blinding procedure

Neither participants nor interventionists (therapists) will know the allocation to each group. The main outcome (Adult Assisting Hand Assessment Stroke (Ad-AHA Stroke)³³) will be rated from videos by external accredited/experienced raters unaware of group allocation or assessment time. Analyses will be performed using study allocation codes. Secondary outcomes such as functional analyses will also be videorecorded. Hence these evaluations, as well as analysis of the neuroimaging data, will follow the same blinding procedure for later analyses. Data will be anonymised and stored in the REDCap register. At the end of the data collection period, these anonymised data will be analysed.

Outcomes

Motor control and motor learning data will be collected at the Stroke Unit of the University Hospital CHU UCL Namur-Site; neuroimaging assessments will be performed at Saint-Luc University Hospital of the UCLouvain in Brussels. All other assessments will be performed primarily at the University Hospital CHU UCL Namur-Site.

The feasibility of HABIT-ILE in adult patients with stroke will be explored by means of a daily logbook filled by the interventionists throughout the whole therapy time. This time-task log will register the time and type of activities performed by each participant during the intervention period. In addition, a semi-structured questionnaire will be presented to the participants at the postintervention assessment to self-report adherence to the intensive programme. Any non-adherence or non-retention (attrition) will be recorded including its reason and will be presented in a CONSORT flow diagram (figure 1).

Primary outcome

In order to assess improvements in bimanual performance after HABIT-ILE, the Ad-AHA Stroke³³ will be used as primary outcome. This observation-based test uses Rasch measurement analysis to assess how effectively people with unilateral UE deficits use spontaneously their affected hand/arm during bimanual tasks.^{33 34} It is scored on a logit-based 0–100 AHA-unit scale, with higher score indicating higher ability. This assessment is reliable and valid for use in adults following stroke.³⁴

Secondary outcomes

Motor control and motor learning assessments

An interactive robotic medical device, the REAplan (www.axinesis.com/en/our-solutions/reaplan/), will be used to assess bimanual motor control and bimanual motor skill learning. At baseline, over three consecutive days, during an asymmetrical bimanual coordination task, the REAplan will record speed, accuracy, coordination, smoothness and force.¹⁵ Likewise, a finger force manipulator³⁵ denominated ‘Dextrain’ will be used to assess changes in finger force tracking dexterity and changes in multifinger tapping dexterity in the paretic hand. The Dextrain (www.dextrain.com) records independent finger movement and forces applied on pistons allowing to calculate the ability to control and release the force applied by the fingers during a tracking task as well as assess the independent finger movement while simultaneous tapping in response to visual instructions during a finger tapping task.^{35 36}

Motor function assessments

The box and block test will be used to measure unilateral gross dexterity³⁷ by quantifying the maximum number of wooden blocks transferred from one compartment to the other during 1 min. Higher scores indicate better performance. A minimal detectable change (MDC) of 5.5 and 7.8 blocks per minute on the more affected and the less affected hand, respectively have been established for

adults with chronic stroke.³⁸ It has also showed an excellent test-retest and inter-rater reliability.³⁹

The Fugl-Meyer Assessment for upper extremity (FMA-UE)⁴⁰ will be used to evaluate changes in UE sensorimotor functions. The maximum score of the test is 66 points; MDC has been set at 5.2 points in adults with chronic stroke.⁴¹ The FMA-UE has also shown an excellent inter-rater and intra-rater reliability.^{42 43}

The Wolf Motor Function Test⁴⁴ will be used to assess quantitative changes in UE motor ability. It presents 17 items, including strength and timed functional tasks. The maximum score is of 75 points; MDC has been set at 0.7 s and 0.1 points for the performance time and functional ability scale, respectively in patients with chronic stroke.⁴⁵

The 6 min walk test (6MWT)⁴⁶ will be used to assess endurance while walking 6 min without pause in a 30 m hallway. A longer distance (in m) indicates a better performance. For the chronic population of adults with stroke, the 6MWT has shown an excellent test-retest reliability and MDC has been estimated at 36.6 m or a 13% change.⁴⁷

Self-perceived ability in activities of daily living

The ACTIVLIM-Stroke questionnaire⁴⁸ will be used to assess activity limitations of adults with stroke during ADLs, involving the use of UE and/or LE. Participants answer to 20 items using a three-level scale (impossible/difficult/easy). It ranges from -6 to +6 logits, with higher scores indicating better performance. The ACTIVLIM-Stroke questionnaire has shown excellent test-retest reliability, good responsiveness and high sensitivity to change.^{48 49}

The ABILHAND questionnaire⁵⁰ will be used to assess participant's perceived difficulty in performing everyday bimanual activities, whatever the strategies involved. Participants answer to 23 items using a three-level scale (impossible/difficult/easy). It ranges from -6 to +6 logits (ie, log odds units), with higher scores indicating better performance. For adults in the chronic stage of stroke, the ABILHAND has shown excellent test-retest reliability,⁵¹ good responsiveness and high sensitivity to change, with an MDC of 0.13 logits.⁵⁰

The modified Rankin Scale (mRS) will be used to assess the perceived degree of disability or dependence in the ADLs of participants regarding their prestroke condition.⁵² It is a single-item scale with six levels of disability, going from 0 ('no disability/no symptoms') to 5 ('disability requiring constant care for all needs').⁵³ The mRS has shown excellent test-retest reliability⁵⁴ and adequate to excellent construct validity,⁵⁵ although less sensitivity to change.⁵⁶

The Stroke Impact Scale (SIS) questionnaire will be used to assess disability and health-related quality of life after stroke.⁵⁷ This self-reported questionnaire assesses the impact of stroke in eight domains: hand function, strength, memory and thinking, mobility, (instrumental) activities of daily living (ADL/IADL), communication, emotion and participation. Domains are scored on a

metric of 0–100, with higher scores indicating better self-reported health. For adults in the chronic stage of stroke, the SIS questionnaire has shown adequate to excellent test-retest reliability in all domains but emotion,⁵⁸ adequate to excellent internal consistency⁵⁹ and an MDC of 24.0 for strength, 17.3 for ADL/IADL, 15.1 for mobility and 25.9 for hand function.⁶⁰

The Canadian Occupational Performance Measure (COPM) is a semi-structured interview⁶¹ used to identify up to five activities that are considered important for the participant within self-care, productivity and leisure areas; these will become therapeutic goals and will be assessed by the participant, on a 1–10 scale, regarding the performance, as well as satisfaction on each goal achievement. The total score is the average of the scores for perception and satisfaction separately. The COPM has shown an excellent test-retest reliability.⁶²

Cognitive functions assessments

Cognitive functions will be assessed at baseline only for demographics purposes.

The Montreal Cognitive Assessment (MoCA) is a rapid screen of cognitive abilities used for adults with stroke.⁶³ In 16 items, it assesses different cognitive domains with a total score of 30. The MoCA presents a moderate-to-excellent inter-rater reliability in adults with stroke.⁶⁴

The Bells test is a pen-paper cancellation test allowing to assess quantitative and qualitative visual neglect in the near extrapersonal space.⁶⁵ The participant must circle 35 bells distributed equally in 7 columns within 280 images presented as distractors. Time and number of circled bells are registered. Six or more omitted bells indicate a unilateral spatial neglect.⁶⁵ The Bells test has presented excellent test-retest reliability.⁶⁶

The Corsi Block-Tapping Task assesses visuo-spatial working memory.⁶⁷ The participants must mimic a tap sequence presented by the assessor from two up to nine identical separated blocks. The average normal subjects are able to repeat the sequence up to five to six blocks.⁶⁸

The Stroop Colour and Word Test assess cognitive interference inhibition.⁶⁹ Participants must read, as fast as possible, one incongruent and two congruent tables involving colours, words (names of colours) and a combination of both. Results can be compared with normative data for persons between 15 and 90 years.⁷⁰

The Trail Making Test assesses cognitive flexibility.^{71 72} This two-part evaluation demands participants to connect in increasing order numbered circles (from 1 to 25) and then circles alternating numbers (1–13) and letters (A–L). The total score is the time required to complete each part. Results can be compared with normative data for persons between 18 and 89 years.⁷³

The arithmetic verbal subtest for working memory and the digit symbol coding performance subtest for processing speed of the Wechsler Adult Intelligence Scale-III (WAIS-III) will be administered to participants. The reliability coefficients of the WAIS-III on these

subtests ranges from 0.82 to 0.88,⁷⁴ considered as good. Results will be compared with normative data.⁷⁵

Neuroimaging assessments

MRI datasets will be acquired in Saint-Luc University Hospital in Brussels using a 3 T MRI (SIGNA Premier, General Electric Healthcare, USA), equipped with a 48-channel head coil. Before the scans, all participants will have to confirm they present no contraindications to MRI. To increase efficacy, participants will undergo a familiarisation protocol to better adapt to the MRI environment. Data, including anatomical (T1 and T2) and diffusion tensor imaging sequences, will allow to assess neuroplastic changes. More precisely, white matter microstructure baseline damage and potential training-induced changes will be quantified in all participants and will be compared between groups both at the macroscopic level using whole-brain tractography and at the microscopic level using voxel-wise, model-based microstructural features.⁷⁶

Statistical analysis

Statistical significance is set to p value <0.05 . Changes in the primary outcome, Ad-AHA Stroke as well as in secondary outcomes will be compared between groups using analysis of covariance (ANCOVA) to adjust for baseline measurement, as suggested by Vickers.⁷⁷ Non-parametric methods will be performed whenever ANCOVA assumptions are not met. The R software⁷⁸ will be used under the supervision of statisticians to perform generalised linear mixed models for the analyses of motor control and motor learning measures using the robotic device, as performed in previous works.¹⁵ Separated generalised linear models (GLM) will be estimated for the corticospinal tract and whole-brain white matter to infer the correlations between microstructure integrity at baseline/after intervention and the intervention outcomes. Finally, an overall GLM will be estimated to combine corticospinal tract and whole-brain microstructure integrity, and robotic outcomes.

ETHICS AND DISSEMINATION

Full ethical approval has been obtained for this study protocol by the Comité d'éthique Hospitalo-Facultaire/ Université catholique de Louvain, Brussels (reference number: 2013/01MAR/069B403201316810) as well as the local medical Ethical Committee of the CHU UCL Namur-site Godinne. Also, the recommendations of the Comité d'éthique Hospitalo-Facultaire and the Belgian law of 7 May 2004, concerning human experiments will be followed. Participants will sign a written informed consent ahead of participation.

Data will be stored in a UCLouvain repository dataverse. Findings will be published in peer-reviewed journals and conference presentations. After contacting the corresponding author and signing a data sharing agreement, a digital object identifier could be shared to access selected data.

Author affiliations

- ¹Institute of Neuroscience, Université catholique de Louvain, Brussels, Belgium
- ²Exercise and Rehabilitation Science Institute, School of Physical Therapy, Faculty of Rehabilitation Science, Universidad Andrés Bello, Santiago, Chile
- ³Neuroimaging platform (NIMA), Université catholique de Louvain, Brussels, Belgium
- ⁴Institute of Information and Communication Technologies, Electronics and Applied Mathematics (ICTM), Université catholique de Louvain, Louvain-la-Neuve, Belgium
- ⁵Neurology Department, Stroke Unit/NeuroModulation Unit (NeMU), Université catholique de Louvain, Yvoir, Belgium

Contributors YB, LD, BM, YV contributed to study design. YB, LD, BM, YV contributed to achieve funding for the research study. DE-K first drafted this protocol. RA, YB, LD, DE-K, BM, YV will supervise the data collection. RA, YB, DE-K will supervise implementation of the training programme. RA, ACdT, DE-K, EH, EG will perform the data collection and implementation of the therapy. All authors contributed to the writing of this manuscript and have critically reviewed and approved the final version.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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ORCID iDs

Daniela Ebner-Karestinos <http://orcid.org/0000-0002-5941-8706>
 Estelle Gathy <http://orcid.org/0000-0002-9878-2420>
 Rodrigo Arandeda <http://orcid.org/0000-0002-0890-5504>
 Laurence Dricot <http://orcid.org/0000-0002-8613-2420>
 Benoît Macq <http://orcid.org/0000-0002-7243-4778>
 Yannick Bleyenheuft <http://orcid.org/0000-0002-6688-932X>

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