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A new dose-finding trial design to identify the optimal therapeutic dose of an upper limb intervention for people after stroke

Submission date
20/03/2014

Recruitment status
No longer recruiting

Registration date
15/04/2014

Overall study status
Completed

Last Edited
22/01/2019

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Stroke is a major cause of death and one of the leading causes of severe disability in many countries. It can cause severe motor impairment which can restrict everyday activities and often independence. Many physical therapies have been explored in the last two decades to improve stroke survivors' motor ability. However, it is not known how much therapy is needed to maximise motor-recovery after stroke. An appropriate amount of training may be a key requirement to enhance recovery after stroke. Research suggest that more therapy is better than less but findings are so far inconclusive. Current national guidelines in the UK recommend a minimum of 45 minutes of daily therapy for people after stroke, a duration not often achieved in UK therapy services and also not supported by research evidence. It is recognised that this target is based on expert opinion rather than scientific evidence. The aim of this study is to fill in the gap of knowledge on the correct amount of therapy after stroke.

Who can participate?
Patients aged over 18 who have moderate difficulty with their arms after stroke

What does the study involve?
A group of three participants enters the study and exercise at the same training dose. At the end of the two weeks, if the dose has been found possible and not harmful, another group of three participants enters the study with an increased training dose. This procedure continues until the ideal treatment dose is reached. Participants exercise five days a week for two weeks at the assigned training dose. For this study the training dose is composed by the number of daily repetition tasks and the task intensity. For the upper limb (arm) training task participants exercise with a three-point frame equipped by a rubber band. They should insert their fingers and thumb into the three point frame and then open the hand to take off the rubber band and then place it on a second identical frame. Each removal and placing of a band counts as one repetition. Participants should move the band from one three-point frame to the other and back again for the number of repetitions assigned.

What are the possible benefits and risks of participating?
Participants undertake a training programme when their usual care is stopped. The social nature of this study may positively impact participants' quality of life. The risk of harm for any participants in this study is low. However, this training can result in the onset or worsening of hand/arm pain or tiredness. This risk is closely monitored and participants are promptly advised. Transcranical magnetic stimulation (TMS) involves exposure to electromagnetic fields and may cause mild discomfort. Such risks are avoided by careful screening of participants.

Where is the study run from?
University of East Anglia (UK)

When is the study starting and how long is it expected to run for?
May 2014 to November 2014

Who is funding the study?
University of East Anglia (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number
102281

ClinicalTrials.gov number

Secondary identifying numbers
IRAS project ID: 102281

Study information

Scientific Title
Establishing a feasible optimal therapeutic dose using a new methodology for stroke rehabilitation

Study objectives
It is feasible to apply a dose-finding trial design commonly used in pharmaceutical development to rehabilitation trial after stroke.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East Anglia - Norfolk, ref: 14/EE/0005

Study design
Single-centre single-arm 3+3 dose escalating design with multiple stage recruitment and observer-blind assessment

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Quality of life

Participant information sheet
Not available in web format, please contact e.colucci@uea.ac.uk to request a patient information sheet

Health condition(s) or problem(s) studied
Stroke

Interventions
Upper limb training task: In detail this intervention is focussed on extension and abduction movements of the fingers and thumb of the participants' paretic hand against a tailored resistance applied by resistance-graded rubber bands.

Intervention Type

Other

Phase
Not Applicable

Primary outcome measure
The commercial therapy device the Cando Digit-Extend Finger Exerciser has been chosen to test participants motor learning and strength improvement due to its similarity with the training task. The Cando Digit-Extend is a professional but easy device. For this study, the device will be used to test the extensor mechanism of all fingers of the paretic hand. Participants will insert the fingers and thumb of their paretic hand in the plastic frame and open their hand against a coded resistance band. With the Cando Digit-Extend training intensity level (resistance levels or exercise effort) can be easily changed using the five coded resistance bands provided (beige xxlight, yellow x-light, red light, green medium and blue hard).
There will be two parts to the measure (mean time 10 minutes):
1. The number of times a participant can extend their fingers (open and close their paretic hand) against the lightest resistance band in one minute
2. The highest level of resistance against which a participant can extend their fingers twice in one minute (level 0: unable to perform, level 1: the lightest band, level 5: the strongest resistance band)

Secondary outcome measures
1. The Modified Box and Block Test (mBBT) will be used for it is similar to the task trained in this study (mean time 15 minutes). The MBBT is a performance-based measurement of unilateral gross manual dexterity. Participants sit on a dining-type chair at a table in front of a divided box. They are asked to pick up an object, between the tip of the index finger and tip of the thumb of the paretic hand and release this into the other side of the box. They are asked to repeat this task as many times as possible in 60 seconds. The test is undertaken three times and each time a different object is used. The objects are: a tennis ball; a 2.5 cm cube; and a 5 cm cube. Five minutes rest will be allowed before changing objects.
2. Upper limb strength elbow flexion/extension and hand muscles with a Myometer (mean time 10 minutes). Measuring grip strength is considered a sensitive method of charting intrinsic neurological recovery and functional recovery. Force values will be obtained during three trials, with the greatest value obtained used for data analysis. Participants will be seated on a dining type chair at a table. They will grip the handle of the myometer and then squeeze it (hand grip strength). Then pinch a specific part of the handle and squeeze (hand grip strength). The upper limb positions for all measurements follow standardized procedures (Fasoli, Trombly et al. 2002). The myometer will be set to zero after the subject is positioned with their hand/digits around the bars at rest. Instruction will be squeeze as hard as you can.
3. Excitability of the corticospinal pathways as assessed by Motor Evoked Potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) (mean time 40 minutes). Single pulse of TMS, using standard figure of eight coil, will be given over the hand and arm areas of primary motor cortex of the stroke and non-stroke hemisphere. MEP data will be recorded and analysed using Signal software. EMG recording of MEPs over both contralateral and ipsilateralbintrinsic hand (first dorsal interosseous and abductor pollicis brevis) and forearm muscles (wrist extensors and biceps) will allow for characterisation of recruitment curves in the muscle at rest. The recruitment curves, for both hemispheres, will be constructed by measuring the amplitude of the motor evoked potential at 100, 110, 120 and 130% of resting motor threshold. The rationale for inclusion of this neurophysiological measure is that the training task is expected to enhance the ability to produce voluntary contraction of paretic muscle by enhancing excitability of connectivity between brain and muscle through the corticospinal pathways. It is therefore

important to measure MEPs as these provide information about change in the neural substrate for improvement in upper limb movement. This measure is therefore expected to be more sensitive to change than any of the other items in the measurement battery.

Overall study start date
12/05/2014

Completion date
30/11/2014

Eligibility

Key inclusion criteria
1. Aged 18+ years
2. Have presence of moderate upper limb paresis/impairment defined as participants able to open and close their paretic hand six times in one minute but unable to do this 25 times in one minute, from starting position of thumb and finger tips close with an extra, extra, light resistance band placed around fingers and thumb
3. Able to imitate action with the non-paretic upper limb. This will be assessed by the Research Therapist
4. Be discharged from stroke rehabilitation services

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
7/8 cohorts will be necessary to target the optimal dose (between 21 and 24 participants)

Key exclusion criteria
Participant should not receive therapy to improve upper limb motor function

Date of first enrolment
01/03/2014

Date of final enrolment
30/11/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of East Anglia
Norwich
United Kingdom
NR4 7TJ

Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/026k5mg93

Funder(s)

Funder type
University/education

Funder Name
University of East Anglia (UK)

Alternative Name(s)
UEA

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
13/06/2017: The publication is currently in press

Intention to publish date

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2017	22/01/2019	Yes	No
HRA research summary			28/06/2023	No	No