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A neurorehabilitation therapy based on a brain machine interface (BMI) for the motor function restoration of the upper limb in chronic stroke patients.

Submission date
31/03/2015

Recruitment status
Suspended

Registration date
07/05/2015

Overall study status
Suspended

Last Edited
28/11/2023

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
If the supply of blood to the brain is restricted or stopped, brain cells begin to die. This is what happens in a stroke. A stroke can cause brain injury, disability and possibly death. People who survive a stroke are often left with long-term problems resulting from the injury to their brain, such as paralysis in one limb or on one side of the body (reduced motor function). Some people need to have a long period of rehabilitation before they can recover their former independence, while many will never fully recover and will need support adjusting to living with the effects of their stroke. The process of rehabilitation is specific to each person. A team of specialists are often involved in rehabilitation, including physiotherapists, psychologists, occupational therapists, speech therapists and specialist nurses and doctors. Brain-Machine-Interfacing (BMI) is being tested as a new way to help with stroke rehabilitation. BMI can turn brain signals into physical movement with the help of a computer-controlled robotic device that the patient wears. This helps the brain communicate with a paralyzed limb. The aim of this study is to test BMI and see if it can bring about better motor recovery in stroke patients which may allow them to regain daily living independence. The system could help establish new connections between the brain and the paralyzed muscles within the nerve system, and encourage new nerve growth that will go around (bypass) the stroke-affected parts of the brain.

Who can participate?
Stroke patients with a severely paralysed arm.

What does the study involve?
All participants have electrodes implanted into their brain which can figure out how they would like to move (e.g. reaching for a cup). This movement is then generated with the help of an upper-limb power-driven outer framework (exoskeleton) that the person wears. Various tests are carried out 2 months before treatment, then again immediately after treatment and then 6 months later at follow up.

What are the possible benefits and risks of participating?
Participants will benefit from intensive rehabilitation from experts and may have improved movement in the stroke-affected limb at the end of the study. The risks involved in participating are mainly related to the general anaesthesia during the surgical implantation procedure. All patients will be duly informed about the risks of the surgery prior to the start of the study.

Where is the study run from?
Hospital Universitario Donostia - Instituto de Investigación Sanitaria Biodonostia (Spain)

When is the study starting and how long is it expected to run for?
October 2016 to December 2025

Who is funding the study?
1. Instituto de Investigación Sanitaria Biodonostia (Spain)
2. Tecnalia Research & Innovation (Spain)
3. Institute of Medical Psychology and Behavioral Neurobiology - University of Tübingen (Germany)
4. University of California Berkeley (USA)
5. University of the Basque Country – EHU/UPV (Spain)

Who is the main contact?
Dr Ander Ramos-Murguialday

Contact information

Type(s)
Scientific

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Protocol serial number
ARM-BMI-2014-01

Study information

Scientific Title
A neurorehabilitation therapy based on a brain machine interface (BMI) for the motor function restoration of the upper limb in chronic stroke patients: Intracranial Stroke MOtor REhabilitation

Acronym
IS-MORE

Study objectives
Incidence of first stroke in Europe is about 1.1 million and prevalence about 6 million. From all stroke survivors showing no active upper limb motion at hospital admission, 14% show complete recovery, 30% show partial recovery and 56% show no recovery and the grand majority retain sensory function. The aim of this study is to induce motor rehabilitation and restoration by contingently and concurrently linking neuronal activity and paralyzed limb movements and by activating neuroplasticity mechanisms in chronic paralyzed stroke patients. Our approach uses an implantable system that links assisted movement of the affected limb with cortical activity in order to promote functional neural pathways through a process based on neuroplasticity. We expect that patients will control reaching and grasping movements of their paralyzed limb using their brain signals and doing so neural plasticity and compensation mechanisms will start re-shaping neural networks involved in motor tasks.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics committee of the Health Care District Gipuzkoa, Spain, 21/10/2014, ref: ARM-BMI-2014-1.

Primary study design
Interventional

Study design
Interventional longitudinal design

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic stroke patients with severely paralyzed upper-limb

Interventions
This study will be undertaken in 4 phases and all patients recruited for this study will undergo the same intervention and will not be divided into different experimental groups:
1. Phase I - Non-interventional (baseline): the patient will not have any intervention besides their regular physiotherapy (if any). This phase will serve as a baseline measure for a non-interventional period of time.
2. Phase II - Current available common and advanced physiotherapies (baseline): in this phase, several currently available common and advanced physiotherapies will be intensively carried out at the hospital:
2.1. Classic physiotherapy
2.2. Mirror therapy
2.3. Assistive robot-aided therapy: passive predefined movements of the upper-limb driven by a robotic exoskeleton attached to the upper-limb of the patient.
2.4. Neurorehabilitation therapy based on a non-invasive BMI activated robotic exoskeleton attached to the upper-limb of the patient (the paralyzed limb of the patient will be moved by the exoskeleton controlled by a non-invasive BMI through predefined trajectories).

The objective of this phase is to give the patient the best combination of non-invasive treatments and to estimate the baseline of possible clinical and functional improvements of the stroke patient due to non-invasive physiotherapy and neurorehabilitation therapy (prior to the interventional phase using the implantable BMI).
3. Phase III - Interventional phase: neurorehabilitation therapy: this interventional protocol will consist in an intensive neurorehabilitation therapy based on a BMI coupled with a rehabilitation robotic exoskeleton. In this phase, the intracranial neural signals will be acquired from an intracortical microarray implanted in the primary motor cortex of the patient. These signals will be decoded into control signals that will drive the robotic exoskeleton attached to the upper-limb of the patient.
4. Phase IV - Follow-up assessment: after the interventional phase, the patient will be discharged from the hospital and after approximately six months the same battery of tests used in the baseline measurements (Phase I & II) will be used to assess long term effects.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome(s)
1. Phase I & II baseline measures carried out on two different days before BMI intervention (with an approximate 2-month interval in between). This will assess the baseline clinical condition of the patient and improve reliability in the pre- and post-intervention scores comparison.
2. Immediately after intervention
3. Six months after intervention completion (follow-up)
4. Fugl-Meyer Assessment (FMA): a stroke-specific, performance-based impairment index.
5. Action Research Arm Test (ARAT): an evaluative measure to assess specific changes in limb function among individuals who have suffered a stroke.

Key secondary outcome(s)
1. Assessment of functional and structural changes in the brain due to intervention: functional and anatomical magnetic resonance imaging (fMRI and aMRI).
2. Assessment of Motor Evoked Potentials (MEPs): Transcraneal Magnetic Stimulation (TMS).
3. Functional stimulation amplitude needed to induce a muscle contraction (motor threshold) will be used to assess muscle fibers status
The following data will be acquired and analyzed for clinical assessment before, during and after intervention:
4. Electromyography data will be acquired on both arms (healthy and paretic) to assess muscle function
5. Electroencephalography data (in non-invasive phase) and cortical array data (in invasive phase) to assess brain activity changes
6. Kinematics data will be obtained via exoskeleton sensors to assess motor performance and range of motion

Completion date
31/12/2025

Eligibility

Key inclusion criteria
Assessment of physical and psychological function and impairment:
1. Wolf-Motor test
2. Goal Attainment Scale (GAS)
3. Motor Activity Log
4. KVIQ-20
5. Modified Ashworth scales (spasticity)
6. Beck Depression Inventory (BDI)
7. Hamilton Depression Rating Scale (HDRS)
8. Berlin Social Support Scale (BSSS)
9. The Schedule for the Evaluation of the Individual Quality of Life-Direct Weighting (SEIQoL-DW) (quality of life)
10. Placebo Questionnaire

Patients will be selected according to strict inclusion criteria, including but not limited to their level of impairment, physiology of the stroke lesion, psychological and cognitive characteristics.

All participants should fulfill the following criteria:
1. Paralysis of one hand with no residual active finger extension
2. Considerable motor impairment in the upper-limb, with MRC (Medical Research Council) below 2 out of 5 (5 = muscle contraction against full resistance, normal; 4 = reduced strength, but contraction can still move joint against resistance; 3 = strength further reduced such that joint can be moved only against gravity with examiner's resistance completely removed; 2 = muscle can only move if resistance of gravity is removed; 1 = only a trace or flicker of movement is seen or felt, or muscle twitching/spasms (fasciculations) are observed; 0 = no movement).
3. Ischemic or hemorrhagic stroke with subcortical damage and, if possible, intact motor cortex.
4. Time since stroke of at least 9 months (chronic stage)
5. Age 18 to 70
6. No psychiatric or neurological condition other than stroke
7. No cerebellar lesion or bilateral motor deficit
8. No pregnancy
9. No claustrophobia
10. No epilepsy or medication for epilepsy during the last 6 months
11. Eligibility to undergo magnetic resonance imaging (MRI)
12. Ability to understand and follow instructions

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex

All

Key exclusion criteria
1. Drug and/or alcohol abuse
2. Psychiatric disorder (including post-stroke depression)
3. Cerebellar damage
4. Bilateral motor deficit
5. Uncontrolled health problems (coronary heart disease, severe heart failure in stage III-IV according to NYHA, severe cardiac arrhythmia, severe edema, severe arthritis, malignant tumor, chronic renal failure)
6. Cognitive impairment (Mini Mental State below 23/30 points). Patients with cognitive or language difficulties that will prevent them giving informed consent and/or follow instructions
7. Pregnancy
8. Drug-resistant epilepsy
9. Pacemakers, metallic implants (ferromagnetic) or claustrophobia, contraindications to undergo magnetic resonance imaging (MRI)

Date of first enrolment
10/04/2015

Date of final enrolment
01/03/2025

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Universitario Donostia
Doctor Begiristain , 117
Donostia - San Sebastián
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20080

Study participating centre
Hospital Universitario Cruces
Plaza de Cruces, S/N
Baracaldo
Spain
48903

Sponsor information

Organisation
Instituto de Investigación Sanitaria Biodonostia (Spain)

ROR
https://ror.org/01a2wsa50

Funder(s)

Funder type
Research organisation

Funder Name
Instituto de Investigación Sanitaria Biodonostia

Funder Name
Tecnalia Research & Innovation

Funder Name
Institute of Medical Psychology and Behavioral Neurobiology - University of Tübingen

Funder Name
University of California Berkeley

Alternative Name(s)
University of California, Berkeley, UC Berkeley, The UC Berkeley, Berkeley, Cal, California, University of California, UCB

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United States of America

Funder Name
Euskal Herriko Unibertsitatea

Alternative Name(s)
Universidad del País Vasco, University of the Basque Country, EHU, UPV/EHU

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Spain

Funder Name
Faculté de Sciences de la Motricité - Université Libre de Bruxelles

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date