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Influence of a structured aerobic physical exercise intervention on cognitive function, emotional state and quality of life in traumatic brain injury patients in the chronic stage

Submission date
03/07/2024

Recruitment status
No longer recruiting

Registration date
11/07/2024

Overall study status
Completed

Last Edited
30/09/2024

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol
Background and study aims
Chronic sequelae in multiple domains (motor, sensory, cognitive, behavioral, etc) are common in persons who have suffered a traumatic brain injury (TBI), particularly after moderate and severe injuries. The treatment of cognitive impairment (working memory, long-term memory, executive function, attention, etc) is challenging and the effects of existing interventions are limited. In non-injured adults, aerobic physical exercise has been shown to affect broad domains of cognitive function, with the largest effect sizes being seen on executive function. Physical activities are often used within sub-acute rehabilitation settings, but limited high-quality evidence exists of how regimented physical exercise regimes can affect cognition in the chronic stages of recovery from moderate-to-severe TBI. The study aims to evaluate the impact of a supervised aerobic exercise intervention, conducted over 20 weeks with three sessions per week, on individuals with chronic TBI. Specifically, the research seeks to assess changes in cognitive function, including attention, executive functions, working memory, and visuospatial memory, as well as quality of life perception and the balance between sympathetic and parasympathetic nervous system activity. Additionally, the study will examine whether this structured exercise program is associated with an increase in overall daily physical activity among the participants.

Who can participate?
Adults (18 to 65 years old) with chronic cognitive impairment as a consequence of a severe TBI suffered from 8 months to years before the inclusion in the study.

What does the study involve?
This study will record the amount of daily physical activity of the participants in daily life during specific periods. During these periods, participants wear a device (Actigraph) which will be provided by the researchers for recording physical activity. A series of parameters will be tested related to heart rate and physical fitness at specific times. During part of the study (20 weeks), participants will be asked to follow an aerobic physical exercise intervention, three times per

week, 30 minutes per session, under the direct supervision of one of the researchers. The total duration of the study will be 60 weeks, but the duration of physical exercise training will only be 20 weeks. The rest of the time the participant will carry out his/her usual activities, including those related to usual care.
At the beginning of the study and at three other times the participants will have a series of tests to assess some cognitive functions (memory, attention, executive function, etc.) and his/her perception of quality of life. This will help determine whether the exercise intervention has helped reduce some of the cognitive alterations experienced by the participants.

What are the possible benefits or risks of participating?
There is no guarantee that participation in this study will involve any benefit for the participant. However, the results of this project might advance the implementation of strategies that can be used to help people who suffer cognitive and/or emotional alterations caused by TBI.
Physical exercise may have some risks, as detailed below, but these risks are usually very low when exercise is carried out under direct supervision:
- The most frequent:
• Fatigue
• Muscle discomfort and stiffness associated with exercise.
- The most serious:
• There are no serious risks derived specifically from participation in this study since the participants will be doing all the exercises under direct supervision. The intensity of the exercise will be based on the individual results of exercise tolerance tests.
• Under no circumstances will the maximum heart rate recommended for age and general health status be exceeded. Therefore, no serious risks are anticipated related to this study.

Where is the study run from?
The study will run in two different neurorehabilitation centers in Barcelona and Sabadell (Catalonia, Spain).

When is the study starting and how long is it expected to run for?
This study started in July 2019. It was running until January 2021.

Who is funding the study?
1. The study is investigator-initiated and funded
2. Using the gymnasium, other premises and neuropsychology tests for the cognitive assessment of the participants were gifted by AVAN Neurologia and INA Memory Center
3. Using Actigraph devices for recording physical activity in daily life was gifted by Dr Myriam Guerra Balic (Department of Physical Activity and Sport Sciences, Blanquerna, University Ramon Llull, Barcelona)
4. Using pulsometers and software for heart rate variability measurement and analysis was gifted by Dr Lluís Capdevila
5. The costs related to trial registration and publication APC are covered by Dr Timothy P. Morris, Northeastern University

Who is the main contact?
Margalida Coll Andreu (Margalida.Coll@uab.cat), Ph.D., Universitat Autònoma de Barcelona.

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Aerobic exercise and cognitive function in chronic severe traumatic brain injury survivors: a within-subject A-B-A intervention study

Acronym
TBI-EXE

Study objectives
Supervised aerobic physical exercise reduces cognitive deficits associated to chronic severe traumatic brain injury

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 02/05/2019, Comisión de Ética en la Experimentación Animal y Humana (CEEAH) (Ethics committee on animal and human experimentation) (Building A (Rectorat). Universitat Autònoma de Barcelona, Bellaterra (Cerdanyola del Vallès), Barcelona, E-08193, Spain; +34 93 581 3578; cerec@uab.cat), ref: CEEAH 4658

Study design
Single-arm within-subject A-B-A design study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Severe traumatic brain injury at the chronic stage

Interventions
Aerobic physical exercise, 20 weeks, 3 sessions per week, 30 minutes per session. Three phases (20 weeks each) were designed as follows:
Phase A1: Ongoing individually tailored outpatient neurorehabilitation
Phase B: Tailored outpatient neurorehabilitation plus scheduled aerobic physical exercise (three sessions per week, 30 minutes/session)
Phase A2: Tailored outpatient rehabilitation without the physical exercise intervention.

Details of the exercise intervention:
The aerobic exercise intervention will be delivered in person within each rehabilitation centre using either cycling rehabilitation trainers, stationary cycle ergometers or MOTOmed. Each session (~30 minutes) will consist of a 5-minute warm-up and cool-down. A hand-held sphygmomanometer will record resting heart rate (HR) and blood pressure before and after each session. The intensity of exercise will be progressively increased with a target HR intensity of 60-80% HR reserve (maximal HR- resting HR) set from the third week onwards. HR zones will be adjusted every four weeks to account for any changes in resting HR. HR will be continuously recorded during the exercise sessions using a wrist pulsometer. Participants will be asked to rate their perceived exertion and comfort/distress every five minutes using Borg's scale (6-20) of perceived exertion and a visual analogue scale, respectively.

Intervention Type
Behavioural

Primary outcome(s)
Cognitive function will be measured using the following set of neuropsychological tests:
1. Trail-making tests A and B
2. Rey-Osterrieth complex figure
3. Wisconsin card sorting test
4. Symbol digits modalities test
5. Letters and numbers
6. Forwards and backwards digit span

The tests will be administered at four different time points:
1. At the beginning of the study (week 1; baseline)
2. Immediately before the exercise intervention (week 20)
3. Immediately after the exercise intervention (week 40)
4. At the end of the study (week 60; follow-up):

Key secondary outcome(s))
1. Physical activity in daily life measured using an Actigraph at three time periods, in the middle of phase A1 (pre-intervention); in the middle of phase B (during the period of exercise intervention), and in the middle of phase A2 (follow-up), on weeks 9-10; 29-30 and 50-51 of the

study. Each recording period has a duration of 7 consecutive days
2. Perceived quality of life measured using the CAVIDACE scale ("Quality of life for brain-injured patients") at the same four times as cognitive testing
3. Sympathetic/parasympathetic balance measured using heart rate variability at the beginning and end of the period of exercise intervention (weeks 20 and 40)

Completion date
27/07/2022

Eligibility

Key inclusion criteria
1. A severe TBI, defined as a score between 3 and 8 on the Glasgow Comma Scale at the time of injury
2. Age range: 18 to 65 years old
3. A minimum of 8 months since injury
4. Lack of medical contraindications to engage in physical exercise of moderate or vigorous intensity
5. Preserved communication abilities to perform neuropsychological assessments, and to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment
6

Key exclusion criteria
1. Drug abuse or addiction

Date of first enrolment
01/07/2019

Date of final enrolment
31/01/2020

Locations

Countries of recruitment
Spain

Study participating centre
AVAN Neurologia
Carrer de l'Estrella 110
Sabadell (Barcelona)
Spain
E-08201

Study participating centre
INA Memory Center
Balmes 399
Barcelona
Spain
E-08022

Sponsor information

Organisation
Autonomous University of Barcelona

ROR
https://ror.org/052g8jq94

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository (https://account.proton.me/login; Proton Drive is an encrypted system to store documents). A persistent web link will be created at a later time. The type of data stored will be data files for statistical analyses (Stata and Jamovi files). To request access please email Margalida Coll-Andreu (Margalida.Coll@uab.cat) at any time. All the participants signed an informed consent form.

Confidentiality
All study-related information will be stored securely at Universitat Autònoma de Barcelona. All participant information will be stored in locked file cabinets in areas with limited access. All data collection and administrative forms will be identified by a coded ID number to maintain participant confidentiality. All records that contain names or other personal identifiers, such as informed consent forms, will be stored separately from study records identified by code number. All local databases will be secured with password-protected access systems.

Participant's study information will not be released outside of the study without the written permission of the participant, and only if the participant wishes the results of his/her outcome measures to be made accessible to the providers of his/her neurorehabilitative care.

Access to data: The principal investigator will have direct access to her own site’s data sets. To ensure confidentiality, data dispersed to project team members will be blinded to any identifying participant information.

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/09/2024	30/09/2024	Yes	No
Participant information sheet			10/07/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan			10/07/2024	No	No