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Combining physical exercise and cognitive training in old age

Submission date
26/08/2019

Recruitment status
No longer recruiting

Registration date
18/09/2019

Overall study status
Completed

Last Edited
06/11/2023

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Age-related cognitive impairments compromise the functional capacity of aging individuals, and create major individual and societal costs. Developing means for preserving and restoring cognitive functioning in old age is therefore of great importance. Pharmaceutical approaches to prevention and treatment have been unsuccessful so far, which makes the search for non-pharmacological routes more important than ever.

Epidemiological studies have found that life-long cognitive performance is associated with various life-style factors, including education, occupational complexity and physical activity . Intervention studies that target a single domain have provided some support for an advantageous role of cognitive training and physical exercise for cognition in old age, but effects tend to be small and inconsistent. It has consequently been suggested that multidomain interventions that target several lifestyle factors at the same time may be needed for optimum effects.

What remains unclear is how such multidomain intervention studies should be designed to optimise preventative effects. Brain-derived neurotrophic factor (BDNF) is essential for neuronal plasticity and increases transiently as a result of physical exercise. BDNF may therefore to be of mechanistic relevance for the interactive effects of physical exercise and cognitive training on cognition.

In this study we investigate the effects of combining physical exercise and cognitive training, in close temporal succession, with a particular focus on BDNF as a relevant mechanism. The study aims to provide concrete information on how a physical training should be combined with cognitive training for effectively combatting the increasingly serious challenge of late-life cognitive impairment. On the mechanistic role of BDNF, the study aimed to establish a role for the transient exercise-induced increases in BDNF for facilitating learning and improving cognition in older adults.

Who can participate?
Older adults aged 65-75 years capable of performing physical exercise.

What does the study involve?
Participants are randomly assigned to one of four groups. Depending on the group participants will be asked to do a combination of physical activity and/or cognitive (brain) training for 12 weeks.

What are the possible benefits and risks of participating?
The benefit of participating in the study is primarily the opportunity to contribute to aging research. It is important to be aware that there are no guarantees that your cognitive abilities will actually improve over the course of the study.
The risks with the study are expected to be minor. The study criteria will ensure that you will not be able to participate in the study if you have an increased risk for complications as a result of the fitness tests or the physical training.

Where is the study run from?
Aging Research Center, Karolinska Institute & Stockholm University, Sweden

When is the study starting and how long is it expected to run for?
September 2017 to March 2018

Who is funding the study?
This research received funding from the European Research Council (ERC) under the European Union's Seventh Framework Programme (FP7/2007-2013) and ERC Grant No. 617280 - REBOOT.

Who is the main contact?
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Protocol serial number
2017/1115-31/4

Study information

Scientific Title
The acute effect of physical exercise on the outcome of working memory training in older adults and its relationship to peripheral levels of brain-derived neurotrophic factor

Acronym
REBOOT-3

Study objectives
H1: Cognition in older adults benefits more from repeated sessions of working memory training when each training session is directly preceded as opposed to followed by physical exercise.

It is predicted that the hypothesized benefit for cognition of the intervention period will encompass both improved knowledge and strategies that are specific to the trained working memory tasks and task-general improvements of working memory ability with relevance for broader cognition. As such, group differences in change in cognitive performance from before to after the intervention period, with better performance when working memory training are preceded by physical exercise, are predicted for

- H1a: trained working memory tasks (combination of task-specific effects and task-general effects on working memory ability)
- H1b: untrained working memory tasks (task-general effects on working memory ability)
- H1c: untrained cognitive abilities (task-general effects on working memory ability with relevance for broader cognition)

For H1, the hypothesized benefit for cognition also encompasses gradual change in working memory performance over the course of the intervention period. The intervention groups are therefore also expected differ in regards to

- H1d: day-by-day change in performance over the intervention period on a trained working memory tasks (combined effect of task-specific and task-general effects on working memory ability)

H2: The relationship between change in peripheral BDNF levels in response to physical exercise at pretest and the outcome of repeated sessions of working memory training is greater when each training session is directly preceded as opposed to followed by physical exercise.

For H2, it is predicted that the acute change in peripheral BDNF levels in response to physical exercise at pretest, in serum and in plasma, will be more closely related to the outcome of the working memory training intervention when each training session is preceded as opposed to followed by physical exercise. As such, group differences are predicted in the strength of the correlation between the acute BDNF change at pretest and change in cognitive performance as a result of the intervention, both in regards to knowledge and strategies that are specific to the trained working memory tasks and to task-general improvements of working memory ability with relevance for broader cognition

- H2a: trained working memory tasks (combination of task-specific effects and task-general effects on working memory ability)
- H2b: untrained working memory tasks (task-general effects on working memory ability)
- H3c: untrained cognitive abilities (task-general effects on working memory ability with relevance for broader cognition)

For H2, it is also predicted that the acute change in peripherapl BDNF levels in response to physical exercise at pretest will be more closely related to progress in the working memory training when each training session is preceded as opposed to followed by physical exercise. As such, group differences are predicted in the strength of the correlation between the acute BDNF change at pretest and

- H2d: day-by-day change in performance over the intervention period on a trained working memory tasks (combined effect of task-specific and task-general effects on working memory ability)

H3: Cognition in older adults benefits more from repeated sessions of working memory training when each training session is combined with physical exercise, irrespective of order, compared to working memory training alone.

For H3, the hypothesized benefit for cognition of the intervention is the same as for H1. Group differences are therefore predicted, with better performance when working memory training is combined with physical exercise, compared to working memory training alone, for

- H3a: trained working memory tasks (combination of task-specific effects and task-general effects on working memory ability)
- H3b: untrained working memory tasks (task-general effects on working memory ability)
- H3c: untrained cognitive abilities (task-general effects on working memory ability with relevance for broader cognition)
- H3d: day-by-day change in performance over the intervention period on a trained working

memory tasks (combined effect of task-specific and task-general effects on working memory ability)

H4: Cognition in older adults benefits more from repeated sessions of physical exercise when each exercise session is combined with working memory training, irrespective of order, compared to physical exercise alone.

For H4, to allow a fair comparison between the cognitive effects of physical exercise only and physical exercise combined with working memory training, predictions are limited to tasks that are not included in the working memory training. As such, group differences in change in cognitive performance following the intervention period are predicted, with better performance when physical exercise is combined with working memory training, compared to physical exercise alone, for

- H4a: untrained working memory tasks
- H4b: untrained cognitive abilities

H5: The acute change in peripheral BDNF levels in older adults will be greater immediately following physical exercise compared to immediately following working memory training.

It is predicted that the acute change in peripheral BDNF levels at pretest, in serum and in plasma, in older adults will be greater immediately following physical exercise compared to immediately following working memory training.

H6: The acute changes in peripheral BDNF levels in older adults following physical exercise and cognitive training will remain after 30 minutes.

It is predicted that the changes in BDNF levels, in serum and in plasma, immediately following physical exercise and working memory at pretest will remain after 30 minutes.

H7: Moderate intensity physical exercise 2-3 times per week over 12 weeks improves physical fitness in older adults.

It is predicted that the maximal rate of oxygen consumption (VO2 max) from pretest to posttest will change more in the intervention groups that receive physical exercise compared to the group that only receives working memory training.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/07/2017, the ethical review board in Stockholm (Regionala Etikprövningsnämnden, Stockholm, Tomtebodavägen 18A, Hiss 1, plan 3, 171 65 Solna; +46 8-52487000; kansli@stockholm.epn.se), ref: 2017/1115-31/4

Primary study design
Interventional

Study design
Longitudinal randomised controlled intervention study

Study type(s)

Quality of life

Health condition(s) or problem(s) studied
Healthy cognitive aging

Interventions
Participants were randomized to one of four intervention groups. All interventions lasted for 12 weeks and involved training visits every second weekday. Participants were randomized to receive either:
1. Physical exercise immediately before cognitive training (PE+COG)
2. Physical exercise immediately after cognitive training (PE+COG)
3. Physical exercise only (PE)
4. Cognitive training only (COG)
in each training session.

The physical exercise sessions consisted of 35 minutes of aerobic exercise at a heart rate corresponding to 65-75% of each participant's individual VO2-max. The cognitive training sessions consisted of 35 minutes of adaptive working memory training.

Randomization was performed in R and three stratifiers were used: age, reasoning ability (score on Ravens Progressive Matrices at pretest) and physical activity level (score on physical activity questionnaire at pretest).

Intervention Type
Behavioural

Primary outcome(s)
Primary outcome variables were eight cognitive composite scores, each composed of two/three individual tests administered at pretest and posttest (12 weeks), which varied systematically in similarity to the tasks in the working memory training, and gradual working memory improvement across the cognitive training period

Key secondary outcome(s)
1. Physical fitness, assessed in a maximum ergometer test at pretest and posttest
2. Acute changes in peripheral BDNF concentrations in response to the allocated intervention, assessed at pretest

Completion date
19/07/2018

Eligibility

Key inclusion criteria
1. Age 65-75 years at the start of the study
2. Ability to attend all study visits
3. Ability to maintain current level of physical activity, in addition to any study intervention, during the whole study period
4. Adequate hearing and normal or corrected eye sight
5. Fluency in the Swedish language

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Total final enrolment
97

Key exclusion criteria
1. Any planned lifestyle changes during the study period (e.g. change of physical exercise routine, diet or leisure activities)
2. Neurological disease, including all dementia types (MMSE<26 excluded), Parkinson's disease or epilepsy
3. Current or ongoing cardiovascular disease (blood pressure up to 200/100 included)
4. History of brain damage, including stroke
5. Uncontrolled metabolic disease, including diabetes (untreated type II included) and Grave's disease
6. Ongoing cancer (<1 year after completed treatment excluded)
7. Psychiatric illness (history of mild to moderate depression and anxiety included)
8. History of head trauma with resulting unconsciousness
9. Color blindness
10. Previous participation in the study or in another study where cognitive tests are included
11. Neuromotor or musculoskeletal dysfunction preventing activity on an exercise bike or treadmill
12. Medications that can affect the fitness tests, such as beta-blockers and beta-stimulants
13. Any ongoing infection
14. Chest pain
15. Fear of needles
16. Medication that can influence the blood analysis, including antiepileptic and antidepressant medication, sleeping medication and cortisone treatment

Date of first enrolment
04/09/2017

Date of final enrolment
06/03/2018

Locations

Countries of recruitment
Sweden

Study participating centre
Aging Research Center, Karolinska Institute & Stockholm University
Gävlegatan 18A, plan 4
113 30 Stockholm
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Sponsor information

Organisation
Aging Research Center (ARC), Institutionen för Neurobiologi, vårdvetenskap och samhälle (NVS), Karolinska Institutet

ROR
https://ror.org/04hmgwg30

Funder(s)

Funder type
Government

Funder Name
This research received funding from the European Research Council (ERC) under the European Union's Seventh Framework Programme (FP7/2007-2013) and ERC Grant No. 617280 - REBOOT.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. Swedish data protection laws prohibit us from putting the data in the public domain, but data can be requested and subsequently transferred for specific and well-defined analyses projects that are in line with the original ethics approval. This requires a data use agreement, which effectively transfers the confidentiality obligations of the institution (Karolinska Institutet) at which the original research was conducted to the institution of the recipient of the data. Please contact the administration manager at ARC for data access requests: marie.helsing@ki.se

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		10/03/2020	06/11/2023	Yes	No
Other publications	Extended blood analysis of blood samples collected as part of the original study	09/06/2023	06/11/2023	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes