Trial Description

Title

Effect of physical activity on brain-derived neurotrophic factor – Association with cognitive dysfunction in depression. An explorative study

Trial Acronym

BDNF-Pilot Study

URL of the trial

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Brief Summary in Lay Language

Depression is a serious mental illness that causes high individual and societal costs. Deficits in attention, concentration and memory are part of this disease and collectively referred to as cognitive deficits. Since cognitive deficits are often perceived as very impeding, have a negative impact on social and professional Rehabilitation, and can persist for Long periods of time research into the causes, diagnosis and treatment of these symptoms is relevant.

One theory suggests a disorder of the growth factor BDNF (brain-derived neurotrophic factor). BDNF is involved in various processes underlying biological models of learning, such as nerve growth and plasticity. BDNF is also associated with depression because depressive people have lower average BDNF serum levels than healthy people. In addition, BDNF is easy to measure in blood serum, which makes it interesting as a potential marker for diagnosis and therapy.

In this study we want to utilize that BDNF in the blood is tranisiently elevated after physical activity. The aim is to provoke this increase and measure its extent. Furthermore, we suspect that the magnitude of the increase allows a prediction of cognitive performance.

We therefore examine people between 18 and 60 years old with a current or past depressive Episode (partially remitted) suffering from subjective cognitive deficits in two groups. The first group performs a stress test on a stationary bicycle, the second group a skill and balance test. We draw blood before and after this activity. Subsequently, cognitive testing is performed with both groups. In addition, we use questionnaires to collect information about the subjective cognitive deficits, the extent of depression, and the quality of life of our subjects.

Brief Summary in Scientific Language

Background: Major Depressive Disorder (MDD) is a severe mental illness causing long-term disability and high individual and societal costs. Cognitive impairment is a symptom of MDD that can sometimes persist well into remission making it an important target for rehabilitation. Etiology of cognitive symptoms in depression is still unclear. Brain-derived neurotrophic factor (BDNF), which is generally lower in MDD patients, has been linked to neuroplasticity and neurogenesis in animal models and humans suggesting a link to cognitive ability. Evidence for correlation

of BDNF to cognitive tasks is inconclusive. However, few studies take into account short term changes in BDNF concentrations. This study is designed to investigate short term BDNF fluctuations caused by physical activity and their association with cognition.
Hypotheses: Primary: The difference between pre- and post-activity serum BDNF (▲BDNF) in a Group performing light, non-exhaustive exercise is less than ▲BDNF in a Group performing strenuous exercise. Secondary: Basal BDNF at rest will be a predictor of Performance in tests of executive function in both Groups. Furthermore, ▲BDNF will be able to predict a significant amount of variance in cognitive variables, summarized by a global cognitive index, in the intervention group but not the active control group.
Subjects: Eligible for participation in this study are adult (18-60) individuals with partially remitted MDD suffering from subjective cognitive impairment. Grounds for exclusion will be major psychiatric or neurological comorbidities (e.g., psychosis, addiction, and bipolar disorder) as well as physical conditions considerably elevating the risk of physical activity such as heart failure, cardiac infarction, dyspnea, or orthopedic conditions.
Method: This study is designed as a randomized and controlled prospective trial with a two group comparison. All participants will be assessed as to their psychopathology, quality of life, and subjective and objective cognitive deficits. Intervention group participants will additionally undergo a strenuous graded exercise test on a stationary bicycle, while control group participants will perform light exercise utilizing stretching and breathing techniques. To evaluate BDNF, blood will be taken before and after the respective physical activity and analyzed via ELISA.

Do you plan to share individual participant data with other researchers?

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Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00015152**
- Date of Registration in DRKS: **2018/08/03**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **S-217/2018 , Ethik-Kommission I der Medizinischen Fakultät Heidelberg**

Secondary IDs

- Universal Trial Number (UTN): **U1111-1218-1614**

Health condition or Problem studied

- ICD10: **F32.1 - Moderate depressive episode**
- ICD10: **F34 - Persistent mood [affective] disorders**

Interventions/Observational Groups

- Arm 1: **Intervention Group: graded exercise test on a stationary bicycle**
  Individuals aged 18-60 with partially remitted depression and subjective cognitive deficits
  Procedure: 1. Standardized diagnostic interview - sociodemographics, illness history and symptoms, quality of life 2. Venipuncture I 3. Graded exercise test - start at 25W, every three minutes 25W increase upto volitional failure 4. Venipuncture II 5. Cognitive testing
- Arm 2: **Active Control Group: light physical exercise (stretching, coordination) for 15 minutes**
  Individuals aged 18-60 with partially remitted depression and subjective cognitive deficits
  Procedure: 1. Standardized diagnostic interview - sociodemographics, illness history and symptoms, quality of life 2. Venipuncture I 3. Test of balance and flexibility 4. Venipuncture II 5. Cognitive testing

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **assessor**
- Control: **Active control (effective treament of control group)**
- Purpose: **Basic research/physiological study**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

BDNF serum concentration in ng/ml, assessed on date of test, before and after physical activity

Secondary Outcome

parameters of cognitive functioning assessed via the test battery COGBAT, assessed on date of test at the end of the procedure

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Zentrum für psychosoziale Medizin - Klinik für Allgemeine Psychiatrie, Heidelberg**

Recruitment

- Planned/Actual: **Planned**
- (Anticipated or Actual) Date of First Enrollment: **2018/08/06**
- Target Sample Size: **80**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **60 Years**

Additional Inclusion Criteria

(1)Outpatients with a current or past-time diagnosis of major depressive disorder
(2)Age between 18 and 60 years
(3)IQ>80 according to the Mehrfachwahl-Wortschatztest B (MWT-B)
(4)Clinically stable patients who are able to provide informed consent
(5)Subjective Cognitive Complaints

Exclusion criteria

(1)Psychiatric co-morbidities as identified by mini international neuropsychiatric interview: current substance (alcohol or drug) abuse and dependence, current or lifetime psychotic disorder and mania, current anorexia, bulimia, PTSD, and panic disorder
(2)Reported current or chronic neurological disorders
(3)Patients with Hamilton Rating Scale for Depression (HAMD-21) scores ≥ 20 will be excluded to avoid confounding with severe depressive symptoms.
(4)Physical fitness: Patients with somatic conditions presenting a risk to the graded exercise test will be excluded, e.g., unstable angina pectoris, symptomatic arrhythmia, symptomatic aortic stenosis, heart failure, acute pulmonary

embolism, acute myocarditis, acute pericarditis, acute aortic dissection, high grade coronary artery disease, uncontrolled hypertension (RR>200/110mmHg), hypertrophic cardiomyopathy, endocarditis, symptomatic congenital and acquired heart defects. Furthermore, patients who cannot sufficiently participate in the graded exercise test due to health issues, e.g. COPD, severe asthma, current severe allergies, severe obesity (bodyweight >180kg, weight limit of the stationary bicycle), orthopedic disabilities will be excluded.

Addresses

- **Primary Sponsor**

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- **Contact for Scientific Queries**

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- **Contact for Public Queries**

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  URL: **https://www.klinikum.uni-heidelberg.de/Neurokognition.5050.0.html**

Sources of Monetary or Material Support

- **Private sponsorship (foundations, study societies, etc.)**

  Stiftung der Landesbank Baden-Württemberg
  Am Hauptbahnhof 2
  70173 Stuttgart
  Germany

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

- **Institutional budget, no external funding (budget of sponsor/PI)**

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  69115 Heidelberg
  Germany

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  E-mail: **[---]***
  URL: **[---]***

Status

- Recruitment Status: **Recruiting planned**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*