

Trial Description

Title

Providing Tools for Effective Care and Treatment of Anxiety Disorders (AD): Outcomes, Mediators and Moderators of Enhanced Extinction Learning (MRI subproject P4: Neural response and Fear Circuitry Activity Related to Extinction Learning and Outcome)

Trial Acronym

PROTECT-AD subproject P4

URL of the trial

<http://www.protect-ad.de>

Brief Summary in Lay Language

PROTECT-AD is a cognitive behavioral treatment study involving highly qualified psychotherapeutic centers at seven German universities. It is our goal to further investigate and optimize existing effective treatments of anxiety disorders. In order to achieve this, we want to investigate the effect of extinction learning in an “intensified” psychological intervention on treatment outcome in adults and children with anxiety disorders. The intensified psychological intervention is characterized by a higher number of exposure trials over a short time period. In the control condition, the exposure trials take place in a weekly interval, analog to standard care.

PROTECT AD subproject P4 investigates the neuro-functional activation patterns in patients with anxiety disorders compared to healthy volunteers and between patients groups with different anxiety disorders. A special focus is on exploring the basic mechanisms of exposure-based behavioral therapy, the extinction learning. Eligible RCT patients with anxiety disorders from all seven PROTECT-AD centers will undergo fear extinction in the MRI scanner before and after exposure-based therapy using functional Magnetic Resonance Imaging (fMRI). We will examine the neuronal correlates of fear extinction and reinstatement. In addition, a paradigm on emotion processing, structural scans and a resting state examination will be conducted.

Brief Summary in Scientific Language

Novel preclinical research evidence suggests extinction learning as the core mechanism of action of exposure-based therapies and provides according strategies to improve the effectiveness of treatment by optimized extinction. A translational research agenda is suggested to examine whether enhanced extinction learning components derived from preclinical research, applied within an “intensified” exposure-based treatment, improves outcomes and influences neural activation pattern in a fear extinction paradigm and face matching task more strongly. As mechanistic subproject of the multicentre randomised clinical trial (PROTECT-AD), we test in n=300 patients with primary AD (compared to a healthy control group: N=100) whether intensified psychological interventions based on augmented extinction learning (IPI) result in stronger outcomes on

subjective, clinical, behavioural, physiological and specifically neural indices as compared to an, otherwise identical, standard research treatment without explicit enhanced extinction (TAU). We hypothesize that enhanced extinction elements (IPI) will result in higher effect sizes and more pronounced neural changes (baseline to post-assessment) in regions of the so called fear network (amygdala, hippocampus, insula and ACC). This will be investigated using a specific extinction learning experiment. We also examine moderators of outcome (i.e. type of diagnosis, comorbidity).

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

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00009687**
- Date of Registration in DRKS: **2015/11/18**
- 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.: **EK 234062014** , **Ethikkommission der Medizinischen Fakultät der Technischen Universität Dresden**

Secondary IDs

Health condition or Problem studied

- ICD10: **F40.1 - Social phobias**
- ICD10: **F40.2 - Specific (isolated) phobias**
- ICD10: **F40.00 - [generalization F40.0: Agoraphobia]**
- ICD10: **F40.01 - [generalization F40.0: Agoraphobia]**
- ICD10: **F41.0 - Panic disorder [episodic paroxysmal anxiety]**

Interventions/Observational Groups

- Arm 1: **Intensified psychological intervention, based on optimized extinction learning (IPI) 12 sessions a 100 minutes, over the course of 6 weeks (2**

sessions per week/week 1 and 2, 3 sessions per week/week 3 und 4, 1 session per week/week 5 and 6)

- Arm 2: **Standard intervention without optimized extinction learning (TAU) 12 sessions a 100 minutes, over the course of 10 weeks (2 sessions per week/week 1 and 2, 1 session per week/week 3 to 10)**
- Arm 3: **No intervention; Healthy control group; Two measurement points correspondent to baseline and post-assessment (12 weeks)**

Characteristics

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

Primary Outcome

PROTECT-AD: Stronger reduction of anxiety symptoms in the IPI group than in the TAU group, Anxiety symptoms are assessed using the HAM-A at Baseline, Post/after session twelve and Follow up/after six months.

PROTECT-AD subproject P4: Stronger changes in neural activation (measured using functional magnetic resonance imaging; fMRI) of fear network regions (amygdala, hippocampus, ACC, insula) in the IPI group than in the TAU group from Baseline to Post/after session twelve. The following experimental fMRI paradigms will be applied:

- 1. Fear extinction paradigm,**
- 2. Emotional reactivity paradigm (face matching task).**

Additionally a resting state activity and a structural scan will be accessed at Baseline and Post-treatment.

Secondary Outcome

Consideration of whole brain data, functional connectivity (predominantly ACC and amygdala) and brain structure (T1). Consideration of behavioural, physiological and clinical measures of PROTECT-AD (DRKS00008743).

Countries of recruitment

- **DE Germany**

Locations of Recruitment

- University Medical Center **Philipps-Universität Marburg, Klinik für Psychiatrie und Psychotherapie, Marburg**
- other **Ruhr-Universität Bochum, Klinische Kinder- und Jugendpsychologie, Bochum**
- other **Technische Universität Dresden, Abteilung für Klinische Psychologie und Psychotherapie, Dresden**
- other **Ernst-Moritz-Arndt-Universität, Lehrstuhl für Physiologische und Klinische Psychologie/Psychotherapie, Greifswald**
- University Medical Center **Charité Campus Charité Mitte, Berlin**
- other **Universität Würzburg, Institut für Psychologie, Würzburg**
- University Medical Center **Uniklinikum Würzburg, Klinik und Poliklinik für Psychiatrie, Psychosomatik und Psychotherapie, Würzburg**
- University Medical Center **Westfälische Wilhelms-Universität Münster, Klinik für Psychiatrie und Psychotherapie, Münster**
- other **Ruhr-Universität Bochum, Lehrstuhl für Klinische Psychologie und Psychotherapie der Fakultät für Psychologie, Bochum**

Recruitment

- Planned/Actual: **Planned**
- (Anticipated or Actual) Date of First Enrollment: **2016/01/01**
- Target Sample Size: **400**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **15 Years**
- Maximum Age: **70 Years**

Additional Inclusion Criteria

- **on or more of the following DSM-V Anxiety Disorders: Panic disorder, Agoraphobia, Social Anxiety Disorder, Specific Phobia**
- **HAMA - Score ≥ 18**
- **CGI - Score ≥ 3**
- **Can attend Therapie regularly (with or without support)**
- **Informed Consent**

- **Healthy control group**
- **No DSM-5 Diagnosis**
- **Informed Consent**

Exclusion criteria

- **Every reason the protocol may not be upheld (e.g. planned hospitalization within study time frame, planning to move away, etc.)**
- **Current Suicidal tendency**
- **DSM-V Bipolar Disorder**
- **DSM-V Psychotic Disorder**
- **DSM-V Borderline PD**
- **Current treatment of other Mental Disorder (Drugs, Psychotherapy)**
- **Current Alcohol, Benzodiazepine or other Substance Use Disorders**
- **Severe medical illness/condition (every serious physical illness, including cardiovascular, kidney, endocrinological and neurological conditions, Hepatitis or other clinical findings that suggest a severe illness and may affect participation in the study)**
- **Pregnancy**
- **MRI exclusion criteria (e.g., metal in body)**

Addresses

■ Primary Sponsor

Technische Universität Dresden, Institut für Klinische Psychologie und Psychotherapie
Mr. Prof. Dr. Hans-Ulrich Wittchen
Chemnitzer Straße 46
01187 Dresden
Germany

Telephone: **+49-(0)351-463-36983**

Fax: **+49-(0)351-463-36984**

E-mail: **hans-ulrich.wittchen at tu-dresden.de**

URL: **<http://www.psychologie.tu-dresden.de/i2/klinische/>**

■ Contact for Scientific Queries

Universitätsklinikum Gießen und Marburg
Mr. PD Dr. Benjamin Straube
Rudolf-Bultmann-Str. 8
35039 Marburg
Germany

Telephone: **06421-58-66429**

Fax: **06421-58-65197**

E-mail: **straubeb at med.uni-marburg.de**

URL: **http://www.ukgm.de/ugm_2/deu/umr_psy/index.html**

■ Contact for Public Queries

Klinische Psychologie und Psychotherapie, Fachbereich Psychologie



Contact for Public Queries

Klinische Psychologie und Psychotherapie, Fachbereich Psychologie

Mr. Dr. Katrin Wambach

Gutenbergstr. 18

35037 Marburg

Germany

Telephone: **+49 (0)6421 282-3681**

Fax: [---]*

E-mail: **wambach at staff.uni-marburg.de**

URL: **http://www.uni-marburg.de/fb04/gremien/ethikkommission**

■ **Collaborator, Other Address**

Universität Würzburg, Institut für Psychologie

Marcusstr. 9-11

97070 Würzburg

Germany

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

URL: **www.klinik.uni-wuerzburg.de**

■ **Collaborator, Other Address**

Westfälische Wilhelms-Universität Münster, Klinik für Psychiatrie und Psychotherapie

Albert-Schweitzer-Campus 1 Gebäude A9

48149 Münster

Germany

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

URL: **www.klinikum.uni-muenster.de**

■ **Collaborator, Other Address**

Technische Universität Dresden, Institut für Klinische Psychologie und Psychotherapie

Mr. Ingmar Heinig

Chemnitzer Straße 46

01187 Dresden

Germany

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

Collaborator, Other Address

**Technische Universität Dresden, Institut für Klinische Psychologie und
Psychotherapie
Mr. Ingmar Heinig
Chemnitzer Straße 46
01187 Dresden
Germany**

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

URL: <http://www.psychologie.tu-dresden.de/i2/klinische/>

■ **Collaborator, Other Address**

**Ernst- Moritz- Arndt- Universität, Lehrstuhl für Physiologische und Klinische
Psychologie/Psychotherapie
Franz-Mehring-Str. 47
17475 Greifswald
Germany**

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

URL: www.klinikum.uni-greifswald.de

■ **Collaborator, Other Address**

**Ruhr-Universität Bochum, Lehrstuhl für Klinische Psychologie und
Psychotherapie der Fakultät für Psychologie
Massenbergstraße 9 - 13
44780 Bochum
Germany**

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

URL: <http://www.kli.psy.ruhr-uni-bochum.de/>

■ **Collaborator, Other Address**

**Charité Campus Charité Mitte
Charitéplatz 1
10117 Berlin
Germany**

Telephone: [---]*

Fax: [---]*

Collaborator, Other Address

Charité Campus Charité Mitte
Charitéplatz 1
10117 Berlin
Germany

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

URL: **www.charite.de**

Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

Bundesministerium für Bildung und Forschung Dienstsitz Bonn
Heinemannstr. 2
53175 Bonn
Germany

Telephone: [---]*

Fax: [---]*

E-mail: [---]*

URL: **www.bmbf.de**

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.