PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Endophenotyping with fMRI: Genetic modulation and treatment response

Trial Acronym

NGFN PLUS TP13

URL of the trial

http://www.ngfn.de/en/tp13_endoph__notypisierung_alkoholabh__ngiger_patienten_mit_fmrt__genetische_modulation_und_behandlungsresponse.html

Brief Summary in Lay Language

Alcohol addiction is one of the most common neuropsychiatric diseases in today's society. Chronic misuse of alcohol not only causes significant physical and psychological damage in afflicted individuals, it also represents a serious social and economic problem. Despite the availability of a range of psychological and medical therapies, the risk of relapse for dependent individuals remains high even after years of abstinence. New, more effective therapies are urgently needed. Approximately 50% of the predisposition to develop an alcohol addiction is genetically inherited. In order to create improved treatment approaches and novel diagnostic tools, an enhanced knowledge of the genetic basis and biology of alcohol addiction is a prerequisite.
The aim of this multi-centre study is to investigate how and which genetic variations increase the risk for developing an alcohol-addiction. To achieve this, scientists in Berlin, Bonn and Mannheim will examine specific brain mechanisms that play important roles in alcohol dependence. Functional Magnetic Resonance Imaging (fMRI), a technique that makes it possible to observe the brain 'at work', will be used to reveal brain mechanisms affected by alcohol addiction such as the processing of reward and punishment, behaviour control and memory. It will then be investigated which genes or gene-gene interactions underlie these neuronal mechanisms. This powerful approach has the potential to uncover 'addiction-pathways' through which genes affect personality, drinking behaviours and success in staying abstinent via their influences on neuronal mechanisms.
A special emphasis of this project lies upon the so-called 'reward system', which processes naturally rewarding stimuli (e.g. food, sex) and which, in alcohol-dependent individuals, changes perceptions and behaviours in such a way that they become progressively more focused on alcohol. Two major neurotransmitters are involved in the workings of the reward system: 'dopamine' and more indirectly 'glutamate'. The project will investigate how dopaminergic and glutamatergic genes influence the neural mechanisms of reward processing, other neural mechanisms, personality, drinking behaviours and therapy success. In the long run, this knowledge might lead to more effective therapies such as the development of new medications.
This large-scale study will be conducted with several hundreds of alcohol-

dependent patients and non-dependent individuals over a period of five years.

Brief Summary in Scientific Language

The mesolimbic dopaminergic reward system is a key structure underlying addictive behaviour in alcohol addiction and is under control of prefrontal glutamatergic neurotransmission. The aim of the present multicenter-study in Berlin, Bonn and Mannheim is to use fMRI in alcohol addiction for endophenotyping in order to study the relevance of genectic variation, in particular in dopaminergic and glutamatergic genes, for addiction. We will use a temporal discounting and a cue reactivity paradigm in alcoholics and healthy controls in order to 1) test the impact of genetic variation on activation of the mesolimbic system in these populations and to 2) to test their predictive effects for treatment outcome in alcoholics. The subproject will thus bridge animal research on genetically determined cue reactivity and human studies in alcoholics. Furthermore, we will link our results to the measurement of glutamate and glutamine with magnetic resonance spectroscopy (MRS) in subproject SP14.

Organizational Data

- DRKS-ID: **DRKS00003341**
- Date of Registration in DRKS: **2011/11/18**
- 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.: **EA1/052/09 , Ethik-Kommission der Charité - Universitätsmedizin Berlin-**

Secondary IDs

Health condition or Problem studied

- ICD10: **F10.2 - Mental and behavioural disorders due to use of alcohol; Dependence syndrome**
- ICD10: **[---]* - [---]***

Interventions/Observational Groups

- Arm 1: **alcohol-dependent patients (currently abstinent) will be investigated using functional magnetic resonance imaging (fMRI) und genetic analysis**
- Arm 2: **healthy control subjects will be investigated using functional magnetic resonance imaging (fMRI) und genetic analysis (as a control group for the alcohol-dependent patients)**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Observational study**
- Allocation: **Non-randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Basic research/physiological study**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

The aim of the present multicenter study in Berlin, Bonn and Mannheim is to use fMRI in alcohol addiction for endophenotyping in order to study the relevance of genetic variation, in particular in dopaminergic and glutamatergic genes, for addiction.

Secondary Outcome

test the impact of genetic variation (within important candidate genes for alcohol dependence using genetic analysis) on activation of the mesolimbic system in alcohol-dependent patients and healthy controls (measured with fMRI) and test their predictive effects for treatment outcome in alcoholics (assessed during 6 months follow-up period)

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2009/06/01**

Planned/Actual: **Actual**

(Anticipated or Actual) Date of First Enrollment: **2009/06/01**

- Target Sample Size: **480**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **75 Years**

Additional Inclusion Criteria

Healthy Controls
- men and women, aged 18 to 75
- legally effective, written informed consent for participation within the study
- right handedness
- no psychiatric disorder according to ICD 10
- no psychotropic substances within the last 7 days

Alcohol-depdent patients
- men and women, aged 18 to 75
- legally effective, written informed consent for participation within the study
- right handedness
- no other psychiatric disorder according to ICD 10
- no psychotropic substances within the last 7 days

Exclusion criteria

- physical disorders, which might interfere with the planned examination (z.B. cerebro-organic disorder)
- MR-contraindication (z.B. pace maker, metalic or electronic implants, metal splinters, Operationsklammern)
- anamnestic manifeste psychiatric axis I disorder and/or axis II according to ICD-10 except alcohol dependence for patients
- medication or drug dependence
- medication or drug abuse (randomisized urin testing)
- insufficient knowledge of German language
- claustrophobia
- for women: pregnancy (exclusion via pregnancy test)

Addresses

- **Primary Sponsor**

  Charité Campus Charité Mitte

Primary Sponsor

Charité Campus Charité Mitte
Charitéplatz 1
10117 Berlin
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **www.charite.de**

■ **Contact for Scientific Queries**

Klinik für Psychiatrie und Psychotherapie CCM
Charité - Universitätsmedizin Berlin
Mr. Prof. Dr. Andreas Heinz
Charitéplatz 1
10117 Berlin
Germany

Telephone: **004930450517001**
Fax: **004930450517921**
E-mail: **andreas.heinz at charite.de**
URL: **[---]***

■ **Contact for Public Queries**

Klinik für Psychiatrie und Psychotherapie CCM
Charité - Universitätsmedizin Berlin
Ms. Dipl. Psych. Katrin Charlet
Charitéplatz 1
10117 Berlin
Germany

Telephone: **004930450517183**
Fax: **004930450517921**
E-mail: **katrin.charlet at charite.de**
URL: **[---]***

■ **Collaborator, Other Address**

Universitätsklinik BonnAbteilung Medizinische Psychologie
Mr. Prof. Dr. Dr. Henrik Walter
Sigmund-Freud-Str. 25
53127 Bonn
Germany

Telephone: **[---]***
Fax: **[---]***

Collaborator, Other Address

Universitätsklinik BonnAbteilung Medizinische Psychologie
Mr. Prof. Dr. Dr. Henrik Walter
Sigmund-Freud-Str. 25
53127 Bonn
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **henrik.walter at charite.de**
URL: **http://www.ukb.uni-bonn.de/quick2web/internet/internet.nsf/directname/home**

- **Collaborator, Other Address**

Klinik für Abhängiges Verhalten und SuchtmedizinZI Mannheim
Mr. Prof. Dr. Falk Kiefer
J5
68159 Mannheim

Telephone: **0621 1703-3522, -3523**
Fax: **0621 1703-3505**
E-mail: **Falk.Kiefer at zi-mannheim.de**
URL: **http://www.zi-mannheim.de/forschung/personen/person/109.html**

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 Berlin
Hannoversche Straße 28-30
10115 Berlin
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **www.bmbf.de**

Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2013/05/31**

Trial Publications, Results and other documents

- Paper **Neural activation during processing of aversive faces predicts treatment outcome in alcoholism.**
- Paper **The dopamine system in mediating alcohol effects in humans.**
- Paper **Dopamine-modulated aversive emotion processing fails in alcohol-dependent patients.**
- Paper **Effect of brain structure, brain function, and brain connectivity on relapse in alcohol-dependent patients.**

** 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.*