Stages in addiction: a functional magnetic resonance imaging (fMRI) study into the neural mechanisms of chronic and non-chronic alcohol dependence and gambling disorder

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON41763

Source
ToetsingOnline

Brief title
Stages in addiction

Condition

- Other condition
- Personality disorders and disturbances in behaviour

Synonym
addiction, substance dependence

Health condition

alcoholafhankelijkheid, gokverslaving

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW van NWO (VIDI beurs)

Intervention

Keyword: Addiction, Alcohol Dependence, Behavior, Magnetic Resonance Imaging, Pathological Gambling

Outcome measures

Primary outcome

Our main study endpoints include 1) The balance between goal-directed and habitual responding under stress as measured by the habit task; 2) the influence of experienced and predicted reward value on the control of goal-directed actions; 3) Brain activation patterns as measured with fMRI during these tasks, a resting-state condition, DTI and 1H MRS; 4) Brain activity (fMRI BOLD responses) during performance of an affective cognitive control task and an affective impulsivity task; 5) Correlations of brain measurements with a number of behavioral tasks and questionnaires (e.g. tests of impulsivity and compulsivity, positive and negative reinforcement, reward anticipation and reward outcome)

Secondary outcome

Not applicable

Study description

Background summary

Different stages can be distinguished in the development of addiction and the end stage is currently seen as a chronic or chronic intermitting brain disorder. In preclinical studies, these different stages are associated with different neurobiological processes and a variety of mechanisms are proposed to be responsible for the development of chronicity in addiction. Some animal models emphasize the change from initial impulsive drug use through the loss of control over this behavior such that it becomes habitual and eventually compulsive. According to dual-system accounts of addiction, this shift of control over behavior is determined by the balance between a goal-directed and a habitual system. Other animal models highlight the motivational change from positive reinforcement to negative reinforcement processes in chronic addiction, although the latter model also explicitly relates to the changes from impulsive (positive reinforcement) to compulsive use (negative reinforcement). Human models of changes in the development of addiction stress the role of loss of control over drug use, and impulsivity has been pinpointed as an important factor relating both to the development of substance misuse, and to relapse in chronic addiction. However, compulsivity has been largely ignored in human research on addiction.

In summary, several mechanisms involved in the shift from non-chronic to chronic addiction have been proposed in animal models, but almost none of them have been tested in clinical samples. We want to translate these hypotheses derived from animal models to the human situation in order to discover what discerns chronic- from non-chronic addiction in humans. We therefore propose an fMRI study to investigate the neurobiological differences between chronic and non-chronic human addicts with either a substance-related addiction (alcohol dependence) or a behavioral addiction (pathological gambling). These two groups are selected in order to compare mechanisms in addictive disorders with neurotoxic effects and addictive disorders without the confounding effects of neurotoxicity of substances on the brain.

Study objective

The main aim of the proposal is to study the processes involved in non-chronic vs. chronic drug seeking behavior in samples of alcohol dependent persons (ADs) and pathological gamblers (PGs) with different levels of chronicity. We thereby rely on knowledge derived from animal work and implement tests of impulsivity, compulsivity, goal-directed and habitual behavior and positive and negative reinforcement.

Study design

Behavioral and neurobiological outcome measures will be used to test how the level of chronicity is related to goal-directed and habitual behavior and positive and negative reinforcement. To model the effect of negative reinforcement on the shift from impulsive to compulsive behavior, as measured

by a habit task, a stress induction vs. neutral control condition (separated by a 1 week interval) is used.
To induce a physiological stress response participants will be subjected to the socially evaluated cold-pressor test (SECPT), which is known to relatively non-intrusively increase salivary cortisol, blood pressure, heart rate and subjective stress ratings by immersion of the participants* hand for a short duration into ice water (lukewarm water in control condition). Simultaneously, participants in the stress condition are monitored by an unfamiliar person and videotaped.

Study burden and risks

The risk associated with participation can be considered negligible and the burden can be considered minimal. Total participation time is approximately 6 hours. Structured diagnostic interviews for psychiatric disorders and personality questionnaires will be administered.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

A structured diagnostic interview, e.g. Composite International Diagnostic Interview (CIDI, World Health Organisation, 1997) is used to screen for inclusion/exclusion criteria. Relevant sections are included: demographics; alcohol use disorders; substance use disorders; depressive disorders and mania; psychotic disorders and post-traumatic stress disorder. The following sections are included from the Diagnostic Interview Schedule (DIS, Robins, 1981): pathological gambling; antisocial personality disorder.
Inclusion criteria:
Alcohol Dependence, chronic group:
- Recent DSM-V diagnosis of AD (<4 months past detoxification).
- Currently in treatment for AD (>3 weeks past detoxification)
- Seeking treatment for at least the third time lifetime and a minimum illness duration of 7 years (chronic addiction).
Alcohol Dependence, non-chronic group:
- Recent DSM-V diagnosis of AD (<4 months past detoxification).
- Currently in treatment for AD (>3 weeks past detoxification)
- Seeking treatment for the first time and with a maximum illness duration of 2 years (non-chronic addiction).
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Pathological Gambling, chronic group:
- Recent DSM-V diagnosis of PG (active gambling <3 months ago).
- Seeking treatment for at least the third time lifetime and a minimum illness duration of 7 years (chronic addiction).
Pathological gambling, non-chronic group:
- Recent DSM-V diagnosis of PG (active gambling <3 months ago).
- Seeking treatment for the first time and with a maximum illness duration of 2 years (non-chronic addiction).
Healthy control group:
- No diagnosis (current or history) of AD or PG.

Exclusion criteria

Exclusion criteria, all groups:
• Current bipolar disorder, psychotic disorder, alcohol or substance dependence, or any cognitive disorder as assessed with the MINI neurological disorders section
• IQ below 80
• insufficient command of the Dutch language
• MRI contraindications such as metal implants, claustrophobia, left-handedness, pregnancy
• recent (<2 weeks) use of psychotropic medication other than naltrexone (smoking and

nicotine dependence is allowed in all groups).
• Endocrinological disorders or regular use of corticosteroids
• Current treatment with tricyclic antidepressant or antipsychotic medication
• Use of other psychotropic medication (apart from SSRI's), or of recreational drugs over a period of 72 hours prior to each test session, and use of alcohol within the last 24 hours before each measurement
• Irregular sleep/wake rhythm (e.g., regular nightshifts or cross timeline travel).;PG group and HC group: more than 21 alcoholic drinks/week for men and more than 15 drinks/week for women, history of AD
PG group: any other current substance dependence than PG.
AD group: current substance dependence other than AD.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-12-2015
Enrollment:	125
Type:	Actual

Ethics review

Approved WMO

Date:	04-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24978
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL51301.018.14
OMON	NL-OMON24978