Impulsivity, a risk factor in relapse to substance use disorder: investigating neural substrates before and after pharmacological challenges.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25130

Source
NTR

Brief title
fMRI modafinil NAC

Health condition

cocaine dependence, alcohol dependence

Sponsors and support

Primary sponsor: Academic Medical Center (AMC)
Source(s) of monetary or material Support: ZonMW, The Netherlands Organization for Health Research and Development

Intervention

Outcome measures

Primary outcome

The main outcome measures are craving ratings, self-report impulsivity, neuropsychological performance (mean reaction time and accuracy) and the fMRI blood oxygen level dependent (BOLD) response. These measures will be evaluated between groups (cocaine/alcohol/control) and within groups (placebo versus medication).

Secondary outcome

Polymorphisms will be evaluated between groups and their relation to brain activation patterns, test performance and self-report measures. Relapse rate will be assessed and related to brain activation patterns and test performance in repsonse to medication.

Study description

Background summary

During the development of substance dependence, drug-associated stimuli become increasingly relevant to the substance user. In addition to the role of motivational cues, deficits in cognitive functioning play a key role in addiction. In particular, cognitive functions that involve behavioural control, and also control over behaviour when confronted with motivationally relevant drug cues, appear to be crucial for the development and course of addictive disorders. We will study the neural substrates of these two processes and their interaction. The interrelation between poor impulse control, motivational relevance of drug cues, and vulnerability to relapse predicts that improving cognitive performance may represent a promising new approach in the treatment of addiction. We therefore present a pharmacological challenge study with (1) a cognitive enhancer (studied in humans with cocaine dependence: modafinil), and (2) an agent influencing the motivational relevance of drug cues in animals (N-acetylcysteine). Thirty alcohol dependent patients, thirty cocaine dependent patients and thirty healthy controls will be tested using neurocognitive tasks on impulsivity and motivational drug cues in an fMRI study both before and after acute administration with N-acetylcysteine, modafinil, or placebo.

Study objective

It is expected that the cocaine and alcohol dependent subjects will display higher impulsivity on impulsivity-related tasks in the current study compared to healthy control subjects and show altered frontostriatal activity associated with impulsivity.

N-acetylcysteine is expected to have its primary effect on motivationally relevant cues (i.e. drug cues, reward cues), and is thus expected to influence mesocorticolimbic and orbitofrontal brain functioning.

Several studies have indicated that modafinil strongly reduces impulsive behaviour. Therefore, it is expected that the inclusion of modafinil will primarily exert its effect on brain areas related to cognitive control, such as the dorsolateral prefrontal cortex and the anterior

cingulate cortex.

Study design

1. First fMRI session with placebo or medication;

2. Second fMRI session with placebo or medication (cross-over design) within two weeks after first session;

3. Follow-up after 3 and 6 months to investigate relapse rate.

Intervention

Cocaine dependent, alcohol dependent patients and healthy controls will receive an acute administration with both NAC/modafinil and a placebo during two fMRI sessions in a double-blind cross-over design. Subjects will be randomly allocated to receive placebo or medication during the first session. During the two sessions, subjects will perform cognitive tasks inside and outside a MRI scanner. Functional and structural MRI images will be obtained. Subjects will also fill out questionnaires and a diagnostic interview will be administered. In addition, urine and DNA samples will be obtained.

Contacts

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Eligibility criteria

Inclusion criteria

1. Male, age 18-60 years;

2 For the alcohol dependent group: current DSM-IV diagnosis of alcohol dependence, but recently detoxified and abstinent and not using benzodiazepines for at least one week;

3. For the cocaine dependent group: current DSM-IV diagnosis of cocaine dependence, but recently detoxified and abstinent and not using benzodiazepines for at least one week;

4. For the healthy control group: matched on gender, ethnicity, age and education to the alcohol and cocaine dependent groups.

Exclusion criteria

1. Current use of prescription or illicit psychoactive drugs;

2. Lifetime history of head injury with loss of consciousness for more than 5 minutes;

3. Serious neurological or psychiatric disorders (e.g. psychosis, dementia, bipolar disorder, major depressive disorder);

4. More than 100 lifetime uses of any class of drug of abuse other than alcohol (alcohol group) or cocaine (cocaine group);

5. Being on an active low-calorie (<1000 calories/day) diet;

6. Unstable medical illness (e.g. hypertension, diabetes, myocardial infarct);

7. Colour blindness;

8. Currently dependent on cocaine for the alcohol dependent group and currently dependent on alcohol for the cocaine dependent group;

9. Less than a lower level education until age 16;

10. With respect to MRI imaging: claustrophobia; presence of non-removable metal objects, use of psychotropic medication;

11. With respect to the medications: use of medication affecting the central nerve system (such as anti-depressants); use of antibiotics, hypersensitivity for modafinil or N-acetylcysteine; history of peptic ulceration, asthma.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2008
Enrollment:	90
Type:	Anticipated

Ethics review

Positive opinion

Date:	26-11-2009
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 33825
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL2005

Register	ID
NTR-old	NTR2122
CCMO	NL24576.018.08
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON33825

Study results

Summary results
N/A