Treating cocaine dependence by targeting underlying cognitive processes

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

Summary

ID

NL-OMON41639

Source ToetsingOnline

Brief title Take Control!

Condition

• Other condition

Synonym

addiction, cocaine dependence

Health condition

cocaïnemisbruik en cocaïneafhankelijkheid

Research involving

Human

Sponsors and support

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

Intervention

Keyword: cocaine, cognition, dependence, treatment

Outcome measures

Primary outcome

- cocaine use
- craving
- working memory
- glutamate concentrations in dACC and striatum

Secondary outcome

none

Study description

Background summary

Dual process models posit that there is a competition between two qualitatively different processing systems that contribute to behavior. Reflective processes include emotion regulation and conscious deliberations, while impulsive processes include automatic appraisals of stimuli in terms of motivational significance and automatic stimulus-response associations. An imbalance between these processing types has been proposed to play an important role in addiction, characterized by an imbalance between a relatively dysfunctional reflective system and a hyperactive impulsive system. These processes have been investigated in cocaine users, in some studies with neuroimaging. Investigating underlying neural processes is important because it can explain changes in neurocognitive performance. Furthermore, these processes appear to predict relapse.

In chronic cocaine users, it was found that WM performance was worse compared to controls and that this was associated with years and quantity of use. When performing WM tasks during fMRI, attenuated responses in prefrontal and cingulate cortices, and striatal regions were found. Using a Stroop task, it was found that cocaine users show increased attentional bais for cocaine-related words. The underlying neural processes of this increased motivation can be investigated using cue reactivity tasks during functional magnetic resonance imaging (fMRI). Higher brain activation in several regions as a response to cocaine-related compared to neutral stimuli have been found in cocaine dependents.

When automatic impulses interfere with personal goals, impulses need to be overridden to achieve that goal. This ability is refered to as executive functioning. Deficits in executive functioning are associated with several substance use disorders and dependencies. Therefore, cognitive control processes are a plausible target in the treatment of substance addiction. For instance, chronic alcohol users show lower levels of working memory (WM), and it has been found that WM training improved working memory, but also reduced alcohol intake for more than 1 month after training in problem drinkers. One recent study tested WM-training in stimulant abusers and found that training reduced cognitive impulsivity (delay discounting). Taken together, these findings suggest that WM-training can strengthen the reflective system in cocaine abusers.

One way to decrease the impact of the hyperactive impulsive system is by using an approach bias training, for which positive clinical effects have been found in alcoholic patients. However, effects on craving were minimal and this method has not been tested in cocaine abusers. Craving is an important predictor of relapse, therefore it is important to know how it is manifested during treatment. A promising drug for treating substance use disorder by diminishing craving is N-acetylcysteine (NAC). NAC is an amino acid cystine prodrug. NAC treatment normalizes glutamate homeostasis, of which its role in the continuation of and relapse into substance abuse has been highlighted. NAC administration prevents relapse to drug-seeking behavior in rats treated with cocaine. In humans, pilot studies have shown that NAC decreases cue-induced craving for cocaine, the rewarding effect of smoking, and marijuana use and craving.

Study objective

The objective of this study is to investigate the effectivity on reducing or cessation of cocaine use of 1) working memory training, 2) N-acetylcysteine, 3) the combination of working memory training and N-acetylcysteine. Clinical measures (cocaine use, craving, impulsivity) and brain processes (cue reactivity, working memory related activation, and glutamate homeostasis) are investigated.

Study design

To study the efficacy of working memory training and/or N-acetylcysteine, a dubble blind, randomised, placebo controlled study will be performed. Participants are randomly assigned to 1 of 2 conditions:

- 1) working memory training + N-acetylcysteine
- 2) working memory training + placebo

Several baseline and post-treatment measures will be obtained. Measurements will also be obtained during treatment by means of ecological momentary assessment (EMA), to monitor craving and cognitive functioning at home. Furthermore, brain activation patterns underlying the cognitive processes and brain glutamate concentrations will be assessed before and after treatment to investigate their mediating role in the alteration of cognitive processes underlying cocaine addiction and, hence, the effectiveness of treatment.

Intervention

25 men receive 25 days of working memory training and 2400 mg N-acetylcysteine per day25 men receive 25 days of working memory training and placebo

Before and after this 25-day period, there is another assessment during which they fill out questionnaires, perform computer tasks and undergo the MRI protocol.

Study burden and risks

Participants will come to the study location twice. During these visits, which will take 3 hours, they fill out questionnaires, perform computer tasks and undergo the MRI protocol. Between these two visits is a 25-day period, during which exists of three components.

1) working memory training

Subjects will train online once daily. The training exists of three different tasks and is performed at home on a pc.

2) N-acetylcysteine or placebo

Subjects will take N-acetylcysteine (2400 mg/day) or placebo twice daily

3) Ecological momentary assessment

At least twice daily, subjects answer several demographic questions (what they used that they, current location, mood) and indicate how much craving they experience. Subsequently, they perform a cocaine Stroop task to measure their attentional bias. Risks:

The risks concerning the MRI scanner are negligible. Also, the risks concerning the N-acetylcysteine are negligible. Several studies have been conducted on the tolerance of similar and higher doses of N-acetylcysteine.

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

male, 18-60 years old, using cocaine at least 4 times per maand

Exclusion criteria

Suffering from a neurological or medical illness; lifetime history of head injury with loss of consciousness for more than 5 minutes; unstable medical illness (e.g., hypertension, diabetes, myocardial infarction); severe stomach problems or ulcers; exclusion criteria for MR imaging such as the presence of non-removable metal objects (e.g. arteriovenous clips, pacemakers) and claustrophobia interfering with MR investigation.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	28-04-2014
Enrollment:	50
Туре:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Reolin, Solmucol
Generic name:	N-acetylcysteine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date: Application type:

29-10-2013

First submission

6 - Treating cocaine dependence by targeting underlying cognitive processes 13-05-2025

Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2015
Application type:	Amendment
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-002606-31-NL
ССМО	NL45240.018.13