Innovative approaches for cocaine pharmacotherapy using fMRI and SPECT: The case of rimonabant

Published: 19-03-2008
Last updated: 10-05-2024

Striatal D2 receptor availability will be ascertained in 30 recent abstinent cocaine addicts by [123I]IBZM SPECT. In addition, we will measure drug craving and impulsivity with questionnaires, fMRI/EEG using cue-reactivity and impulsivity paradigms...

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

Summary

ID

NL-OMON31595

Source
ToetsingOnline

Brief title
CoDoRi

Condition

- Other condition

Synonym
cocaine addiction, drug dependence

Health condition

verslaving

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cocaine, Craving, Dopamine, Rimonabant

Outcome measures

Primary outcome

Research assesing the availability of striatal D2 receptors.

Craving and impulsivity.

Research assesing the respons towards cocaine-associated "cues".

Rimonabant may induce an increased availability of striatal D2 receptors. This

could subsequently reduce craving to cocaine and/or impulsivity in human

cocaine users.

Secondary outcome

not applicable

Study description

Background summary

Cocaine addiction creates clear medical and social problems worldwide. Until now, there is no proven effective medication for the treatment of cocaine dependence. Treatment of cocaine addiction is hampered by high rates of relapse even after prolonged periods of drug abstinence. Disruptions in the dopaminergic system are implicated in the etiology of drug addiction, including drug craving and impulsivity, and this may contribute to relapse in cocaine addicts. For example, striatal dopamine D2 receptor availability in chronic cocaine users has been shown to be less than in controls, and low D2 receptor availability promotes cocaine self-administration in non-human primates and

rats. The concentration of striatal D2 receptors may be negatively correlated to craving, which contributes to relapse. If striatal D2 receptor availability were increased, then perhaps relapse by cocaine addicts may be prevented. Rimonabant (SR141716A) is a selective cannabinoid receptor 1 (CB1) receptor antagonist that may increase the availability of D2 receptors, and could attenuate relapse induced by re-exposure to cocaine or cocaine-associated cues in rats. Rimonabant is therefore a promising new pharmacological agent to decrease the risk of relapse in cocaine addicts. The effects of rimonabant on the neurobiology of cocaine addiction, drug craving, impulsivity and relapse may be elucidated by comparing striatal D2 receptor availability, drug craving and impulsivity in abstinent cocaine addicts maintained on rimonabant to those taking a placebo.

Study objective

Striatal D2 receptor availability will be ascertained in 30 recent abstinent cocaine addicts by [123I]IBZM SPECT. In addition, we will measure drug craving and impulsivity with questionnaires, fMRI/EEG using cue-reactivity and impulsivity paradigms. Relapse will be assessed by checking urine samples every week.

Study design

Participants will be divided into two groups: one group will receive rimonabant (n=15; 20 mg/day) and the other will receive placebo (n=15) for 2 months (double-blind, randomized study design). Drug craving and impulsivity will be assessed three times: at the beginning of the trial, after intake of the first tablet (to assess acute effects) and at the end of the trial (after 2 months). D2 receptor availability will be assessed twice: at the beginning of the trial and at the end. In addition, each participant will receive cognitive-behavioral therapy in 45-minute weekly sessions for the duration of the trial.

Study burden and risks

The burden for each participant consists of exposures to each of the following:2 IBZM SPECT scans, 3 fMRI/EEG scans, and questionnaires and neuropsychological testing. In addition, one venous blood sample (to assess the concentration of rimonabant) and weekly urine specimens (for benzoylecgonine tests) will be obtained. Participants will also ingest either rimonabant or placebo daily for 2 months.
The risks for the participants are: radiation burden (within the WHO criteria for research in human) and possible side effects of the rimonabant (this is a registered drug with a mild profile for side-effects) or placebo.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Male, aged 18-60 years;
2) Current DSM-IV diagnosis of cocaine dependence, but recently detoxified and abstinent.
3) Able to provide written informed consent and to comply with all study procedures.

Exclusion criteria

Exclusion Criteria:
1) Currently dependent on any substance other than cocaine or nicotine;
2) Severe neurological or psychiatric disorders (e.g., depression, psychosis, bipolar illness, dementia, or any diseases that require psychotropic medications);
3) Serious medical illnesses

4) Known hypersensitivity or allergy to rimonabant, or receiving chronic therapy with medication that could interact adversely with one of the medications under study, within 30 days prior to randomization;
5) Drugs known to influence binding to DA2 receptors, including neuroleptics, and methylphenidate
6) Received a drug with known potential for toxicity to a major organ system within the month prior to entering treatment
7) Clinically significant abnormal laboratory values;
8) Any disease of the gastrointestinal system, liver, or kidneys which could result in altered metabolism or excretion of the study medication

Study design

Design

Study phase:	3
Study type:	Observational invasive
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2008
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	123I-IBZM
Product type:	Medicine
Brand name:	rimonabant
Generic name:	SR141716A
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-005456-17-NL
CCMO	NL19664.018.07