Investigating the role of dopamine in healthy and pathological gambling: A pharmaco-fMRI study

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Study 1:- Determine whether loss aversion behaviour (i.e. increased sensitivity to losses compared to gains) is modulated by dopamine levels using a pharmacological challenge- Assess whether this effect is accompanied by the modulation of brain...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Impulse control disorders NEC
Study type	Interventional

Summary

ID

NL-OMON36024

Source
ToetsingOnline

Brief title
Dopamine and gambling

Condition

- Impulse control disorders NEC

Synonym
Pathological gambling; gambling addiction

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Decision-making, Dopamine, Gambling, Reward

Outcome measures

Primary outcome

- Blood Oxygenation Level Dependent (BOLD) signal as measured with functional magnetic resonance imaging (fMRI)

- Behavioral performance on computerized tasks

- Psychophysiological recordings, e.g., electrodermal activity, blood pressure, heart rate and eye tracking

Secondary outcome

- Subjective measurements ,e.g., self-report questionnaires, visual analogue scales

- Blood plasma levels of prolactin and sulpiride

Study description

Background summary

Study 1:
People often avoid risks with losses even when they might earn a substantially larger gain, indicating a differential sensitivity to gains and losses. This behaviour, termed "loss aversion", has been associated with dopamine-rich areas such as the ventral striatum, but causal evidence linking loss aversion and dopamine is still missing. The first goal of this study is to use pharmaco-fMRI in healthy subjects to provide such evidence. We will further test the hypothesis that the risk-seeking behaviour typically observed in pathological gamblers might reflect a reduced loss aversion resulting from a dysregulated dopamine function.

Study 2:
Near-misses occur when an unsuccessful outcome is proximal to the designated win. These near-misses have been shown to recruit reward-related brain areas

during gambling, raising the possibility that despite their nonwin status, near-misses are able to enhance dopamine transmission in these areas. We will test this hypothesis in healthy subjects, and further seek to understand whether the persistent gambling behaviour observed in pathological gamblers might result from a heightened sensitivity to the rewarding effect of near-misses, in relation to a dysregulated dopaminergic transmission within the reward circuit.

Study objective

Study 1:
- Determine whether loss aversion behaviour (i.e. increased sensitivity to losses compared to gains) is modulated by dopamine levels using a pharmacological challenge
- Assess whether this effect is accompanied by the modulation of brain activity in the ventral striatum using functional magnetic resonance imaging (fMRI)
- Determine whether exacerbated risk-taking observed in pathological gamblers results from reduced loss aversion driven by abnormal ventral striatal activity
- Assess whether acute dopamine receptor blockade restore loss aversion and ventral striatal activity to normal levels in pathological gamblers

Study 2:
- Determine whether the brain responses to wins and near-misses in a reward task are modulated by dopamine levels using a pharmacological challenge
- Assess whether this modulation is mediated by brain activity changes in the reward system, specifically in the ventral striatum, insula and midbrain
- Determine whether acute dopamine receptor blockade normalizes midbrain responses to near-misses in pathological gamblers

Study design

Subjects will have to lie in an fMRI scanner and perform two decision-making/reward tasks successively. These tasks will be performed on two occasions: once after administration of a placebo substance and once after administration of 400mg sulpiride. A within-subject, double-blind, placebo-controlled, cross-over design will be employed. Behavioral and fMRI data will be analyzed for each task following a 2 drugs (sulpiride/placebo) x 2 groups (controls/pathological gamblers) factorial design.

Intervention

Each subject will receive a placebo and 400mg sulpiride on separate testing days.

Study burden and risks

Subjects will have to lie down and stay still in an fMRI scanner while performing two 30 min tasks involving making decisions and observing their outcomes. These tasks will have to be performed twice: once after administration of a placebo substance and once after administration of 400mg sulpiride. We expect no serious adverse events following the administration of sulpiride, since extensive previous experience has shown only rare and mild side effects, restricted to headaches and transient drowsiness. Subjects will further have small samples of their blood taken twice during each testing sessions.
On the day preceding each drug session, subjects will have to adhere to some simple restrictions with respect to medication, alcohol and drug intake. Also, on the morning of each scanning session, subjects will also have to refrain from smoking and stimulant containing drinks.

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

All groups: males volunteers between 18 and 55 years of age, predominant right-handedness
Pathological gambling group: *active* pathological gamblers, as assessed by a score >= 5 on the SOGS questionnaire and the presence of 5 or more DSM-IV criteria for the diagnosis of pathological gambling
Control group: score <= 1 on SOGS questionnaire and none of DSM-IV criteria for pathological gambling

Exclusion criteria

- neurological disorders
- DSM-IV axis I psychiatric disorders other than pathological gambling / nicotine dependence
- current psychiatric treatment
- heart problems
- claustrophobia
- metallic implants
(See p. 14 on the research protocol for more details)

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-01-2012
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO Date:	14-07-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL36779.091.11