Investigating dopamine synthesis capacity in (pathological) gamblers: An explorative Positron Emission Tomography study

Published: 17-01-2013
Last updated: 26-04-2024

Objective 1:- Determine whether baseline dopamine synthesis capacity levels in the striatum are different between pathological gamblers and healthy controlsObjective 2:- Determine whether pathological gamblers show different reward and punishment...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Impulse control disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON37017

Source
ToetsingOnline

Brief title
Dopamine synthesis capacity and gambling

Condition

- Impulse control disorders NEC

Synonym
gambling addiction, pathological gambling

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen

Source(s) of monetary or material Support: NWO

Intervention

Keyword: dopamine, gambling, PET, reward

Outcome measures

Primary outcome

- Baseline dopamine synthesis capacity in the striatum measured

with[18F]fluoro-dopa (F-DOPA) Positron Emission Tomography (PET)

- Behavioural performance on computerized tasks measuring reward and loss

sensitivity

Secondary outcome

- Self-report questionnaires

Study description

Background summary

Question 1:
Presently, several lines of evidence point to a prominent role of brain dopamine (DA) in pathological gambling (PG). This neurotransmitter has been implicated in drug addiction, which shares striking similarities with PG. By analogy, it was proposed that gambling-induced reinforcement is associated with bursts of DA in the brain reward system. However, whether PG is characterized by similar DA dysfunctions as drug addiction is still unclear. Therefore, our first goal of the study is to clarify whether pathological gamblers suffer from an abnormal baseline DA synthesis capacity, as compared to healthy controls.

Question 2:
There is evidence that pathological gamblers show enhanced sensitivity to rewarding feedback while being less sensitive to punishing feedback. This abnormal reward processing is thought to play a role in gambling behavior spiraling out of control. Despite converging arguments, whether abnormal reward and loss sensitivity in PG is a result of DA dysregulation remains elusive. To

answer this question, we will investigate potential correlations between individual dopamine synthesis capacity levels and behavioral measures of reward sensitivity.

Question 3:
Currently, Dr Sescousse and Prof Cools from the Donders Institute are using pharmacological manipulations to test the causal role of DA in gambling behavior (ABR number NL36779.091.11). Specifically, they are testing the hypothesis that PG is characterized by a higher sensitivity to monetary gains compared to losses when making risky decisions and that these distortions can be toned down following acute drug-induced blockade of DA D2 receptors by sulpiride.
Importantly, the effects of dopaminergic drugs on reward sensitivity vary greatly between different individuals as a function of baseline levels of DA. Therefore, combining the data obtained in the study by Dr Sescousse et al. with PET DA baseline synthesis capacity measures will provide an invaluable piece of information to fine-tune analyses and improve our understanding of the complex interplay between DA, reward sensitivity and gambling.

Study objective

Objective 1:
- Determine whether baseline dopamine synthesis capacity levels in the striatum are different between pathological gamblers and healthy controls

Objective 2:
- Determine whether pathological gamblers show different reward and punishment sensitivity compared to healthy controls.
- Assess whether basal dopamine synthesis capacity levels are related to measures of reward and punishment sensitivity.

Objectiven 3:
- Determine whether the dopaminergic drug effects on reward and loss sensitivity found in the study by Dr. Sescouse et al. (ABR number NL36779.091.11) can be predicted from individual differences in baseline dopamine synthesis capacity levels.

Study design

Subjects will visit the Radboud University on two occasions: once for an intake session and a MRI structural brain scan, and once for the PET scan (the PET-CT scanner is located at the department of nuclear medicine of the Radboud University Nijmegen Medical centre).
Importantly, we aim to re-test participants included in the study currently conducted by Dr. Sescousse et al. (project number 2011/204). This will have the advantage of decreasing the burden on those participants, as they will not have

to come for an intake session and MRI scan (i.e. they will only come once for the PET scan).

A group of 24 pathological gamblers will be compared to a group of 2 matched non-gambling control participants in a between-subject design. The PET scan session will start with completion of informed consent, after which subjects will ingest carbidopa (150 mg) and entacapone (400 mg). A waiting period of 1h is necessary for carbidopa and entacapone to reach maximal efficacy (delay based on prior work and half-life, see Pharmacokinetics carbidopa and entacapone Table). During that time, all subjects will be invited to perform a computerized task to measure reward sensitivity.

Approximately 1 hour after carbidopa and entacapone intake, subjects will be guided to the PET scanner where they will be invited to lie down and relax. Patients are positioned as comfortable as possible, in a supine position, with the head slightly fixated in a headrest to avoid movement. First a low dose CT is made for attenuation correction (this takes 1 minute). Then a 89-minute dynamic PET-scan will-be made of the brain. The scan starts immediately after the bolus injection of the [18F]fluoro-dopa (F-DOPA; max 5 mCi) into an antecubital vein. PET data acquisition will take approximately 1h30. After completion of the PET session (approximately 2h30 in total) the subject may go home.

Study burden and risks

Subjects will visit on two occasions: once for an intake session and a MRI structural brain scan, and once for the PET scan. Importantly, we aim to re-test participants included in the study currently conducted by Dr. Secousse et al. (ABR number NL36779.091.11). This will have the advantage of decreasing the burden on those participants, as they will not have to come for a second intake session and MRI scan.
On the day preceding each drug session, subjects will have to adhere to some simple restrictions with respect to medication, alcohol and drug intake (i.e., not take drugs and alcohol).
All subjects will be scanned 60 min after administration of an oral dose of 150mg of the peripheral decarboxylase inhibitor carbidopa and 400 mg entacapone. Carbidopa is a decarboxylase inhibitor which prevents the peripheral decarboxylation of [18F]fluoro-dopa (F-DOPA) and entacapone is a catechol-O-methyl transferase (COMT) inhibitor, which is one of the metabolites of F-DOPA, both will therefore result in greater availability of tracer to the brain. Carbidopa and entacapone does not penetrate the blood brain barrier and has no central nervous system effects. Furthermore, participants will have to lie and relax in a PET scanner for 90 min while being intravenous injected with F-DOPA. The F-DOPA will be given in tracer amounts. There are no additional risks associated with F-DOPA because it is not pharmacologically active when given in tracer amounts (max mSV/5 mCi). This is much lower than most

diagnostic CT protocols.

Contacts

Public
Radboud Universiteit Nijmegen

Kapittelweg 29
Nijmegen 6525 EN
NL
Scientific
Radboud Universiteit Nijmegen

Kapittelweg 29
Nijmegen 6525 EN
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Males volunteers between 18 and 65 years of age
- Predominant right-handedness
- Gambling status:
- Gambling group: *pathological* or *problem* gamblers, as assessed by a score >= 4 on the SOGS questionnaire and the presence of 4 or more DSM-IV criteria for the diagnosis of pathological gambling (assessed using DIS-T)
- Control group: score <= 2 on SOGS questionnaire and none of DSM-IV criteria for pathological gambling

Exclusion criteria

- Current psychiatric treatment (excluding cognitive behavioural therapy)
- Major depressive disorder, post-traumatic stress disorder and substance/alcohol abuse/dependence (except nicotine dependence) in the 6 months prior to the start of the study
- Lifetime history of other DSM-IV axis I disorders and related psychiatric treatment
- Average use of more than 4 alcoholic beverages daily.
- Self-reported inability or unease to cease smoking during the whole testing session
- Use of psychotropic medication, or of recreational drugs over a period of 1 week prior to each test session, and use of alcohol within the last 24 hours before each measurement.
- (History of) neurological treatment
- (History of) epilepsy

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-03-2014
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO

Date:	17-01-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	12-12-2013
Application type:	Amendment
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	NL41522.091.12