The role of dopamine and noradrenaline in probability and reward value processing.

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This study aims to clarify whether the brain dopamine and noradrenaline system underlie the electrocortical responses (event-related potentials) that are sensitive to cues signalling reward and probability, the P200 and P300.

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

Summary

ID

NL-OMON44020

Source
ToetsingOnline

Brief title
The role of dopamine and noradrenaline in expected utility processing.

Condition

- Other condition

Synonym
Medication will be used to study the effect on subjective value and probability processing in the brain.

Health condition

De medicatie wordt gebruikt om het effect hiervan te bestuderen op de verwerking van subjectieve waardevolheid en waarschijnlijkheid in het brein.

Research involving

Human

Sponsors and support

Primary sponsor: Universiteit Utrecht
Source(s) of monetary or material Support: NWO open competitie

Intervention

Keyword: dopamine, noradrenaline, subjective probability, subjective value

Outcome measures

Primary outcome

Medication sessions:

- Cue specific P200 ERP relative to no cue

- Cue specific P300 ERP relative to no cue

Independent variable: dopaminergic antagonism by haloperidol and noradrenergic antagonism by clonidine.

Secondary outcome

- Reaction times, percentage omissions and percentage correct responses

Independent variable: dopaminergic antagonism by haloperidol and noradrenergic antagonism by clonidine.

- Velocity scaling, which will measure bradykinesia

- Spontaneous motor activity measurement, by using an actigraph

- Event related potentials in response to the target

- Questionnaire scores (BIS, BAS, ACS, STAI, POMS)

- Low frequent resting state EEG activity

Study description

Background summary

The way humans behave is greatly affected by the principle 'expected utility'. Expected utility is the product of subjective value of the outcome of an act and the probability of that outcome. In our prior study (approved by the METC, protocol number 12/238, NL39997.041.12) we observed an anteriorly localized brain potential (the P200) that was sensitive to cues signaling reward and it was also sensitive to cues signaling the probability of an upcoming target. Specifically, the P200 was larger for cues signaling reward compared to cues signaling no reward. And the P200 was also larger for cues signaling high compared to low target probability. We also observed a more posteriorly located brain potential (the P300) that was sensitive to cues signaling reward. This P300 was larger for cues signaling reward compared to no reward.
The current study aims to clarify whether the brain dopamine and noradrenaline system are involved in the processing of reward value and probability. More specifically, we want to investigate whether these neurotransmitter systems underlie the the brain potentials sensitive to reward and probability (the P200 and P300). We expect that the effect of reward on the posterior P300 decreases under noradrenaline antagonism by clonidine, specifically. Moreover, we expect that the effect of reward and probability on the anterior P200 decreases under dopamine antagonism by haloperidol, specifically.

Study objective

This study aims to clarify whether the brain dopamine and noradrenaline system underlie the electrocortical responses (event-related potentials) that are sensitive to cues signalling reward and probability, the P200 and P300.

Study design

The main part of the study consists of 3 medication sessions. This is a placebo-controlled, double blind cross-over study.
EEG will be measured during each of the medication sessions.

Intervention

During each of the three medication sessions 2 mg haloperidol, 150 microgram clonidine or placebo will be administered to included individuals. The time between sessions is at least 1 week.
During each session one of these drugs (haloperidol, clonidine or placebo) will be administrated (in a double blind fashion).
The order of the sessions (haloperidol/placebo/clonidine) will be balanced

across participants.

Study burden and risks

We expect this study to be a moderate risk study. There is, however, a possibility that transient side effects occur.
Mostly reported side effects for haloperidol are sedation and extrapyramidal side-effects. Mostly reported side effects for clonidine are a dry mouth and sedation. For a complete overview of reported side effects, see IB.
Strict measures will substantially reduce the risk of side effects to occur. First, there are strict in/exclusion criteria (including no medication use, no history of serious medical conditions, no low blood pressure, see protocol section 4.2/4.3). Second, the study will be run in the hospital, where medical care is available when needed. Finally, drug effects will be monitored (by means of actigraph measurements, velocity scaling and the POMS questionnaire).

In our opinion the burden associated with participation is acceptable. It could be that participants feel a bit tired, because of the medication on the one hand and because of doing the task on the other hand. To keep the experimental sessions as comfortable as possible, participants will pause several times during the task. Of course, participants have the right to withdraw from the study when they want to.
The behavioral task during which EEG will be measured takes about 1 hour. During a large part of the study (between drug administration and drug peak level) participants do not have to perform a task.

In our opinion it is justified to perform the experiment. First, because in our opinion the burden associated with participation is acceptable (see above). Second, this study will have great implications on understanding and possible treatment of psychiatric disorders (see introduction of the protocol)

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, non-smoking, age between 18-45 years and passing the screening (assessing medical history and blood pressure/heart rate)

Exclusion criteria

Psychopathology, current medication use, (history of) serious medical condition(s), low blood pressure

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-06-2015
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Clonidine HCL
Generic name:	Clonidine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Haloperidol
Generic name:	Haloperidol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	25-01-2016
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 27311
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-004411-36-NL
CCMO	NL51144.041.14
OMON	NL-OMON27311