The neurobiological basis of bias; A mechanism implicated in visual spatial attention.

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

Summary

ID

NL-OMON35172

Source
ToetsingOnline

Brief title
The pharmacology of attention

Condition

- Other condition

Synonym
Neurobiology of (visuospatial) attention

Health condition

Geen aandoening; geneesmiddel wordt gebruikt om selectief een aandachtssysteem te inhiberen dmv noradrenergisch antagonisme

Research involving
Human

Sponsors and support

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

Intervention

Keyword: attention, erp, neurobiology, pharmacology

Outcome measures

Primary outcome

Behavioural measures

In the VSC paradigm: the validity effect in ms (RT valid cued target - RT invalid cued target).

A larger validity effect reflects either more bias, or less disengagement.

In the stop task paradigm: the stop signal reaction time (SSRT); SSRT reflects inhibition and related disengagement.

Neurophysiological (Event Related Potentials, task related brain activity) endparameters in the VSC:

1) Parietal cue Event Related Potential (ERP) components. These are the Anterior Directing Attention Negativity (ADAN) and the Late Directing Attention Positivity (LDAP). Both are related to bias.

2) P1 ERP (following a validly cued target); associated with bias.

3) Late Positive Deflection (LPD) ERP (following an invalidly cued target);

associated with disengagement.

Neurophysiological (ERP) endparameters in the stop task:

1) N2 ERP (following the onset of a stopsignal), associated with disengagement.

2) LPD ERP (following the onset of a stopsignal), associated with

disengagement.

Secondary outcome

not applicable

Study description

Background summary

For the development of better pharmacological treatment of various pathologies in which attention and impulsivity
are implicated, such as ADHD, it is crucial to gain knowledge about the neurobiological basis.
Two neurobiological mechanisms are implicated in visuospatial attention, bias and disengagement. bias refers to
increased sensory information processing due to the orientation of attention. Disengagement refers to the
interruption of that attentional set, making processing of non attended stimuli possible. The dominant theory
posits that bias rests on cholinergic functioning and disengagement depends on noradrenergic functioning.
Results of pharmacological research are inconsistent and suggest the opposite. In this research, the noradrenergic part of an alternative model which states the opposite of the dominant model but accounts beter for pharmacological results is
proposed and evaluated.

Study objective

The goal of the current investigation is to test the noradrenergic part of a new model that accounts better for results of pharmacological research. This

model states that the cholinergic system underlies disengagement, and that the noradrenergic
system underlies bias. Two assumptions are made in this model: 1) Two opposing mechanisms underlie bias and
disengagement, 2) Sedators impair but do not enhance these mechanisms, and stimulants do the exact opposite.
Clonidine will be used to selectively inhibit activity in the noradrenergic system. In line with the new model, it is expected that noradrenergic inhibition specifically results in a decrease in bias. In this research, explicit reference to brainactivity indices is made which is necessary since disengagement and biasmechanisms are not dissociable in only behavior measures.

Study design

A double blind placebocontrolled, crossover design will be incorporated in which the order of the conditions
(placebo and clonidine) and of the computertasks (Visual Spatial Cuing task and Stop task) are
counterbalanced across participants.

A pilot is envisaged, this pilot is aimed on veryfing the ERPs in the computertasks. If unexpected
results are found in the pilot, the experiment is either ceased or an addendum of the protocol will be
submitted to the METC before the experiment is continued.

For the medication study an interim analysis is planned after 6 participants completed both sessions.
The effect size will be calculated pertaining to the effect of 100 microgram Clonidine on the dependent electrophysiological variables.
We continue the experiment with the 100 microgram dose if the effect of Clonidine on at least one electrophysiological variable results in a power above 80% with alpha set at 0.05. If the interim analysis suggests the sample size must be increased, we submit another amendment.

Intervention

Clonidine results in less noradrenaline turnover and in effect inhibits the noradrenergic system.
Each participants receives all conditions, 1x clonidine, and 1x placebo, spread across two days.

Study burden and risks

Participants will perform in a relatively long experiment. For the medicationstudy, the experiment consists of two sessions each lasting about 5.5

hour + 1 hour medical screening. During these sessions, participants perform on two short and two long computer tasks.
EEG will be recorded during the long computertasks. The duration of the short computer tasks is in total approximately 30 minutes whereas the duration of the long computer tasks is in total approximately 2 hours including short breaks. After the short computer tasks, Clonidine or placebo will be adminstered. No serious adverse events have been reported following 200 microgram Clonidine. However, our researchgroup experienced that side effects, plausibly in combination with the specific procedures, have resulted in a significant burden for participants. As a result, 100 microgram Clonidine will be administered to participants as significantly less side effects are expected with half of the original dose. The medicationstudy will take place in the UMC Utrecht. At the start of the experiment, participants will be informed (again) that they may withdraw at any time from the experiment.

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

Passing the physical/medical evaluation (in which cardiovascular functioning and blood pressure is
evaluated) is a prerequisite.

Exclusion criteria

Diagnosis of psychopathology.
Current drug use
Low blood pressure.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2010
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Clonidine
Generic name:	Clonidine

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-07-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-02-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	19-07-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-08-2010
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-013502-14-NL
CCMO	NL28618.041.09