The neurobiological basis of bias and disengagement; Two neurotransmitter mechanisms implicated in visual spatial attention.

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Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON33564

Source
ToetsingOnline

Brief title
The pharmacology of attention

Condition

- Other condition

Synonym
Neurobiology of (visuospatial) attention

Health condition

Geen aandoening; geneesmiddelen worden gebruikt om selectief aandachtssystemen te inhiberen dmv noradrenergisch dan wel cholinergisch antagonisme

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Utrecht
Source(s) of monetary or material Support: 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 (ERP) endparameters in the VSC:

1) Parietal cue ERP components (ADAN + LDAP), related to bias.

2) P1 valid cued target ERP, related to bias.

3) LPD invalidly cued target ERP, related to disengagement.

Neurophysiological (ERP) endparameters in the stop task:

1) N2 stop signal ERP, related to disengagement.

2) LPD stop signal ERP, related to disengagement.

Secondary outcome

not applicable

Study description

Background summary

For the development of beter 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, 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 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.

Two drugs, Clonidine and Mecamylamine are used to selectively inhibit activity in respectively the noradrenergic or the cholinergic system. In line with the new model, it is expected that noradrenergic inhibition, in contrast to cholinergic inhibition, results in a decrease in bias. Likewise it is expected that cholinergic inhibition, but not noradrenergic inhibition, results in an impairment of disengagement.

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, clonidine, mecamylamine) and of the computertasks (Visual Spatial Cuing task and Stop task) are counterbalanced across participants.

Two pilots are envisaged, one pilot is aimed on veryfing the ERPs in the computertasks, the other pilot's aim is to estimate the least sufficient dose for mecamylamine to render an effect in our paradigm.

Intervention

Clonidine results in less noradrenaline turnover and in effect inhibits the noradrenergic system.
Mecamylamine is a nicotinic acetylcholine receptor antagonist and hence, inhibits the cholinergic system.

Each participants receives all conditions, 1x mecamylamine, 1x clonidine, and 1x placebo, spread across three days.

Study burden and risks

Participants receive three conditions, each lasting 300 minutes, and in two of these conditions a drug is administered. Side effects of the drugs may occur. Although these side effects seem trivial, especially clonidine may cause a sensation of sedation, fatigue and a dry mouth. Participants will be extensively informed about possible adverse effects.
Risks are thought to be minimal, no serious adverse events have been reported and furthermore, all research with medication will be done at the UMCU. The experiments are relatively long (300 min for eacht condition), and participants have to perform a rather monotonous task. 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:	Will not start
Enrollment:	48
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Clonidine
Generic name:	Clonidine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Inversine
Generic name:	Mecamylamine

Ethics review

Approved WMO

Date:	04-03-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Not approved

Date:	24-03-2009
Application type:	First submission
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	EUCTR2009-010385-37-NL
CCMO	NL25704.041.09
Other	trialregister, nr nog niet binnen