Dopaminergic modulation of neuronal response to a stimulus-reward task in people with 22q11 deletion syndrome and healthy volunteers: a functional MRI study.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Disturbances in thinking and perception
Study type	Interventional

Summary

ID

NL-OMON29870

Source
ToetsingOnline

Brief title
The role of dopamine in reward processing.

Condition

- Disturbances in thinking and perception

Synonym
delusion, psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NARSAD

Intervention

Keyword: dopamine, fMRI, psychosis, reward

Outcome measures

Primary outcome

Blood oxygen level dependent (BOLD) contrast measured during a modified

reversal learning task within the MRI scanner.

Secondary outcome

1. Level of catecholamine synthesis, measured by blood levels of:

* homovanillic acid (HVA)

* 3-methoxy-4 hydroxyphenethyleneglycol (MHPG),

* VMA

* prolactine

and urine levels of:

* HVA

* MHPG

* VMA

* dopamine (free and conjungated) and norepinephrine (free and conjungated)

2. Score on modified reversal learning taak

3. Possible extrapyramidal side-effects

4. Subjective experiences

5. Depressive and positive and negative symptoms

Study description

Background summary

The neurobiological aspects of psychotic symptoms are still not fully understood, but dopaminergic neurotransmission is thought to play an important role. How dopaminergic disturbances can cause the experience of psychosis is still a matter of study.
It is presumed that dopamine plays a central role in rewards, motivation and the attribution of salience.
It is possible that a dysregulation in dopaminergic neurotransmission leads to aberrant assignment of salience to external objects and internal representations, which subsequently leads to psychotic symptoms. In previous imaging studies looking at neuroanatomical substrates of rewards, e.g by drugs or financial rewards, it was found that mainly brain areas rich in dopamine were involved, like the orbitofrontal cortex (OFC) and the ventral striatum. In this study we want to investigate if dopaminergic modulation during a reward-task leads to changes in these and/or other areas.
People with velo-cardio-facial syndrome are, by carrying a deletion on chromosome 22q11, at greater risk for the development of a psychotic disorder.
In a recent study of our research group, we have found a disturbed dopaminergic neurotransmission in non-psychotic individuals with VCFS. VCFS is therefore a unique research model to investigate psychosis, and the role of dopamine in abberant assigment of salience and the experience of rewards in the general population. Therefore, we also want to look at differences in brain activity after dopaminergic modulation between healthy indiviuals and people with VCFS.

Study objective

Main goal is to gain more insight in the role of dopaminergic neurotransmission in rewards, motivation and the attribution of salience in the etiology of psychosis.
Primary question is whether a change in blood oxygation level dependent (BOLD) fMRI activity is being measured after temporary acute dopamine depletion with alpha-metyrosine (AMPT) during a stimulus-reward task in healthy volunteers and people with VCFS.

Study design

A stimulus-reward task is being carried out within an MRI-scanner, one time with baseline conditions and one time after temporary dopamine depletion with AMPT. This will take place in two seperate sessions, with an interval of two weeks and in randomized order.

Intervention

Temporary acute dopamine depletion with alpha-metyrosine (AMPT).

Study burden and risks

Possible side effects are stiffness (extrapyramidal symptoms), dysphoria, transitory anxiety, tiredness, sedation and sleeping problems. In a previous study of our research group with 24 comparable individuals, in reaction to the proposed dose of AMPT only sleepiness was reported. There have not been any reports of longer lasting side effects, which would also not be expected farmacologically, because of the de half-life of 3.4-3.7 hours. In addition, there is a burden in time of 1 day and 1 daily period.

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

20 individuals with 22q11 deletion syndrome with no psychiatric history and no use of psychiatric medication, age 18 till 50 years.
20 healthy volunteers, matched for age and gender, with no psychiatric history and no use of psychiatric medication.

Exclusion criteria

Pregnancy, presence of metals that are not allowed in MRI-investigation.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2006
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Demser

Generic name:	metyrosine

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2006-003979-12-NL
CCMO	NL12429.018.06