Het dopamine systeem en cognitieve achteruitgang bij patiënten met VCFS.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26307

Source
Nationaal Trial Register

Brief title
VCFS , del22q11.2

Health condition

velocardiofacial syndrome
del22q11.2
dementia
dementie
velocardiofaciaal syndroom

Sponsors and support

Primary sponsor: Governor Kremers Centre /
Department of Clinical Genetics
Maastricht, the Netherlands
Source(s) of monetary or material Support: Governor Kremers Centre /
Department of Clinical Genetics
Maastricht, the Netherlands

Intervention

Outcome measures

Primary outcome

Catecholaminergic metabolites (in plasma: (homovanillic acid (HVA), 3-methoxybenzophenone-4 hydroxyphenethyleneglycol (MHPG), vanillylmandelic acid (VMA,) and in urine (HVA, MHPG, VMA, dopamine (free and conjugated) and norepinephrine (free and conjugated)), prolactine and proline in plasma and for COMT and PRODH polymorphism screening.

Secondary outcome

1. Vineland-S;

2. Dementiascales DMR: Dutch version: DVZ;

3. Psychiatric symptomatology: Mini PAS-ADD Behavioural scales: ABCL and SGZ.

Study description

Background summary

Background of the study:
Velocardiofacial syndrome (VCFS) is a genetic syndrome caused by a microdeletion on chromosome 22q11.2. The clinical symptoms are very variable. One of the symptoms is a learning disability, mostly mild or borderline. There is a subgroup of patients with VCFS that suffer from chronic serious psychotic symptoms. For those symptoms there are, up till now, insufficient treatment options. Some of these patients experience severe cognitive deterioration. In those patients the clinical picture fulfils the DSM-IV criteria of dementia. There are also patients with a pre-existing low IQ. In pre-existing research dopaminergic mechanisms are thought to play an important role in psychopathology concerning VCFS (2, 3, 12)(1, 2, 10). We hypothesize that dopaminergic neurotransmission in those two groups is more disrupted in comparison with healthy people and non-psychotic VCFS patients without cognitive decline. Disrupted dopaminergic neurotransmission is likely to be partially caused by COMT haploinsufficiency. The COMT gene is located on 22q11.2 and therefore thought to be of importance for the psychopathological (e.g. psychosis, cognitive decline) mechanisms in VCFS.

In the same chromosomal region the PRODH gene is located, which encodes for the enzyme proline dehydrogenase (PRODH), responsible for proline degradation. Proline probably modulates COMT (elevated proline levels seem to have a negative effect on the dopamine catabolic capacity) and because of PRODH haploinsufficiency this can play a role in dopaminergic metabolism in VCFS (36)(31).

Objective of the study:
The aim of this study is to measure dopaminergic metabolic outcomes which gives an indication of the dopaminergic transmission investigate dopaminergic neurotransmission in people with VCFS and pre-existing or acquired cognitive impairment. Particularly we are interested in the dopaminergic neurotransmission related to the COMT genotype.

Study design:
This study is an observational case-control study.

Study population:
The study population consists of two groups of 22 patients with VCFS with an IQ of 55 or below. One group will consist of VCFS patients with a premorbid IQ >55 (normal for VCFS) who develop a subsequent IQ decline and one group will consist of patients with a premorbid IQ <55. In an earlier study (MEC 04/200) two groups of both 22 persons were studied. One group consisted of patients with VCFS without psychiatric history and IQ > 55 without cognitive decline. The other group consists of healthy controls. The results of these studies will be taken into account in this study.

Primary study parameters/outcome of the study:
Blood and urine samples will be collected to determine dopaminergic markers. Also we will obtain blood samples to determine erythrocyte COMT activity, proline levels in serum and COMT and PRODH polymorphisms.

Secundary study parameters/outcome of the study:
Behavioural and psychiatric parameters will be obtained though several questionnaires. Medication status wil be added.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
The study protocol will be explained to carers of VCFS patients and they will be asked for consent for participation in this study. Blood and urine samples for this study will be collected once at the same time of a regular routine clinical blood monitoring (preferable coinciding with the yearly recommended Ca level monitoring in VCFS).

This study will be carried out with VCFS patients and a low IQ, who are not able to give consent. The study is group related; it is only possible to extent the knowledge of VCFS and decline in cognitive functioning using this unique population. The risks which include taking a blood and urine sample once, are negligible and the burden of participation to the study is minimal. Understanding the dopaminergic neurotransmission mechanisms is important in order to gather further insight in the mechanisms of deterioration in combination with the occurrence of serious psychotic symptoms. Investigation of the study populations will extent the knowledge of VCFS and the decline in cognitive functions in these patients.

Study objective

COMT and/or PRODH polymorphisms are debt to cognitive deterioration in velocardiofacial syndrome.

Study design

N/A

Intervention

N/A

Contacts

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Eligibility criteria

Inclusion criteria

1. Deletion 22q11.2;

2. IQ < 55.

Exclusion criteria

IQ > 55.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2009
Enrollment:	44
Type:	Anticipated

Ethics review

Positive opinion

Date:	08-06-2009
Application type:	First submission

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
NTR-new	NL1735
NTR-old	NTR1845
Other	METC AZM : 26039.068.09
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A