Het dopamine systeem en cognitieve achteruitgang bij patiënten met VCFS.

Gepubliceerd: 08-06-2009 Laatst bijgewerkt: 18-08-2022

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

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON26307

Bron
NTR

Verkorte titel
VCFS , del22q11.2

Aandoening

velocardiofacial syndrome
del22q11.2
dementia
dementie
velocardiofaciaal syndroom

Ondersteuning

Primaire sponsor: Governor Kremers Centre /
Department of Clinical Genetics
Maastricht, the Netherlands
Overige ondersteuning: Governor Kremers Centre /
Department of Clinical Genetics
Maastricht, the Netherlands

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

N/A

Contactpersonen

Publiek

L.J.M. Evers
Maastricht University Center, Department of Clinical Genetics
Maastricht
The Netherlands
+31 (0)6 53985979

Wetenschappelijk

L.J.M. Evers
Maastricht University Center, Department of Clinical Genetics
Maastricht
The Netherlands
+31 (0)6 53985979

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Deletion 22q11.2;

2. IQ < 55.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

IQ > 55.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm

Controle: N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-09-2009
Aantal proefpersonen:	44
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	08-06-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1735
NTR-old	NTR1845
Ander register	METC AZM : 26039.068.09
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
N/A