Genetic causes of craniofacial disorders

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The objective of the study is to identify genetic causes of developmentalanomalies of the face and skull (craniofacial anomalies), such as orofacial clefting, craniosynostosis, abnormal dental development and rare craniofacial syndromes.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Congenital and hereditary disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON40561

Source
ToetsingOnline

Brief title
GenCFA

Condition

- Congenital and hereditary disorders NEC

Synonym
congenital anomalies of the face and skull

Research involving
Human

Sponsors and support

Primary sponsor: Genetica
Source(s) of monetary or material Support: Ministerie van OC&W,Grant funding exome sequencing for orofacial clefting (coordinator: T. Roscioli;Sydney;Australia)

Intervention

Keyword: CFA, Craniofacial, genetic

Outcome measures

Primary outcome

Identification of new genetic causes of developmental craniofacial disorders.

Secondary outcome

Not applicable.

Study description

Background summary

The aim of the study is to identify new genetic causes of craniofacial developmental anomalies. We will focus on several disorders comprising orofacial clefting, cranioynostosis and/or abnormal tooth development.
In nonsyndromic form, these disorders are all relatively common developmental anomalies. They can also be part of a syndrome (syndromic forms) or occur within families (familial forms). . These disorders can be caused by strongly penetrant mutations in Mendelian genes, interactions between multigenic and environmental factors, and/or stochastic factors. However, especially in nonsyndromic forms, there is not much known about the genetic factors that are associated with the disease. The genetic cause of these craniofacial disorders is only identified in a small number of patients. The use of next generation sequencing techniques will increase this number.
Genetic diagnoses will allow optimal treatment and management of the disorder. Moreover, it is a prerequisite for adequate genetic counseling to patients and their families. Furthermore, understanding the molecular background of these disorders will pave the way for possibilities for development of therapy.

Study objective

The objective of the study is to identify genetic causes of developmentalanomalies of the face and skull (craniofacial anomalies), such as orofacial clefting, craniosynostosis, abnormal dental development and rare craniofacial syndromes.

Study design

Individual patients and families will be selected by a clinical geneticist or other medical specialists involved in the craniofacial/cleft team. The selection will be based on the phenotype and/or numbers of affected persons

within a family. The recruited patients will be seen by the principal investigator (PI). During this visit a (family) history will be taken, the patient will be physically examined and a blood sample will be obtained for the isolation of DNA.
Within routine diagnostics known causes of craniofacial disorders will be investigated using targeted DNA gene tests and/or microarray analysis. When no causative defect is identified, next generation sequencing (whole exome or whole genome sequencing) will be performed in the patient and, depending on the probable mode of inheritance, possibly in other affected individuals in the family.
The patient and/or his/her relatives will be counselled about the risks and benefits of next generation sequencing by the PI prior to inclusion in the study. The results of the investigations will be discussed with the patient or his parents by the PI. If there is an unsollicited finding this will be reported to the "Commissie Toevalsbevindingen" (committee of unsollicited findings) of the Radboud University Medical Center. If the Committee decides it is necessary to inform the patient about the unsollicited finding, this will be done by the PI.
If segregation analysis in affected or non-affected family members of gene variants that have been identified by exome or genome sequencing is necessary, they will be asked for permission by the (legal representatives of the) patient himself. The PI will subsequently inform about the study, acquire permission of the family member, perform physical examination and obtain a blood sample.

Study burden and risks

The only physical burden is a venipuncture. There is a small chance of unsollicited findings when whole exome or genome sequencing is performed.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Patients with congenital craniofacial anomalies, such as orofacial clefting, craniosynostosis, disorders of teeth development and syndromes with a distinct craniofacial phenotype.

Exclusion criteria

Not applicable

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting

Start date (anticipated):	31-12-2014
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	16-07-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL46589.091.13