The role of GPR161 and its modifiers in spina bifida: association studies in a human cohort.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON29737

Source
ToetsingOnline

Brief title
UMCG SB

Condition

- Neurological disorders congenital

Synonym
cleft spine, spina bifida

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: subsidie aanvraag voor het Prinses Beatrix fonds is in voorbereiding

Intervention

Keyword: candidate genes, genetic epidemiology, spina bifida

Outcome measures

Primary outcome

The allele frequencies of the candidate genes in spina bifida patients and

their parents.

Secondary outcome

n.a.

Study description

Background summary

Spina bifida is a complex disease trait underlying multiple genetic and environmental factors. We recently demonstrated that the spina bifida phenotype in the vacuolated lens (vl) mouse is due to a mutation in Gpr161, a gene encoding a previously uncharacterized orphan G protein coupled receptor (GPCR). As we observed modification of the phenotype characteristic for vl we concluded that modifier genes are present. Subsequent analysis identified six modifier loci.

Study objective

Now that we have identified the gene underlying the vl mutation and have strong candidates for its genetic modifiers in mouse, we want to investigate their role in human spina bifida. Therefore, our aim is to test GPR161 and its modifier loci for association with spina bifida in human.

Study design

To enable gene association testing in human, we will set up a cohort of 500 spina bifida patients and their parents. Using a parent-parent-affected offspring trio design has the advantage that it has more power to detect association, is immune for population stratification, enables the construction of haplotypes, and allows (in part) for checking of genotype errors compared to a case-control design.

Study burden and risks

Participants are asked to donate blood for DNA isolation (neonates 4 ml; all other participants 10 ml). There is no risk related to participation. Since neonates with spina bifida are planned for operation, blood withdrawal can be performed from the intravenous catheter during operation. In all other spina bifida-participants we will strive to obtain samples during vena punctures for other clinical purposes. For the participants, there is no personal direct benefit attached to cooperate with the study. The results of the study will contribute to the knowledge and benefit for the whole spina bifida patient-group.
The study is group related because a large number of the necessary patients for this study are minors.

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

All spina bifida patients and their biological parents registered at the spina bifida team Groningen will be asked to participate in the study. In addition, we will include new spina bifida patients born during the time of the study.

Exclusion criteria

Patients with a known direct, iatrogenic cause for spina bifida (such as administration of anti-epileptic drugs during pregnancy) will be excluded from the study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	1500
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL12182.042.06