Genetics of primary headache disorders and associated syndromes

Published: 22-11-2012
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To evaluate to what extent primary headache disorders are caused by genetic factors and to identify genes and pathways involved in the pathophysiology of these disorders.

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

Summary

ID

NL-OMON50526

Source
ToetsingOnline

Brief title
Genetics of headache

Condition

- Neurological disorders congenital
- Headaches

Synonym
headache, pain in the head

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO / ZonMW,Hersenstichting

Intervention

Keyword: cluster headache, genetics, headache, migraine

Outcome measures

Primary outcome

The identification of genetic factors involved in primary headache disorders

and associated syndromes, the comparison of genetic profiles of patients and

controls and the determination of the relative importance of genetic factors.

Secondary outcome

not applicable

Study description

Background summary

Primary headache disorders are at least partly determined by genetic factors. Current treatment is not optimal and the burden of disease is large, both for the individual patient and society. A better understanding of disease pathophysiology is needed to identify novel treatment targets. The identification of genes involved in primary headache disorders will help pinpointing molecular pathways and profylactic treatment targets.

Study objective

To evaluate to what extent primary headache disorders are caused by genetic factors and to identify genes and pathways involved in the pathophysiology of these disorders.

Study design

The genetic study designs applied can be divided into case-control studies and family-based studies.

Overview of amendments and addenda
Research protocols:
- p133/99: Genetics of primary headache syndromes (1999); revised in 2012 as P12.201

- p.07.079: Biochemical profiling of brain and cerebrospinal fluid in migraine patients (2007)

Amendments/ addenda:
1. Title: Patient recruitment cluster headache
Content: Recruitment of cluster headache patients and their relatives for a survey to describe the clinical spectrum of cluster headache
Function: Addendum to P12.201
Date: 18-02-2000

2. Title: Migraine website
Content: Patient recruitment for headache research through the project*s website
Function: Addendum to p.07.079 and P12.201
Date: 13-12-2007, revised version submitted with P12.201

3. Title: Endothelial function in TREX1 mutation carriers 1.0
Content: Endothelial function tests in patients with RVCL and CADASIL
Function: Addendum to p.07.079 and P12.201
Date: 20-06-2008

4. Title: Endothelial function in TREX1 mutation carriers 2.0
Content: Extension of version 1.0 with capsaïcin test
Function: Extension of addendum #3 to p.07.079 and P12.201
Date: 04-05-2009

5. Title: Hypothalamic functioning in migraine; a diary study into the premonitory and headache phases
Content: Diary study/ questionnaires to collect additional clinical information from patients recruited via the headache research project*s website
Function: Addendum to p.07.079 and P12.201
Date: 15-05-2009

6. Title: Recruitment of a control cohort for questionnaire studies and genetic studies in the perspective of the LUMINA program
Content: Recruitment of controls for headache research through the project*s website
Function: Addendum to p.07.079 and P12.201
Date: 14-03-2011

7. Title: Recruitment of ex-(pre-)eclampsia patients
Content: Recruitment of ex-(pre-)eclampsia patients for genetic research and questionnaires via the headache research project*s website
i.c.w. UMCG
Function: Addendum to p.07.079 and P12.201
Date: 17-04-2012

8. Title: Gene expression profiling and epigenetics in patients with primary headache disorders and associated syndromes
Content: Extension of the genetic studies described in P12.201 with a buccal swab for DNA isolation, RNA isolation, measurement of general blood markers to be used as a reference (e.g. leukocyte count + differentiation) and biobanking of plasma and serum, with the possibility to assess gene expression and epigenetic markers not only cross-sectionally, but also in a follow-up design (in different disease states or with different environmental factors). Only selected patient groups are invited for these additional measurements, other participants still follow standard procedures described in P12.201.
Function: Addendum to P12.201
Date: Submitted to METC LUMC in November 2013

9. Title: Biobanking at headache clinic
Content: From different patients group we will collect blood samples to store in the LUMC Biobank. In the future, these samples can be used for analyses of interest.
Function: Addendum to P12.201
Date: Submitted to METC LUMC in Oktober 2018

Study burden and risks

Case-control studies:
- Completion of at least two questionnaires, visit to a local laboratory for blood withdrawal.

Family-based studies:
- Proband: completion of a questionnaire and an address list of relatives who want to participate, drawing a pedigree of the family. House visit for direct interview and obtaining DNA, or a telephone interview with blood withdrawal at a local laboratory. If it is not possible to obtain a blood sample for DNA isolation, a saliva kit is used instead.
- Other relatives: completion of a questionnaire. House visit for direct interview and obtaining DNA, or a telephone interview with blood withdrawal at a local laboratory. If it is not possible to obtain a blood sample for DNA isolation, a saliva kit is used instead.
- Affected minors of any age, and unaffected minors between 12 and 18 years old are included in these non-therapeutic family-based studies, because they provide indispensable information for genetic studies that cannot be obtained using non-related control subjects. In order to minimize the burden of participation, information is also obtained from the parents and saliva kits are preferred for minors aged <12 years.

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

A) Case-control studies
- Aged 18 years or older
- Written informed consent
- Diagnosed with a primary headache syndrome according to the International Headache Society criteria., B) Family-based studies
- Probands diagnosed with a primary headache syndrome according to the International Headache Society criteria and their affected and unaffected family members.

Exclusion criteria

Inability to give informed consent, or to obtain informed consent from a legal representative.
Healthy family members younger than 12 years of age.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-11-2012
Enrollment:	15000
Type:	Actual

Ethics review

Approved WMO Date:	22-11-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	07-05-2014

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	06-07-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL41600.058.12