Connection Interrupted: Genetic causes and clinical characteristics of hereditary optic neuropathies

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON56244

Source
ToetsingOnline

Brief title
Connection Interrupted

Condition

- Other condition
- Eye disorders congenital
- Congenital eye disorders (excl glaucoma)

Synonym
Hereditary optic atrophies

Health condition

oogzenuw aandoeningen

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Stichting Bartimeus

Intervention

Keyword: Electrophysiology, Genetics, Hereditary, Optic Atrophy, Visual impairment

Outcome measures

Primary outcome

Identification of pathologic genetic variants in known disease associated genes

or new disease associated genes in hereditary optic neuropathies. Clinical

characterizations of hereditary optic neuropathies.

Secondary outcome

Not applicable.

Study description

Background summary

Hereditary optic neuropathies are a group of rare genetic diseases characterized by vision loss at the early years of life. Little is known about the underlying genetic mechanisms and the clinical characteristics of these diseases. Although new mutations are being reported regularly, in a large group of patients the underlining genetic changes cannot yet be detected with standard diagnostic panels due to unclear genetic variations in known disease-associated genes or mutations in thus far unknown disease-associated genes. More extensive genetic analyses are needed for detection of these mutations in known disease genes and identification of potential novel disease-associated genes. As relatively little is also known on genotype-phenotype correlations in hereditary optic neuropathies, better understanding of these correlations is also needed.

Study objective

The goal of this study is to identify the genetic causes underlying hereditary optic neuropathies and establish genotype-phenotype correlations. This will lead to more reliable prognosis predictions, better genetic counselling and hopefully form a base for therapeutic approaches in the future.

Study design

Molecular genetic and retrospective clinical studies.

Study burden and risks

Some of the subjects of this study will be children. There are negligible risks for the subjects. Retrospective data collection poses no risk for the participants and only in selected cases one-time blood sampling, which is considered as a low risk procedure, will be 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)
Babies and toddlers (28 days-23 months)

Inclusion criteria

• Clinical diagnosis or suspicion of hereditary optic neuropathy based on fundus examination supported with additional clinical examinations, such as optical coherence tomography, perimetry or visual evoked potentials
• No underlying mutation detected with standard diagnostic panels which sequence most common disease-associated genes for hereditary optic neuropathies (In the second part of the study where we focus on secondary objectives, we will also include subjects with HON with a known mutation)

Exclusion criteria

Patients with optic atrophy with a known etiology other than hereditary optic neuropathies, such as:

• Vascular (e.g. arteritic and non-arteritic ischemic optic neuropathy)
• Compressive (e.g. secondary to papilledema, tumour, bony growth, thyroid eye disease, chiasmal compression, disc druses, increased intraocular pressure)
• Inflammatory (e.g. systemic lupus erythematosus, Behcet*s disease, sarcoidosis, demyelination (MS))
• Infectious
• Traumatic optic neuropathy
• Metabolic (e.g. diabetes mellitus)
• Neoplastic,
• Radiation optic neuropathy
• Toxic & nutritional (e.g. Medications such as ethambutol, amiodarone, antiretroviral drugs; alcohol, vitamin deficiencies). In some toxic optic neuropathies, toxic agents can precipitate neuropathy in an susceptible optic nerve with underlying genetic disorder. Selective cases where initial diagnosis is toxic optic neuropathy but clinical features suggest an underlying hereditary optic neuropathy will be also included in the study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-10-2022
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO Date:	31-03-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-08-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.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	NL77704.018.21