Molecular Basis of Parry-Romberg syndrome

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Our first aim is to find the cause of Parry-Romberg syndrome. The subsequent aim is to study the pathogenesis of the entity. The final aim is to find an effective management for the disorder.

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

Summary

ID

NL-OMON37608

Source
ToetsingOnline

Brief title
Molec Parry-Romberg

Condition

- Congenital and hereditary disorders NEC

Synonym
Progressive hemifacial atrophy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Etiology, Pathogenesis, Progressive Hemifacial Atrophy

Outcome measures

Primary outcome

Detection of the gene causing Parry-Romberg syndrome.

Secondary outcome

Understanding of the molecular and cellular mechanisms leading to the various

manifestations of Parry-Romberg syndrome.

Study description

Background summary

Parry-Romberg syndrome consists of slowly progressive atrophy of bone and the soft tissues of essentially half the face accompanied most frequently by contralateral Jacksonian epilepsy, trigeminal neuralgia, and ipsilateral changes in the eyes and hair. The consequences for the disorder for individual patients is significant due to the often enormous disfigurement it causes. The cause is inkonwn, no therapy is available.

We have recently hypothesized that Parry-Romberg syndrome might be a laminopathy. Laminopathies are a series of disorders caused by abnormal functioning of lamin A/C which is an important part of the cytoskeleton of both the nucleus and lamina within the cells. The classical phenotype is Hutchinson-Gilford progeria syndrome but other entities such as restrictive dermopathy, familial partial lipodystrophy and dilated cardiomyopathy are well known as well
We reasoned that in Parry-Romberg syndrome there is not only atrophy of skin, subcutaneous fat tissue and facial muscles, but also of bone. We had access to a biopsy taken from the affected part of a face of a patient obtained during surgery for patient care purposes. Indeed the main characteristics of a laminopathy were found. These were only present in the cells from the affected part of the face and not in peripheral blood cells, indicating mosaicism. The genes known to cause laminopathies were tested and found to be negative.

The present study is aimed to evaluate this in a few more patients, and perform next generation sequencing techniques in both fibroblasts derived from the

affected facial area and from leukocytes, and search for differences between the genomes from the two tissues. Results of patients who show signs of abnormal nuclear morphology in affected tissues will be coupled and compared, which increases the chance to detect the causative gene.

Study objective

Our first aim is to find the cause of Parry-Romberg syndrome. The subsequent aim is to study the pathogenesis of the entity. The final aim is to find an effective management for the disorder.

Study design

Prior to be enrolled in the study, all individuals known with Parry-Romberg syndrome known to us will receive written information about and invitation to participate in the study. Subsequently they will be contacted by phone and if the possible participant is considering participating, he/she will be invited to the clinic.
Blood sampling will be performed by experienced technicians in either AMC or VUmc. Skin biopsies will be taken by an experienced oral surgeon under local anaesthesia. The site will be chosen together with the participant.
Histological studies to show abnormal nuclear morphology will be performed in all skin biopsies (Prof Nicolas Levy, Marseille, France).
Total genome sequencing using the 454 or Solid Genome Analyzer will be performed in at least one Parry-Romberg individual in DNA derived from the affected face region and from leukocytes. If inconclusive results will be obtained from this individual, the DNA of other participants from the affected facial region will be studied this way as well. If the total genome sequencing leads to discovery of a gene that is likely to be causative for Parry-Romberg syndrome, Sanger sequencing of this gene will be repeated in the DNA derived from the affected facial region in all available patients.
Depending on the nature of the detected gene further functional studies will be performed in a lab (Dr Carlos Lopez-Otin, Burgos, Spain) that has an extraordinary experience in performing such studies in laminopathies.

Study burden and risks

Possible adverse event: blood sampling can result in minor hematoma. The (small) biopsy wound may develop into scar tissue but this is unlikely to happen in an atrophic skin. If possible the biopsy will be taken in the anterior hairline or other localization that is less well visible. The localization of the biopsy will be chosen together with the participant. The biopsy is an essential part of the study. Personal contacts with patients have learned us that the affected persons are eager to find the cause of the disorder and know well no management strategy exists at present. The impact of the disorder of the patients on their life is significant and therefore we

think taking small biopsies in as few patients as possible is acceptable. There are no literature data that taking a biopsy accelerates (or decelerates) the disease process.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Diagnosed with Parry-Romberg syndrome
* Patients able to read and understand the written information
* 18 years of age or older

Exclusion criteria

none

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-04-2012
Enrollment:	3
Type:	Actual

Ethics review

Approved WMO

Date:	11-04-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL39498.018.12