Fabry Findings

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What is Fabry?

Fabry disease is a rare, genetic condition which is estimated to affect around 1 in 100,000 people.[1]

In Fabry, an absence or reduced level of an enzyme called α-galactosidase A (α-Gal A), means that the body cannot break down certain types of fats, called globotriaosylceramide (GL-3) and plasma globotriaosylsphingosine (lyso-Gb3), and GL-3 builds up in a variety of cells in the body.[1]

This build-up causes damage to tissues and organs and leads to a range of symptoms and complications, which vary from one person to another.[1]

Disease progression is influenced by the sex of the individual (male or female) and how the disease presents, called its **phenotype**, which is classified as either **non-classical** (mild form) or **classical** (severe form).

Symptoms and complications vary from one person to another [1]

SKIN

- Sweating less than normal
- Small dark red/purple spots located between the belly button and the knees

KIDNEYS

- Protein in urine
- Decreased kidney function
- **Kidney failure**

EYES AND EARS

- Hearing loss (in children)
- Ringing in ears
- Cloudy vision (cataracts)

BRAIN AND NERVES

- Burning in the hands and feet
- Intolerance to heat/cold
- Vertigo/feeling dizzy
- Pain
- White matter lesions
- Depression
- **Mini stroke (TIA)**
- **Stroke**

STOMACH AND BOWELS

- Feeling sick/being sick
- Diarrhoea
- Pain/bloating after eating
- Difficulty managing weight
- Feeling full after eating a small amount of food

HEART

- Irregular heart beat
- Enlarged heart
- **Heart attack**
- **Heart failure**

OTHER

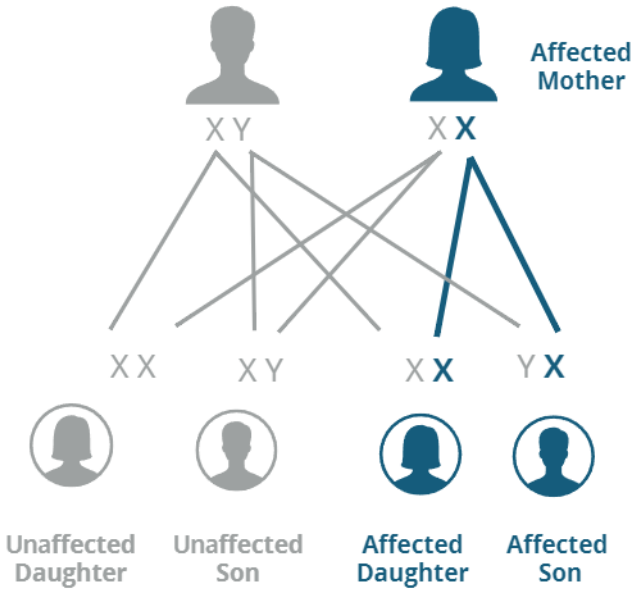
- Tiredness that is not relieved by rest or sleep
- Shortness of breath
- Cough/wheezing

Inheritance

As Fabry disease is an X-linked disorder it can be passed to children by either parent

Mother

A mother with Fabry has a 50% chance of passing her **X mutation** to any of her children



Fabry is caused by a **mutation** in the α-galactosidase A gene (GLA) on the X chromosome

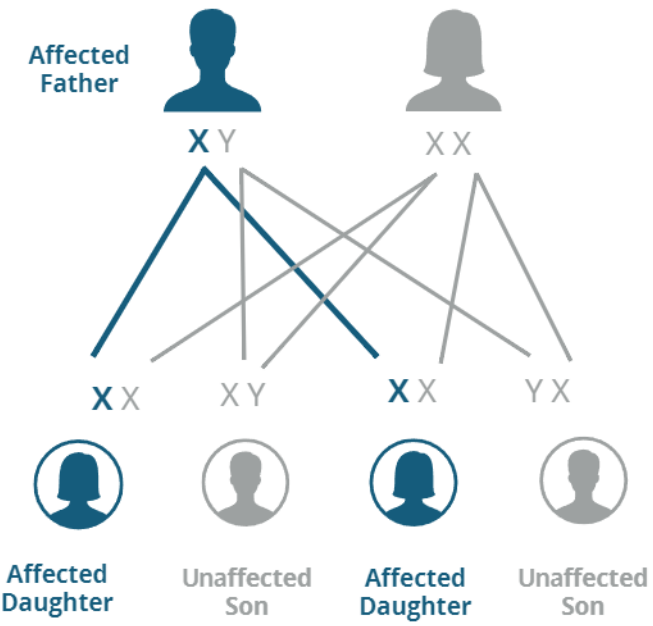
More than 1000 different mutations which cause Fabry disease have been identified [2]

The mutation type may indicate what symptoms an individual will have, when they will appear and how bad they will be or will become

A mutation is a permanent alteration in the DNA sequence that makes up a gene

Father

A father with Fabry passes his **X mutation** to all of his daughters. His son's do not inherit Fabry because they inherit his Y chromosome



Fabry and the brain

A lesion is an area of injury or disease within the brain

Structure

Fabry disease can cause white matter **lesions** (WML) in the brain.[1]
WML are present in around half of individuals with Fabry and increase with age.[3]

Depression

Between 15 and 62% of people with Fabry experience depression [4]

Studies have shown that up to two-thirds of people with Fabry disease experience depression;[4] although the cause is not clear. Depression may be a symptom of the disease itself; be related to the structural changes in the brain; or a reaction to living with a progressive condition.[5]

Cognitive impairments and complaints

Studies in people with Fabry disease have shown a range of cognitive impairments and subjective cognitive complaints [6,7]

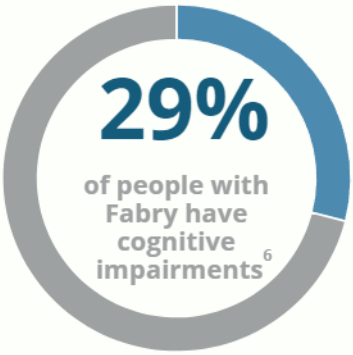
Definitions

COGNITIVE IMPAIRMENT
When a person has trouble remembering, learning new things, concentrating or making decisions that affect their everyday life

OBJECTIVE COGNITIVE IMPAIRMENT
Is one that has been measured using a test

COGNITIVE COMPLAINT
When a person identifies that they have a problem e.g. remembering or concentrating

SUBJECTIVE COGNITIVE COMPLAINT
Is one that the person has identified them self and reported to their doctor



Cognitive impairments are present in around one-third of people with Fabry disease.[6]

Whilst sex (male/female) and phenotype (i.e. how the disease presents) are known predictors of progression of Fabry, little is known if and how these factors relate to cognitive impairments and complaints, in those with the disease

Research news

'Predictors of objective cognitive impairment and subjective cognitive complaints in patients with Fabry disease'
was published in Scientific Reports

The study

'Predictors of objective cognitive impairment and subjective cognitive complaints in patients with Fabry disease' was recently published in *Scientific Reports.*[8]

Objective cognitive impairment is one that has been measured using a test

A subjective cognitive complaint is one that the person has identified them self and reported to their doctor

Depressive symptoms include: feelings of sadness, not feeling like eating, difficulty in staying focussed and not sleeping well

The researchers looked at the relationship between: **objective cognitive impairment, subjective cognitive complaints** and **depressive symptoms.**

The study then went on to explore the **risk factors** and **interrelationships** associated with **cognitive problems** in Fabry disease.

An interrelationship is the way in which two or more things affect each other because they are related in some way

The assessments

In the study **objective cognitive impairment** was assessed using a series of tests, **subjective cognitive complaints** were captured via a **structured interview** and **symptoms of depression** were measured with a depression scale.

During a structured interview a series of set questions are asked in a particular order...

'Predictors of objective cognitive impairment and subjective cognitive complaints in patients with Fabry disease'

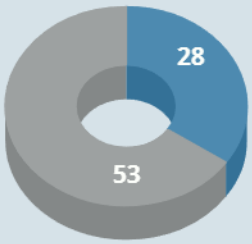
The findings

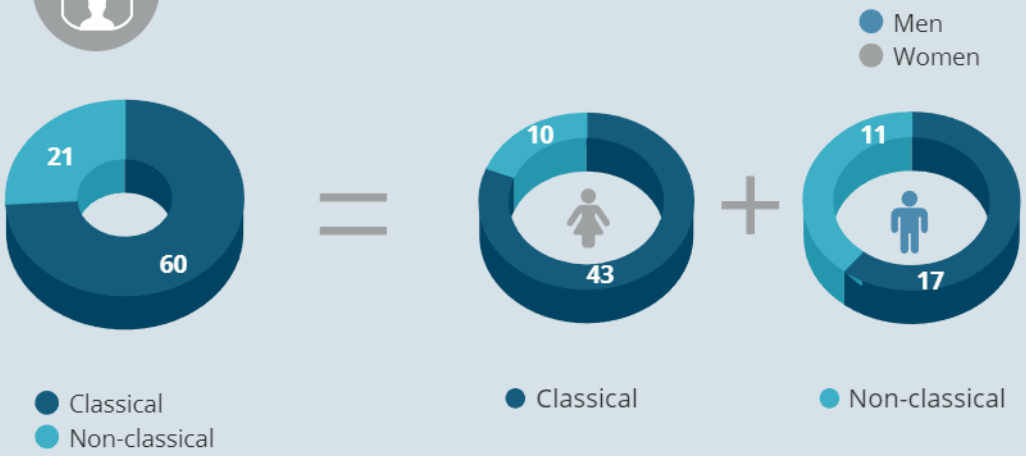
81
participants with an average age 44.5 years

A group of **men and women** with **non-classical** (mild) and **classical** (severe) **Fabry disease** were studied.

The **average age** of the group was **44.5 years (range 19 to 76 years).**

Women made up 65% of the group





Seventy-four percent of the group had the classical form of Fabry disease

81% of women and 61% of men had classical Fabry disease

WMLs were found in 43 patients (59%)

Ten patients (12.3%) had a history of stroke; none of these were women with non-classical disease

Subjective cognitive complaints

Whilst subjective cognitive complaints were reported by around two-thirds of the group, there was no relationship to sex or phenotype

*relating to memory, attention and/or executive functioning (analysing, planning, organising and completing tasks)

Subjective cognitive complaints
LINKED TO

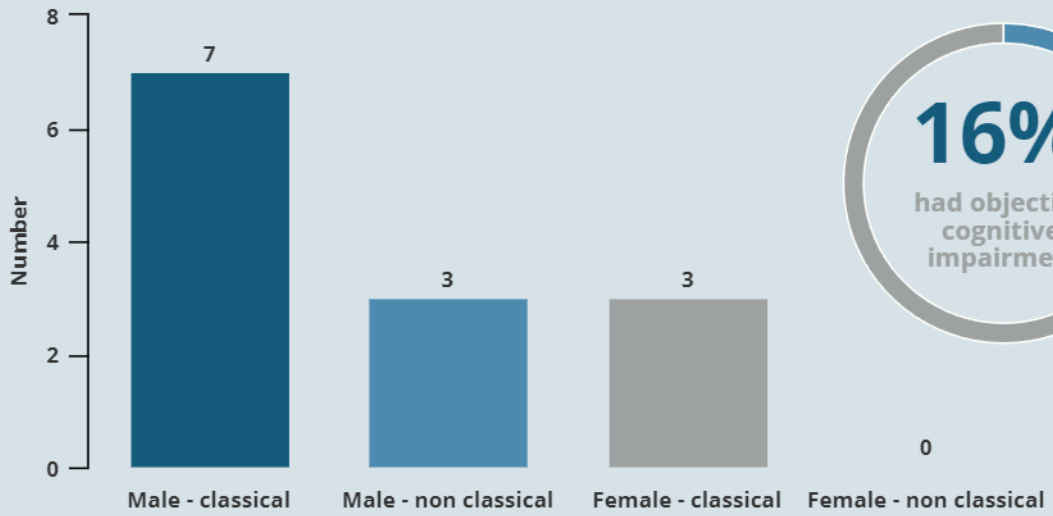
- Depression in the past
- Current depressive symptoms

*However, subjective cognitive complaints were **not** linked to objective cognitive impairment*

'Predictors of objective cognitive impairment and subjective cognitive complaints in patients with Fabry disease'

Objective cognitive impairment

Objective cognitive impairment was found in 13 of the group, mostly in men with classical disease. There were no reports in women with non-classical disease.



Lower pre-morbid IQ was associated with a higher chance of objective cognitive impairment

A history of stroke was associated with a higher chance of objective cognitive impairment

There was no link between objective cognitive impairment and depression

Pre-morbid IQ – is an estimate of intelligence before the identified onset of a disease or dysfunction of the brain

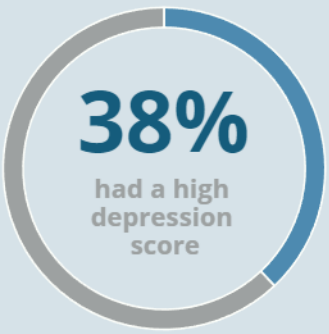
Objective cognitive impairment

RISK FACTORS

- Male
- Previous stroke
- **Pre-morbid IQ**

Depression

Twenty-two patients (27%) reported a history of depression or current depression



Thirty-one patients had a **high depression score**

High depression score and history of depression

LINKED TO

- Subjective cognitive complaints

Findings in brief

'Predictors of objective cognitive impairment and subjective cognitive complaints in patients with Fabry disease'

Objective cognitive impairment

Objective cognitive impairment was present in 1 in 6 people with Fabry

Objective cognitive impairment was most common in men, with classical Fabry

Objective cognitive impairment was linked to:

- Sex
- Stroke in the past
- Pre-morbid IQ

Subjective cognitive complaints

Subjective cognitive complaints were reported by 2 in 3 people with Fabry

Sex and phenotype did not affect subjective cognitive complaints

Subjective cognitive complaints were linked to:

- History of depression
- Current depression

References

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7. Sigmundsdottir L, Tchan MC, Knopman AA, Menzies GC, Batchelor J, Sillence DO. Cognitive and psychological functioning in Fabry disease. Arch Clin Neuropsychol. 2014;29(7):642-50.
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Find out more

Fabry International Network
Fabrynetwork.org

Fabry Support and Information Group (FSIG)
Fabry.org

The National Fabry Disease Foundation (US)
Fabrydisease.org

Society for Mucopolysaccharide Diseases (UK)
Mpssociety.org.uk

Canadian Fabry Association
Fabrycanada.com

Fabry Australia
Fabry.com.au

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