Cerebellar Ataxia Research Update

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Friday 7th & Saturday 8th October 2022

Sponsored by

PTC THERAPEUTICS measured by moments

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Overview

Ataxia UK activities and the process of research

Developments in diagnosis and treatment of ataxia

European and global ataxia research initiatives

Clinical trials and taking part in research

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Ataxia UK activities and the process of research

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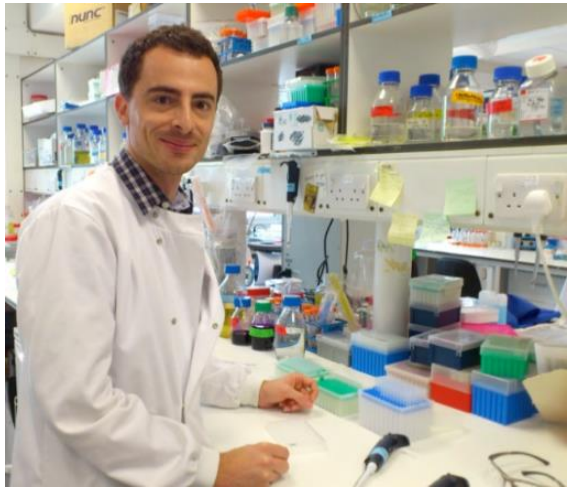
Ataxia UK research activities

Fund research projects mostly small grants to get initial results



2022 Impact Report
Every £1 Ataxia UK spent on research projects raised almost £5 in further funding for ataxia research

Organise research conferences

International Congress for Ataxia Research
ICAR 2022

ATAXIA Ataxia UK
FARA Friedreich's Ataxia Research Alliance
NAF National Ataxia Foundation

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Ataxia UK research activities

Ataxia UK links researchers and ataxia community:

- Recruitment to studies
- Patient engagement in research

Work with pharma and biotech companies:

- Encourage involvement in ataxia research
- Assist with programmes
- Collect useful information

Engagement at all stages of research

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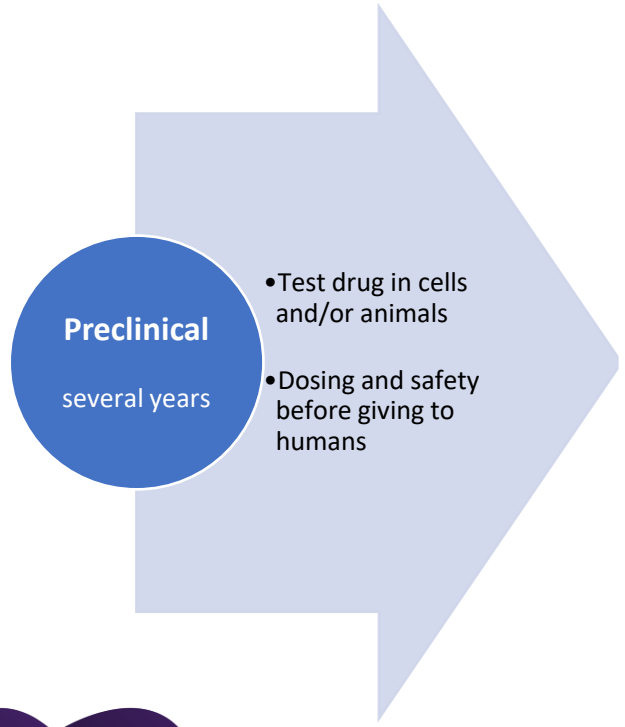
The process of research



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*for rare conditions such as ataxia, the numbers of people in trials are much smaller and the different phases of trial might be combined

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Developments in diagnosis of ataxia

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Inherited ataxias

Advances in knowledge of genes that cause ataxia mean more inherited ataxias can be identified

- Whole genome sequencing (WGS) now available on the NHS
- We now know WGS can also detect repeat-expansion disorders, such as the SCAs
- WGS can aid in the discovery of new conditions

Discovery of a genetic cause of CANVAS

- Genetic mutation in RFC1 gene was discovered by UK-based researchers
- If you have no specific ataxia diagnosis and are interested to find out if you have CANVAS, speak to your neurologist. Tests can be organised via the researcher that identified the mutation (contact research@ataxia.org.uk).

RFC1 mutations may be common cause of late onset ataxias

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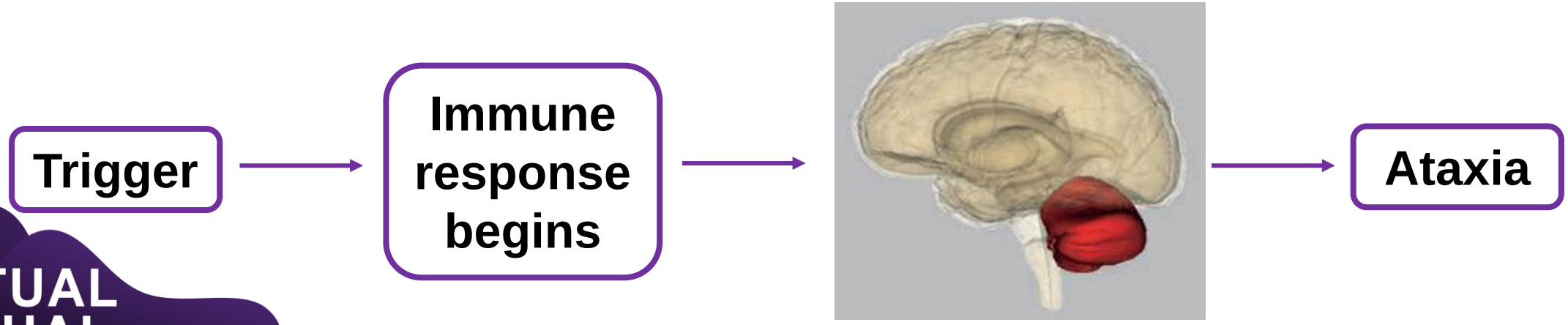
Non-inherited ataxias

Prof Marios Hadjivassiliou from the Ataxia UK-accredited Sheffield Ataxia Centre is a leading expert in non-inherited ataxias.

- **Gluten ataxia**

- **Primary Autoimmune Cerebellar Ataxia (PACA)**



Primary autoimmune cerebellar ataxia (PACA)

Prof Marios Hadjivassiliou and Dr Priya D Shanmugarajah (Sheffield Ataxia Centre) have published two papers on PACA

PACA is a type of immune-mediated cerebellar ataxia

- These ataxias are caused by the body launching an unnecessary immune reaction against the cerebellum (the balance centre) causing damage.
- Sometimes the trigger of this immune response is known (e.g. gluten). If the trigger is unknown, the condition is PACA.

How neurologists can diagnose PACA

- There is no definitive test for PACA
- Prof Hadjivassiliou describes a comprehensive list of clues that neurologists should look for when considering the possibility that someone has PACA.

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A diagnosis of PACA can be made if certain criteria are fulfilled, and if an experienced neurologist or ataxia specialist has ruled out other causes (such as genetic ataxia).

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Primary autoimmune cerebellar ataxia (PACA)

A potentially treatable form of ataxia

- The team from the Sheffield Ataxia Centre treated 22 PACA patients with an immunosuppressive drug called Mycophenolate, which reduces the immune response that causes the ataxia.
- Their results using brain scans and ataxia rating scales showed that those receiving treatment improved or stabilised and those who did not got progressively worse.

If you have been diagnosed with idiopathic ataxia and would like to explore the possibility that you might have PACA, we recommend that you speak to your neurologist about these publications.

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Developments in treatments for ataxia

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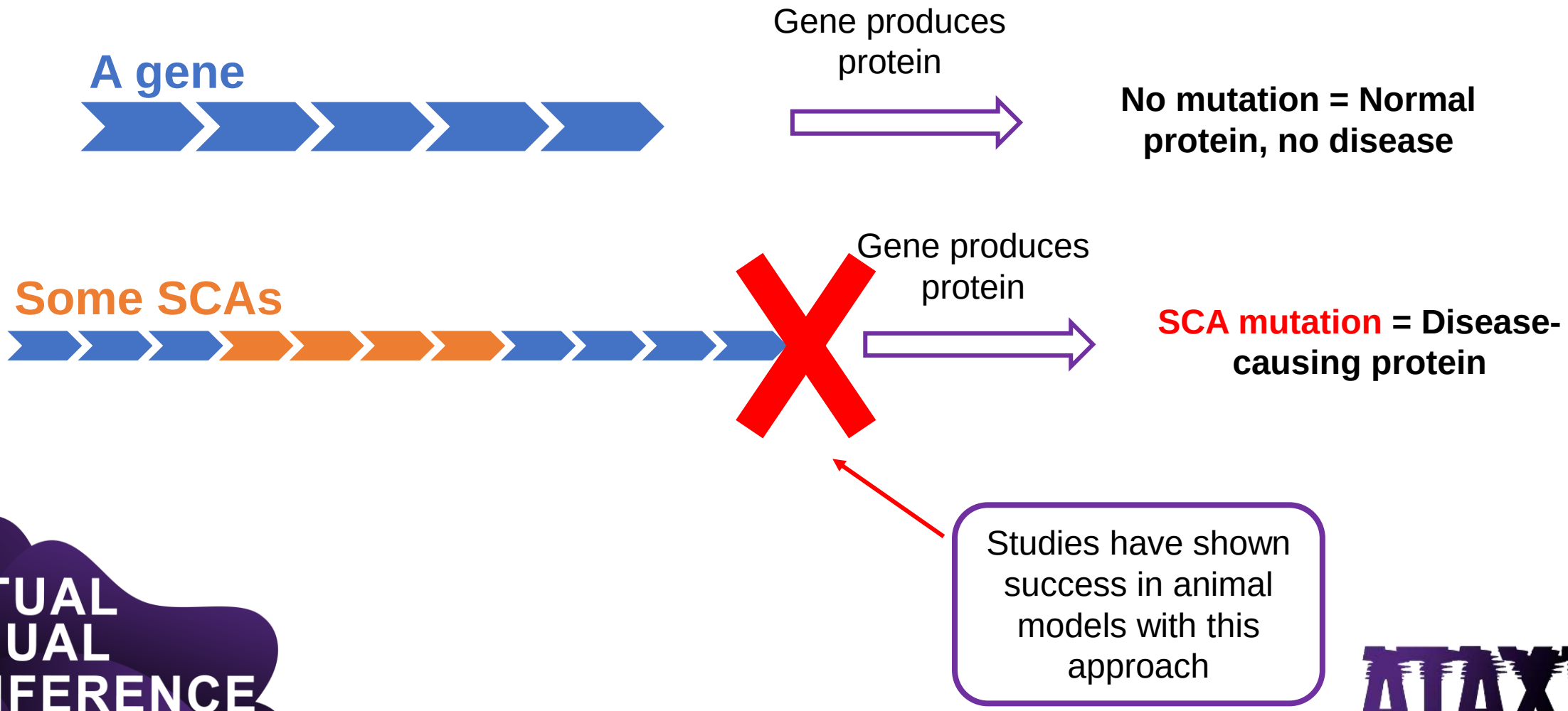
Genetic approaches in SCAs



Genetic approaches in SCAs

- **VICO Therapeutics**
  - SCA therapy VO659
  - Planning to start trials in SCA1 and SCA3

- **Q-State Biosciences**
  - Identified ASOs for SCAs
  - Shown positive results in cell and animal models

- **Ataxia UK-funded project on SCA1**
  - A type of gene therapy called SMaRT

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Examples of Ataxia UK-funded projects

- Two research groups in Portugal looking at nanobodies as a treatment for SCA3, and using anti-depressants to treat SCA3.

- Funded two projects on spastic ataxia type 8, aiming to conduct a natural history study and develop gene therapy. These grants were made possible by a generous donation from the DVS Foundation.

- Ataxia UK and US Foundation CureDRPLA have a research programme working on DRPLA. DRPLA research update tonight at 5pm.

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Speech therapy projects

- Ataxia UK have funded projects on speech therapy for people with ataxia
- Speech therapy focusing on good voice production and clear articulation can help some people with ataxia to improve their speech and their confidence in communicating
- ClearSpeechTogether – peer support model tested in collaboration with Ataxia UK – recently published as a successful method of providing speech therapy
- Prof Lowit is currently testing one more therapy to decide on the best approach, before finalising plans for a larger trial

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European and global ataxia research initiatives

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European research initiatives

Cerebellum and emotional networks (CEN) project

- Investigating neuronal basis of emotions
- Focuses on the role of the cerebellum
- 8 academic and 7 industry/charity partners, including Euro-ataxia

TREAT-ARCA

- Group of researchers studying autosomal recessive cerebellar ataxias
- Focus is on testing treatments in animal models of ARSACS and CoQ8A-ataxia
- Euro-ataxia representing people with ataxia, with support from Ataxia UK

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European research initiatives

PROgression chart of SPAstic ataXias (PROSPAX)

- Large study taking place across Europe (including the UK) and Canada
- Aim to study spastic ataxias over time to learn about progression – starting with ARSACS and SPG7
- Will also learn about biomarkers and animal models
- In order to become ready for clinical trials
- Euro-ataxia representing people with ataxia, with support from Ataxia UK

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euro ataxia

PROSPAX

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Ataxia Global Initiative

Network of Ataxia Specialists worldwide

- For rare and common ataxias
- Researchers, pharma, patient groups (Ataxia UK – Exec Committee)
- Get consensus on standardised data and sample collection to help with trials
- Coordination of joint research projects globally
- Education and training
- Young investigators initiative

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ATAXIA GLOBAL INITIATIVE

worldwide platform for clinical research in ataxias

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Clinical trials and taking part in research

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Symptom relief trial

- Applying a **low electrical current** to the scalp may alleviate symptoms of ataxia.
- Cerebellar transcranial Direct Current Stimulation (tDCS)
  - Ataxia UK funded a tDCS trial in Italy
  - Range of ataxias (FA, SCAs, MSA)
  - Results in 2021 showed improvements in ataxia rating scales
  - Results in other studies have shown mixed results
- Transcranial Alternating Current Stimulation (tACS)
  - Ataxia UK are funding tACS trial by same group
  - tACs could potentially be more effective than tDCS

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IntraBio symptom relief drug trial

- IntraBio announced positive results from their IB1001 clinical trial in Niemann Pick Type C (NPC) and Tay Sachs.
- Neurodegenerative conditions with **ataxia** as a symptom.
- IB1001 targeted the ataxia symptom – including showing an improvement in the SARA score as part of the trial.
- Currently carrying out a trial in ataxia-telangiectasia and looking at developing IB1001 for other neurodegenerative conditions.

Orphan drug designations (US and EU) include SCAs

IntraBio

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Seelos Therapeutics trehalose trial

- Phase 2/3 trial, testing trehalose in people with SCA3
- One year trial with 245 participants, from up to 30 sites
- Recruitment has begun in the US - STRIDES

- Research studies of the trehalose in cells, animals, and humans with SCA, show that high doses may help to clear out damaging molecules in cells in conditions such as SCA

SEELOS THERAPEUTICS

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Biohaven SCA trial

- Troriluzole is a symptom relief treatment

- Phase 3 trial: 1 year, focus on SCA1, SCA2, SCA3, SCA6, SCA7, SCA8 and SCA10, higher dose, 218 participants
  - Main measure used to see if treatment worked (f-SARA score) was not improved by troriluzole
  - However, when only looking at participants with SCA3, they did see an improvement in the f-SARA score in people taking troriluzole
  - Biohaven plans to discuss these results with the regulatory agency in the US (the FDA) to see if there is a way to move this programme forward

SCA3 natural history study - recruiting

- **ESMI**
- Aims to create a patient registry and carry out a natural history study to assess how SCA3 progresses over time
- Recently identified possible biomarkers for SCA3
- Multi-centre European SCA3 project coordinated at the German Centre for neurodegenerative diseases in Bonn, and involving 5 countries

London Ataxia Centre is recruiting: If you have been diagnosed with SCA3 and are interested in taking part, please contact the team at uclh.ataxia@nhs.net

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SCA6 gait project - recruiting

- Ataxia UK is funding a study looking at balance and gait in people with SCA6
- Taking part will involve one visit to the study site, and wearing a sensor at home for 7 days
- The researchers expect that this project will generate useful data in support of using gait measurements in future clinical trials

The site in Newcastle is recruiting: If you have been diagnosed with SCA6 and are interested in taking part, please contact the team at mito.ataxia.study@ncl.ac.uk.

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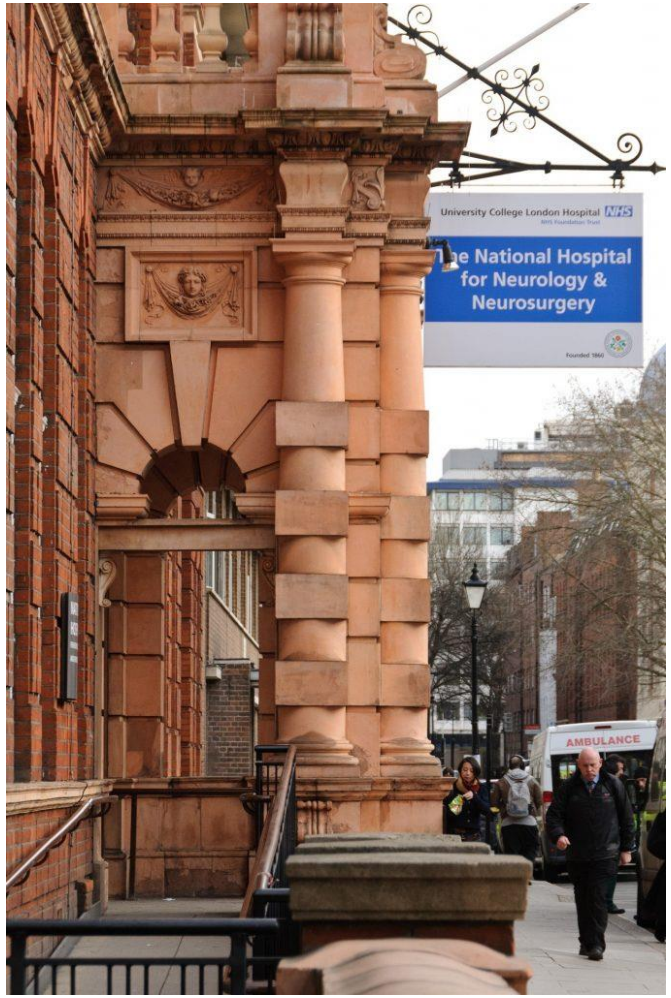
ARSACS project - recruiting

Taking a measurement from the eye (called OCT) to find out whether this can be used to diagnose ARSACS, and to better understand the clinical features of ARSACS.



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Healthcare research

Google's AI for Social Good programme

Project Euphonia

Collecting speech samples from people with speech difficulties in order to improve voice recognition technology – for example to improve Google Assistant.

Moving from child to adult healthcare services

NCEPOD

The aim of this study is to produce a report for clinicians and other professionals about how to improve the care they deliver, and guidance for young people and families on what care you should expect to receive

Google

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Upcoming opportunity – SCA3

Biogen

Biogen are starting a Phase I clinical trial for SCA3 treatment BIIB132.

Small trial taking place in 21 sites (total of 48 participants), including UK.

- BIIB132 is antisense oligonucleotide (ASO) - it can block the ability of a gene to make a protein
- Trial will be the first in-human study of this treatment
- Recruitment for UK sites not yet open

Join Ataxia UK to be kept informed of new research opportunities!

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All studies can be found on our website ataxia.org.uk

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Thank you for listening!

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www.ataxia.org.uk

Please contact ecutting@ataxia.org.uk or research@ataxia.org.uk if you have any further questions!

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