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Friedreich ataxia: balance and gait study

Submission date
31/10/2023

Recruitment status
No longer recruiting

Registration date
02/11/2023

Overall study status
Ongoing

Last Edited
13/08/2024

Condition category
Nervous System Diseases

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Friedreich's ataxia (FA) is an inherited genetic condition. FA affects the part of the brain that controls movement and balance (the cerebellum). It also affects the nerves which carry signals from the brain to the rest of the body. People with FA experience symptoms that get worse over time. These include movement and balance difficulties, speech and swallowing issues, and muscle weakness. Other symptoms can include diabetes mellitus and heart problems. Many people with FA live with significant physical disability and reduced life expectancy. Currently, there is no cure for FA, and more research on this rare condition is needed. Performing clinical trials in rare conditions like FA is challenging. Current clinical rating scales and many outcome measures are subjective. The results may differ depending on who performs the assessment. Often, assessments are not sensitive enough to detect changes over a short time frame. Instrumented assessments of gait and balance, may be useful as alternative outcome measures. They are already used to assess gait and balance issues (ataxia) in some conditions. They are less subjective than current measures and may be better at detecting changes. This study will investigate instrumented assessments of gait and balance in FA. This will be in a specialist gait laboratory and via wearable sensors. It will investigate if these assessments show a consistent pattern. It will also check if these assessments are sensitive enough to measure changes in FA over a year compared to current outcome measures.

Who can participate?
People aged 14 to 65 years, years and above with a confirmed diagnosis of FA

What does the study involve?
Participants will attend the study centre in Newcastle upon Tyne for three visits over 12 months. These will take place at baseline (the start), month 6 and month 12.

Visit assessments will include clinical assessments including physical examination and review of medical history, standard clinical rating tools for FA and tests of upper limb coordination. Participants will also complete questionnaires about ataxia, quality of life and fatigue. Assessments of balance and gait will be performed in a gait laboratory and using wearable sensors. Following each visit, participants will continue wearing a wearable sensor for seven days at home.

Data collected in this study will be combined for analyses with data collected via a separate protocol (under separate approvals and governance) undertaken at the Hertie Institute for Clinical Brain Research and Centre for Integrative Neuroscience, in Germany (Tübingen).

What are the possible benefits and risks of participating?
There will be no direct benefits to individual participants. The study will provide data on the severity and progression of FA. It will investigate new methods for measuring ataxia in FA and will inform the design of future research.

The study involves tests of balance and walking and there may be a risk of falling or becoming tired. The assessments are delivered in an area designed for this type of activity. All staff are trained and experienced in delivering these assessments. Opportunities for regular breaks will be provided.

Study questionnaires include questions on quality of life and well-being. These questions may be distressing for some participants. Participants can contact study staff at any point if they are worried or have difficulty with a questionnaire.

Where is the study run from?
Newcastle University (UK)

When is the study starting and how long is it expected to run for?
June 2023 to August 2026

Who is funding the study?
The French Friedreich's Ataxia Association (AFAF) (France)

Who is the main contact?
Dr Yi Shiau Ng, yi.ng@newcastle.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
328273

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 57586, IRAS 328273

Study information

Scientific Title
A longitudinal laboratory and real-world study of gait and balance in people with Friedreich ataxia

Study objectives
Gait and balance problems have been identified by people with ataxias as the main symptoms that they would like to be addressed in clinical trials.

A number of clinical rating scales are commonly used in both clinical practice and research to determine the severity of ataxia. However, there are a number of limitations in using such measures including their semi-quantitative and subjective nature, inter-rater variability (differences depending on who performs the assessment), and lack of sensitivity to detect change over shorter time periods (e.g., 6-12 months), with ceiling effects.
Also, the small effect size of studies using clinical rating scales as the primary outcome means a large sample size is required, which is a significant barrier to the delivery of clinical trials, especially in rare conditions such as Friedreich's Ataxia.

The availability of robust clinical outcome measures that are reliable and sensitive to change is therefore essential for future clinical research in this condition.

Recent work has shown that instrumented measures of gait have the potential to be feasible and reliable outcome measures for people with ataxias.

This study aims to:
1. Identify outcome measures that can reliably detect disease progression in Friedreich's Ataxia over a short period (one year)
2. Validate instrumented measures of gait (including in a specialist gait laboratory and via wearable sensors) against traditional clinical rating scales for Friedreich's Ataxia.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 30/08/2023, East of England - Cambridge South Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)207 104 8171; cambridgesouth.rec@hra.nhs.uk), ref: 23/EE/0173

Study design
Observational single UK centre longitudinal study (12-month follow-up per participant)

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Friedreich ataxia

Interventions
This study is a collaboration between the Wellcome Centre for Mitochondrial Research, Newcastle, UK, and the Hertie Institute for Clinical Brain Research and Centre for Integrative Neuroscience, Tubingen Germany. Data collected at both centres (under separate protocols and separate regulatory permissions) will be combined as part of the analyses. This registration relates to the UK study and data collection only.

Participants in the study will be assessed at study visits at Baseline, Month 6, and Month 12. Study visit assessments will consist of:
- Collection of medical history and results from previous clinical assessments
- Clinical rating scales of Friedreich's Ataxia, ataxia and cognition
- Functional assessments of upper limb coordination and gait
- Instrumented assessment of gait in a gait laboratory
- Participant completed questionnaires (Participant Reported Outcomes) of balance, ataxia, quality of life and fatigue (collected remotely via an online system)

Study visits will last approximately four hours each.

Following each visit, participants will undergo habitual activity monitoring (via wearable sensor) in a free-living environment (at home) for seven days.

Following completion of the Month 12 visit assessments (at the end of the seven-day activity monitoring period) study participation will be complete.

Intervention Type
Mixed

Primary outcome(s)
Balance and gait measured using stabilometry (force plate analysis), an instrumented walkway (GaitRite) and wearable sensors (Ax6 and Opal) at baseline, month 6 and month 12

Key secondary outcome(s))
1. Investigate how balance and gait outcomes are influenced by wearable sensor location and configuration (i.e. single sensor vs. 3 Opal sensors) measured using gait data generated in a

specialist gait laboratory and in the real world at baseline, month 6 and month 12
2. Validate gait outcomes measured using the wearable sensors against gait outcomes measured via the instrumented walkway at baseline, month 6 and month 12
3. Compare data collected in the real world via wearable sensor with data from clinical rating scales, questionnaires and gait laboratory assessments at baseline, month 6 and month 12

Completion date
31/08/2026

Eligibility

Key inclusion criteria
1. Genetically confirmed Friedreich's Ataxia
2. Aged 14 to 65 years
3. Able to stand and walk unaided for at least 20 m
4. Able to provide informed consent
5. Able to follow instructions and comply with the study protocol
6. Willing to wear a small sensor on the lower back for seven consecutive days
7. No other known neurological or musculoskeletal disorder affecting balance and mobility

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
14 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Lacking the capacity to provide informed consent
2. Enrolled in interfering therapy or clinical drug trial currently or within last 3 months
3. Pregnancy at the time of enrolment
4. Any other reason, which in the opinion of the recruiting investigator would preclude involvement in the study

Date of first enrolment
01/11/2023

Date of final enrolment
31/08/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Newcastle Clinical Ageing Research Unit (CARU)
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation
Newcastle University

ROR
https://ror.org/01kj2bm70

Funder(s)

Funder type
Research organisation

Funder Name
l'Association Française de l'Ataxie de Friedreich (AFAF)

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study have not yet been finalised and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Adult version 3.0	17/10/2023	02/11/2023	No	Yes
Participant information sheet	Older children version 3.0	17/10/2023	02/11/2023	No	Yes
Participant information sheet	Parent version 3.0	17/10/2023	02/11/2023	No	Yes
Protocol file	version 3.0	17/10/2023	02/11/2023	No	No