

Welcome to another edition of our newsletter!

We are ataxia researchers based in Melbourne, Australia. We study various types of ataxia using tools such as brain imaging, clinical testing, and digital devices. This newsletter is made for people with ataxia and their families. It aims to help keep you up-to-date with our research and provide you with other ataxia information and resources.



In this edition, we are excited to share with you:

- Updates on new ataxia research funding and projects
- Results from ongoing ataxia research studies
- Special features to help you learn more about ataxia topics



We hope you find this information useful. Please get in touch with us at harding.lab@monash.edu if you would like further information on any of these topics - we would love to hear from you!

*The Melbourne Ataxia
Team*

NEW ATAXIA RESEARCH FUNDING



Associate Professor Ian Harding has been awarded a prestigious Investigator Grant from the Australian National Health and Medical Research Council for his research on “Hereditary Cerebellar Ataxias: Next-Generation Biomarker Discovery on a Global Scale”.

This 1.5 million dollar grant will fund A/Prof Harding’s ongoing research program, which uses tools including brain scans, computer-based assessment tasks, and clinical assessments to learn more about hereditary cerebellar ataxias and how these conditions progress differently in different people.



Researchers from Monash University and the MJD Foundation (MJDF) were awarded a \$40,000 Community Grant from the auDA (au Domain Administration) Foundation to collaborate on a new online clinical and educational monitoring platform for people living with Machado-Joseph Disease (MJD or spinocerebellar ataxia type 3) in the Northern Territory.



Dr Louisa Selvadurai, A/Prof David Szmulewicz, and Dr Lewis Tang at the auDA Community Grants announcement event in Melbourne

This work will be led by Dr Louisa Selvadurai, alongside A/Prof Ian Harding, A/Prof David Szmulewicz, and the Director of Research, Clinical Services and Education at MJDF, Libby Massey.

The project aims to address geographic, cultural, and language barriers to specialist clinical care and education for the MJD community.

The first stage of the project involves developing the platform, the clinical monitoring assessments, and the educational materials with input from people with MJD and their health and support workers.

SCA-REMOTE STUDY

UPDATES FROM THE STUDY TEAM AT MONASH UNIVERSITY



In this study, individuals with SCA1, 2, 3, or 6 and controls have been completing monthly online assessments of their movement, thinking skills, speech, and mood/wellbeing.

Dr Louisa Selvadurai analysed monthly mood questionnaire scores from 19 individuals with SCA6 and 12 Controls over 10 or more months.

- As a group, people with SCA6 tended to rate their mood as lower than the Control group did
- In both the SCA and Control groups, mood scores could be quite different month-to-month (i.e., scores were **variable**)
- In people with SCA6, people with **lower mood** tended to have **more variability** in their mood scores across months



These results indicate that it is important to assess the mood of people with SCAs, at multiple times. We also need to look further into how we can support people whose mood is low or who find their mood changing a lot.



Congratulations to Chiara Lo Giudice who successfully completed her Psychology Honours thesis on *"Impaired Cognitive Function and Associations with Depression and Fatigue in Spinocerebellar Ataxias"* as part of the SCA-Remote team. Chiara made an invaluable contribution to participant assessments and data analyses for SCA-Remote in 2023. Chiara summarises her thesis findings below:



Spinocerebellar ataxias, a group of progressive diseases that effect people's movement and coordination, may also impact people's cognitive (thinking) skills. We found that as a group, people with SCA performed worse than controls on tasks examining thinking skills, however their performance did not decrease significantly compared to controls over one year. Worse depression symptoms were related to worse performance for people with SCA. These results indicate that difficulties with thinking skills and depression symptoms should be assessed to ensure individuals experiencing these symptoms are supported.

THANK YOU

We are greatly appreciative of all our SCA-Remote participants for their invaluable and ongoing contributions to this project! We could not do this work without you and we look forward to sharing more updates in the next newsletter.

STUDY RESULTS FROM THE FA-APP

USING SMARTPHONES TO LEARN ABOUT FREIDREICH ATAXIA



The Cerebellar Neurodegeneration Research Group (CNRG) at Monash University has been conducting research using the “FA App”. This smartphone app allows people with Friedreich ataxia (FA) to take part in virtual research studies from anywhere in the world. The app also provides important news, education, and connections to others in the FA community.

CNRG researchers designed a study in which participants use the FA App to complete finger-movement tasks, reaction time tasks, speech tasks, and surveys about their mood and wellbeing. This has allowed the team to collect data about many different features of FA, particularly features outside movement difficulties.

Researcher Sarah Wallis analysed study data from 32 individuals with FA and 27 controls without FA. People with FA tended to have worse performance than the controls on some tasks, but not others.

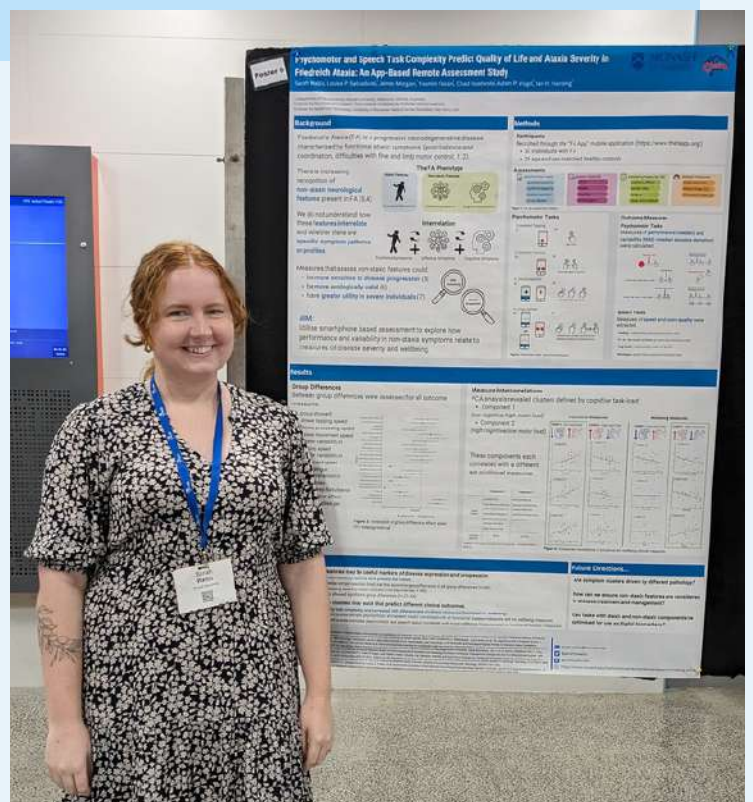
An interesting finding was that different tasks seemed to be related to different aspects of a person's functioning. How a person rated the **severity of their ataxia** was related to how they performed on tasks that needed higher motor skills but lower cognitive (thinking) skills.

On the other hand, how a person rated their **wellbeing** (such as their mood) was related to their performance on tasks needing lower motor skills but higher cognitive skills.

These results tell us that it is important to measure wellbeing as well as the severity of motor symptoms, to better understand people with FA.

Sarah presented these new results at the recent meeting of the Australasian Cognitive Neuroscience Society in Sydney, Australia (November 2023).

Learn more about the FA App:
<https://www.thefaapp.org/>



Sarah Wallis at the Australasian Cognitive Neuroscience Society meeting

FEATURE: OTOLITH ORGAN FUNCTION IN CANVAS

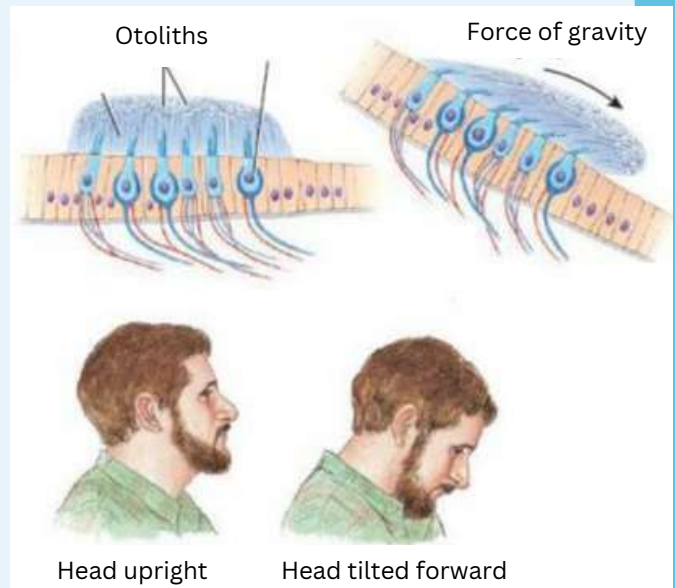
Dr Manju Mammen and A/Prof David Szmulewicz from the Cerebellar Ataxia Clinic at the Royal Victorian Eye and Ear Hospital tell us about their research on how the organs in our ear are affected in a type of ataxia called CANVAS

What is CANVAS?

CANVAS is a disease in which people suffer from difficulties with balance and coordination due to cerebellar (brain coordination centre), and vestibular (inner ear balance system) dysfunction, along with a reduced sense of feeling (sensation) in different parts of the body.

What are the otolith organs?

The inner ear balance system is made up of three balance canals (semicircular canals) that measure movement that takes place in a circular pattern, and small organs containing 'ear stones' (otolith organs) which measure movement in straight lines (up/down, forward/backward).



How the otolith organs work

Otolith organ structure is normal in CANVAS - what about function?

From previous research we performed, we know that in CANVAS the actual semicircular canals and otolith organs are normal. However, we have previously shown that in CANVAS, semicircular canal function is always reduced and this is because the messages from the semicircular canals to the brain are not travelling as they normally would. In a recent study, we looked at how the otolith organ messages in CANVAS are affected, namely whether they are similarly affected to the semicircular canals.

Evaluating otolith function in CANVAS

Otolith function is assessed using a test known as Vestibular Evoked Myogenic Potentials (VEMP). We performed VEMPs in 35 people with CANVAS and found that approximately half had normal VEMPs. This is somewhat surprising as the otolith organs and the semicircular canals share similar means of communicating balance information to the brain, and yet semicircular function is markedly reduced in all people with CANVAS.

What might these results mean?

Although we are yet to confidently explain these results, one option is that there may be a subtle difference in the nerves which carry information from the otolith organs to the brain (as compared to those which link the semicircular canals to the brain). We hope that a better understanding of the way in which CANVAS affects people will help with the development of treatments.

FEATURE: THE VISUALLY ENHANCED VESTIBULO-OCULAR REFLEX IN CEREBELLAR ATAXIA RESEARCH

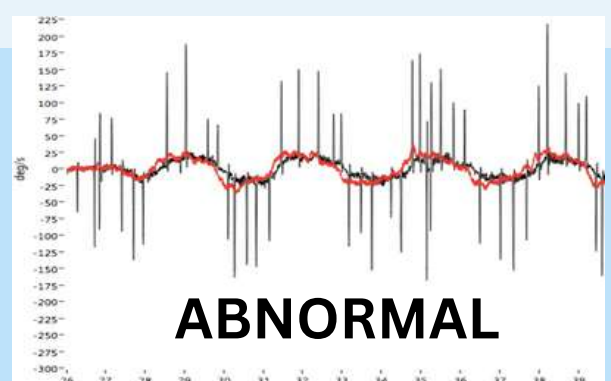
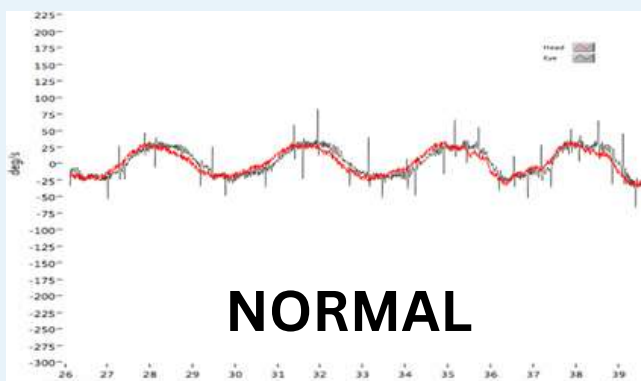
Dr Lewis Tang and A/Prof David Szmulewicz from the Cerebellar Ataxia Clinic at the Royal Victorian Eye and Ear Hospital tell us about a reflex that is useful to measure in ataxia

The vestibular (balance) system is often impaired in cerebellar ataxia

The underlying mechanism of Cerebellar Ataxia is complex, but broadly speaking it is the result of impairments to the cerebellum. More recently, we are coming to understand that the vestibular system (inner ear balance mechanism) is frequently impaired as well. This is not surprising as the two systems are closely linked and must work together to allow us to be coordinated. The symptoms of ataxia may understandably worse if both systems are impaired.

The visually enhanced vestibulo-ocular reflex (VVOR) uses the cerebellum and vestibular systems and can be measured.

One example of the combined function of the cerebellum and the vestibular system is the Visually Enhanced Vestibulo-Ocular Reflex (VVOR). It allows us to sustain stable vision during head movements. In ataxic conditions, disruptions in VVOR often manifest as visual instability (blurry vision during movements) and dizzy sensations. Real life examples of this includes staring at a sign whilst going up or down an escalator. We can record and confirm VVOR abnormalities, by using special goggles that record eye movements while the examiner slowly turns your head side-to-side or up and down. Below are examples of what our recordings may look like.



Why is it useful to measure the VVOR for ataxia diagnosis and monitoring?

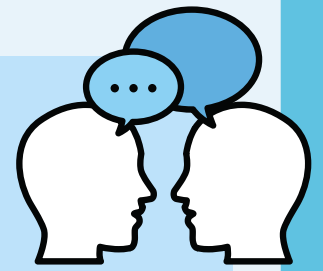
Being able to identify abnormalities in VVOR aids us in diagnosis as it narrows the number of conditions that a given person may have. It also allows us to track the evolution of certain diseases to help us understand it further. A current example is our CANVAS natural history trial.

VVOR is an easy to acquire test of ataxia which means it can potentially serve as a goal post (what drug companies call “biomarkers”) for the development of therapies for cerebellar ataxia. A real-life example of biomarkers being applied is in the recently FDA-approved Omaveloxolone for treatment of Friedreich’s Ataxia.

SPEECH AND ATAXIA

Updates from Professor Adam Vogel, University of Melbourne:

- The Neuroscience of Speech research group at the University of Melbourne and industry partner Redenlab were chosen to support the global Friedreich ataxia natural history study (UNIFAI) – working across 50 sites globally providing speech testing to patients in 10+ languages.
- Professor Vogel co-lead the digital biomarkers working group within the Ataxia Global Initiative with colleague Dr Andreas Traschütz from the University of Tübingen, Germany



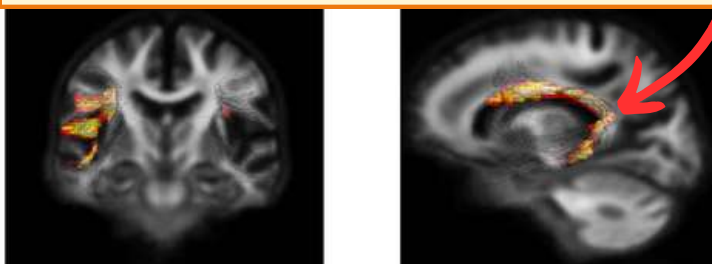
ATAXIC DYSARTHRIA IN MULTIPLE SCLEROSIS

Monash University PhD candidate Kathie Kenyon shares her research

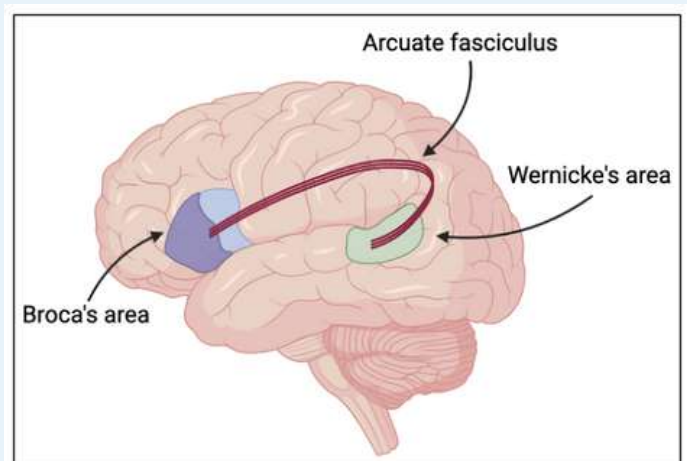
Ataxic dysarthria is a disorder that impacts the motor aspects of speech production. While Kathie's PhD has focused on dysarthria in people with multiple sclerosis (MS), it is also common in SCAs! This type of ataxia is associated with **cerebellar damage**, and is characterised by slower speaking and reading rates, lack of loudness and pitch control and longer pauses during speech.

Kathie uses brain imaging techniques, which help us identify and understand changes in brain structure and function associated with diseases like MS and SCAs. Kathie's research has shown that damage **outside of the cerebellum** is also linked to symptoms of ataxic dysarthria in people with MS. Here's one example of her findings!

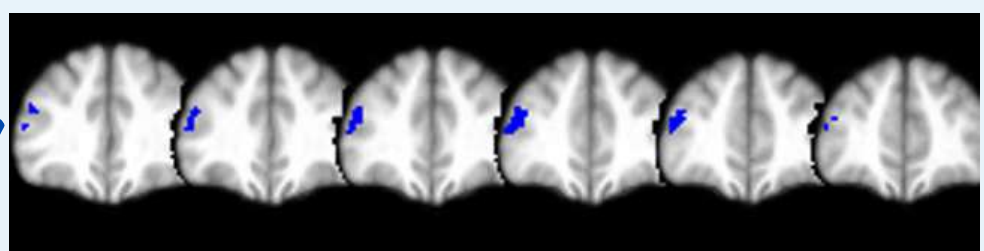
1) More damage in the left **arcuate fasciculus** (a specific bundle of brain connections) is related to slower reading rate in MS.



Highlighted area = damage to arcuate fasciculus that is related to reading rate in people with MS.



2) There is higher brain activity in **Broca's area** during speech in MS compared to people without MS. This is likely to compensate for brain damage.



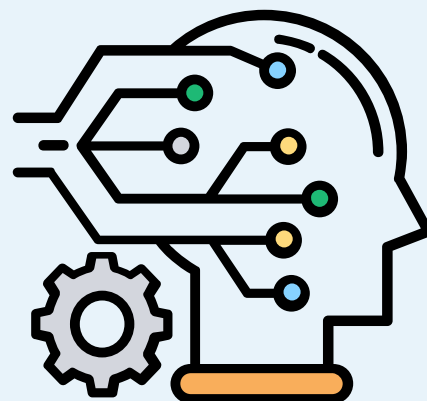
Blue = more brain activity during speech in people with MS compared to healthy people

USING MACHINE LEARNING TO PREDICT PERSONAL DISEASE PROGRESSION AND DEVELOP BIOMARKERS FOR FRIEDREICH ATAXIA

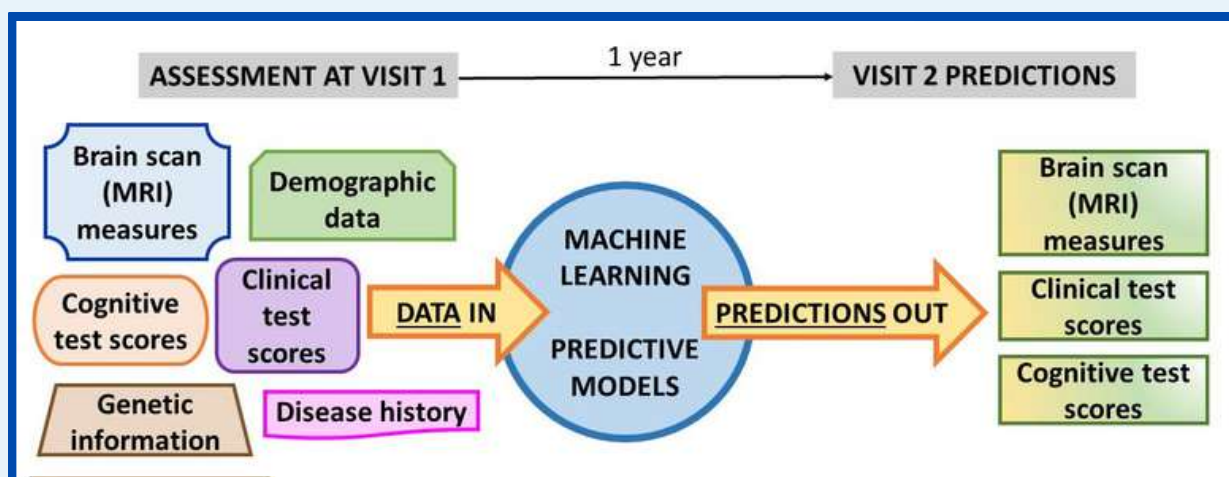
Dr Susmita Saha from Monash University is using artificial intelligence to learn from ataxia data

Machine Learning is a type of Artificial Intelligence in which a computer takes data and uses it to **find patterns** and **make predictions**.

Dr Susmita Saha, alongside fellow investigators A/Prof Ian Harding, Prof Nellie Georgiou-Karistianis and collaborator Dr Paul Harrison, applied machine learning to longitudinal data (data collected on the same people more than once over time) which has been collected from individuals with Friedreich ataxia (FA).



Dr Saha aims to determine whether we can use multiple types of data (such as brain imaging data, clinical data, and genetic data) to predict how an individual with FA will progress over one year (from Visit 1 to Visit 2) in their clinical, cognitive, and brain imaging measurements.



Using machine learning to predict Visit 2 scores from Visit 1 data.

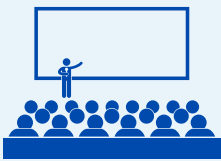
A secondary aim of this work is to use the prediction information, or “models”, to develop a new biomarker for FA. A **biomarker** is something that can be measured objectively to indicate a person’s disease severity and disease progression.

This new biomarker would combine multiple types of brain imaging data to allow for more precise and reliable tracking of FA progression compared to current measures.

In the future, we may be able to use predictions about how different people with FA progress over time in order to identify FA subgroups - for example, “fast progressors” and “slow progressors”. In clinical trials, researchers could then investigate whether different subgroups respond differently to a treatment.

ATAXIA RESOURCES - CONFERENCES

Ataxia conferences, symposia, and forums targeted to people with ataxia and their families are offered by various ataxia organisations. These are valuable ways to keep up-to-date with advances in ataxia research, even if you cannot attend in person. Recent conferences have shared recordings of the presentations given:

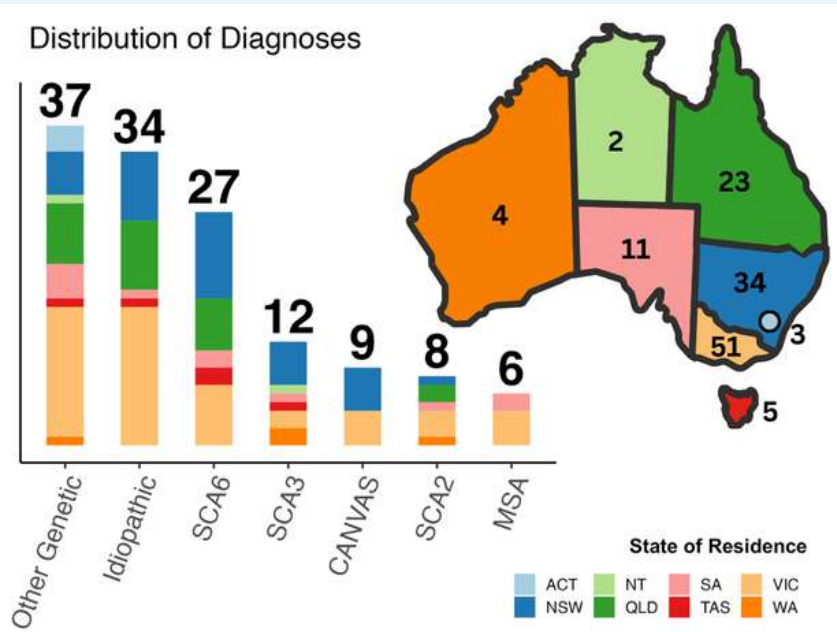


- fara Australia (Friedreich Ataxia Research Association) Patient & Family Information Forum (29 February 2024, Brisbane, Australia):
<https://www.fara.org.au/news/watch-all-presentations-from-our-recent-patient-and-families-information-forum>
- National Ataxia Foundation (USA) Annual Ataxia Conference (30 March - 1 April 2023, Las Vegas, USA/virtual):
<https://www.ataxia.org/2023aac/>



Information about the upcoming 2024 Annual Ataxia Conference (30 May - 1 June 2024, Orlando, USA/virtual) can be found here:
<https://www.ataxia.org/2024AAC/>

AUSTRALIAN CEREBELLAR ATAXIA REGISTRY (CARE)



Located in Australia and interested in Ataxia research?
Sign up to CARE!

CARE is the go-to for researchers looking to recruit for new studies. CARE also allows us to:

- Better understand the number of Australians living with ataxia
- Attract drug companies looking for sites to run ataxia clinical trials
- Help plan future ataxia research

You don't have to have ataxia to get involved! Friends and family are also welcome to join and play a vital role in our research.



Sign up with the link or scan the QR code with your phone!
<https://www.monash.edu/medicine/ccs/neuroscience/research/harding-group/australian-cerebellar-ataxia-registry>

Thank you for your participation in and your support of our research!
Please contact us at any time at the CNRG Lab, Monash University:



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