MELBOURNE ATAXIA RESEARCH NEWSLETTER

JULY 2023

Introducing

The Cerebellum and Neurodegeneration Research Group

CNRG

To better recognise the diverse range of researchers and research projects that our lab includes we have rebranded from "The Harding lab" to "The Cerebellum and Neurodegeneration Research Group".

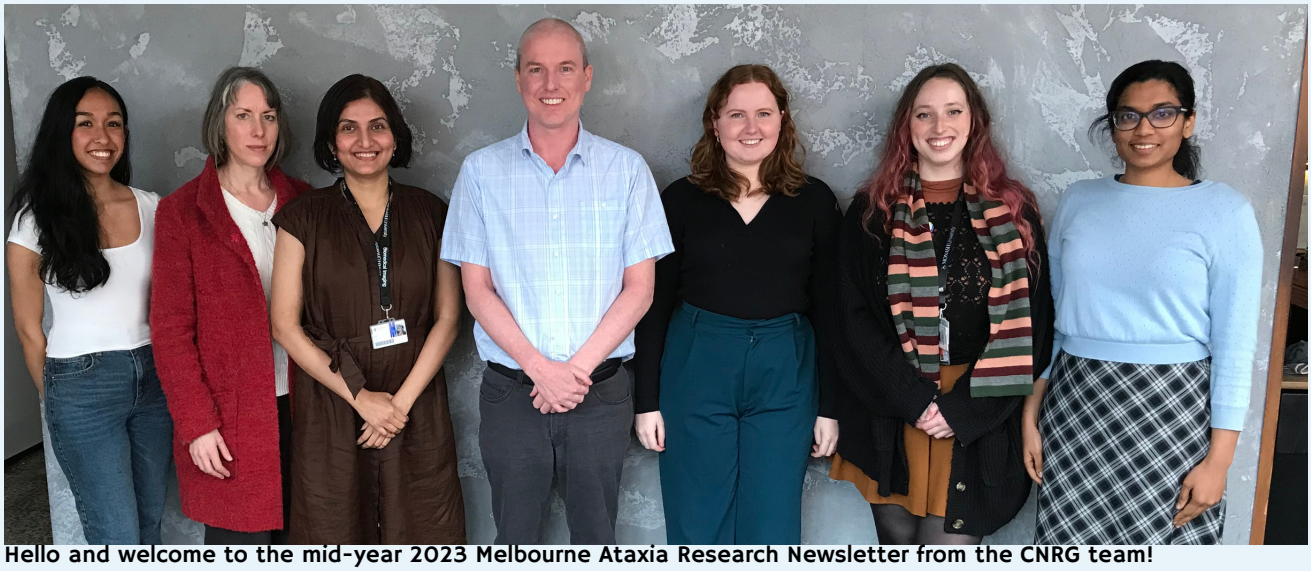
Our research group uses brain imaging and behaviour tracking to better understand neurodegentative diseases, with a focus on the cerebellum.

This newsletter contains research updates from the CNRG crew, our collaborators and the broader ataxia research community, as well as some useful ataxia resources.

Getting social!

To celebrate our rebrand we have expanded our social media presence. You can now get in touch or stay up to date by following us on twitter or facebook. On these accounts we will post participation opportunities, research updates and much more which you can share with friends, family and community groups!

@CNRGMonash @CNRGMonash



Hello and welcome to the mid-year 2023 Melbourne Ataxia Research Newsletter from the CNRG team!

NOW RECOGNISED BY THE NATIONAL ATAXIA FOUNDATION AS A CENTRE OF EXCELLENCE!

The National Ataxia Foundation (NAF) in the USA recently designated our Cerebellar Ataxia Clinic & Research Program an Ataxia Centre of Excellence (clinical lead: A/Prof David Szmulewicz; research leads: Dr Ian Harding, A/Prof David Szmulewicz, Prof Paul Lockhart).

Only 4 sites outside of the USA currently hold this designation. The NAF is the peak global ataxia patient support and advocacy group that also supports and coordinates research activity. We are incredibly honoured to receive this designation, and excited to represent Australian efforts in ataxia care and research on the global stage!

NAF National Ataxia Foundation | ATAXIA Center of EXCELLENCE

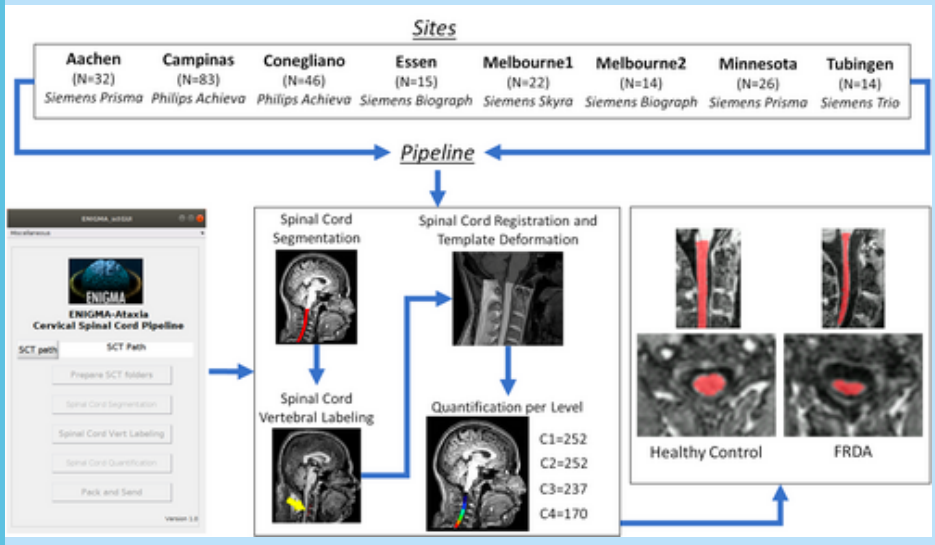
Experts in Care & Collaboration

You can find out more about NAF's Centers of Excellence with the link below.
https://www.ataxia.org/ace/

THE ENIGMA-ATAXIA COLLABORATION

DR IAN HARDING LEADS THE WORLDWIDE ENIGMA-ATAXIA COLLABORATION

ENIGMA-Ataxia pools MRI data collected at over 20 sites globally to perform large-scale analyses of brain and spinal cord changes using data from hundreds of people with genetic ataxias.



In our latest work, we show for the first time that spinal cord changes are evident in SCA1, SCA2, and SCA3, but not in SCA6. We also show that these changes get worse with disease progression. These results help us to clarify the key parts of the nervous system that are impacted by these diseases.

SCA-REMOTE STUDY

The SCA-Remote study has entered its third year! Since May 2021, participants from around the world have been completing our monthly online activities to help us learn more about how different symptoms change in spinocerebellar ataxias types 1, 2, 3, and 6. More than 200 people have now joined this unique study.

This now allows us to start analysing this exciting new data. Our research questions include:

- For people with SCAs, how does movement, speech, thinking skills, and mood change over one year or two years? Is this different to people without SCAs?
- Are people with SCAs more likely to show "ups and downs" in their performance on the online activities compared to people without SCAs?
- Different people with SCAs may experience different rates of symptom progression. Is there a way to group people with similar rates of symptom progression so that we can predict future progression and start to understand why some people progress at different rates to others?

This year we also welcomed Chiara Lo Giudice to the SCA-Remote team. Chiara is currently completing her Honours in Psychology at Monash University. For her research thesis, Chiara will use data from SCA-Remote to investigate how cognition (thinking skills) may change over time in SCA and how other non-motor symptoms be related to any cognitive changes. Chiara has also been collecting new data for SCA-Remote by conducting Zoom assessment sessions with our participants.

HONOURS STUDENT CHIARA LO GIUDICE

Keep an eye out for the outcomes of Chiara's thesis project in our next newsletter!

THE SCA-REMOTE TEAM

Principal investigator: Dr Ian Harding
Project lead: Dr Louisa Selvadurai
Honours student: Chiara Lo Giudice

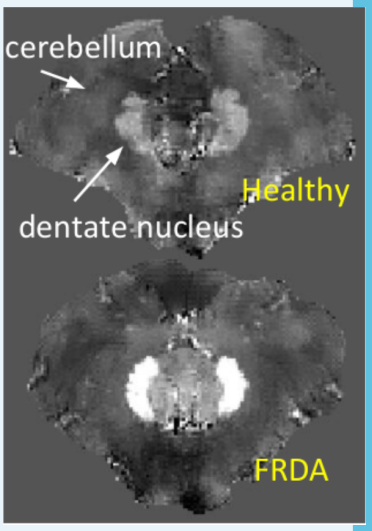
Research coordinator: Sarah Wallis
Co-investigators: Associate Professor David Szmulewicz, Professor Adam Vogel
Clinical collaborator: Dr Klshore Kumar

UTILISING ARTIFICIAL INTELLIGENCE TO PREDICT DISEASE PROGRESSION IN FRIEDREICH'S ATAXIA

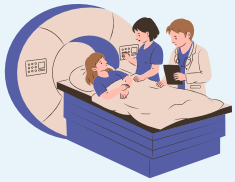
DR. SUSMITA SAHA IS INVESTIGATING BIOMARKERS OF FRIEDREICH'S ATAXIA USING AI MODELS TO PREDICT DISEASE PROGRESSION

Dr. Susmita Saha is currently analysing the MRIs of those with Friedreich's ataxia and those without, comparing biomarkers including cerebellum structure and iron accumulation between the two groups. These biomarkers are then tracked over time to investigate their progression as part of a global, large-scale study named TRACK-FA, led by Professor Nellie Georgiou Karistianis and Dr. Ian Harding among others.

Dr. Saha is now developing artificial intelligence models that predict disease progression using MRI measures, clinical and cognitive scores, demographic data, disease history, and genetics. These models have great potential to aid in drug development, clinical trial recruitment, and comprehensive treatment outcome assessment.



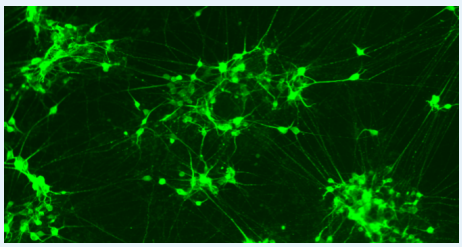
MRI OF AN INDIVIDUAL WITH FRIEDREICH'S ATAXIA COMPARED TO A HEALTHY INDIVIDUAL



USING STEM CELLS TO UNDERSTAND RFC1-CANVAS AND IDENTIFY POSSIBLE TREATMENTS

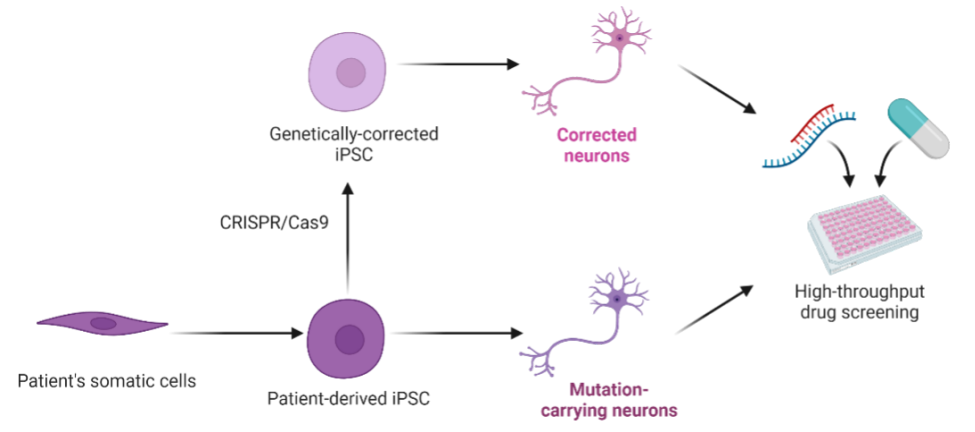
PHD STUDENT KAYLI DAVIES AND PROFESSOR PAUL LOCKHART HAVE GENERATED THE FIRST PATIENT-DERIVED STEM CELL MODELS TO STUDY RFC1-CANVAS

Kayli and Professor Lockhart have reprogrammed skin cells from individuals with RFC1-CANVAS using cutting-edge stem cell and gene editing technologies to create a model with the RFC1 gene mutation and a model in which the RFC1 gene mutation is corrected.



NEURONS GENERATED FROM THE CANVAS STEM CELL MODEL

THE PROCESS OF CREATING RFC1 GENE MODELS

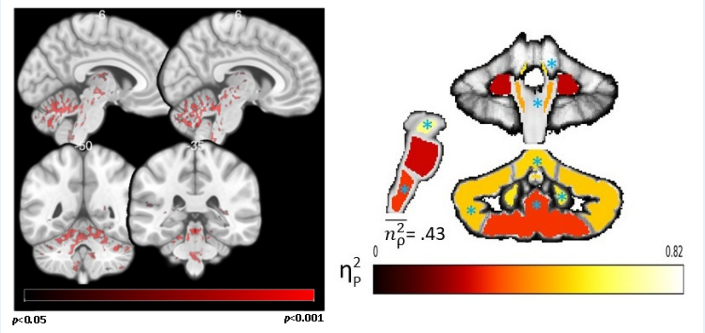


These models are now being grown into brain cells in the lab. This will help us to understand how mutations in the RFC1 gene cause the disease, and offer a way to rapidly screen large numbers of drugs for potential treatment options.

FREE-WATER IMAGING IN FRIEDREICH'S ATAXIA

DR LARA FERNANDEZ AND DR IAN HARDING ARE INVESTIGATING A NOVEL BIOMARKER OF DISEASE IN FRIEDREICH'S ATAXIA CALLED 'FREE-WATER'

Neuroimaging allows us to look at the structure and function of the brain and how conditions like ataxia cause it to change over time. Neuroimaging can help us determine early indicators of a disease. This information may be used to aid clinicians in a diagnosis, and in the development of suitable treatment programs for an individual.



AREAS OF THE BRAIN AND BRAIN STEM WHICH SHOW DIFFERENCES IN FREE-WATER BETWEEN INDIVIDUALS WITH FRIEDREICH'S ATAXIA AND HEALTHY INDIVIDUALS

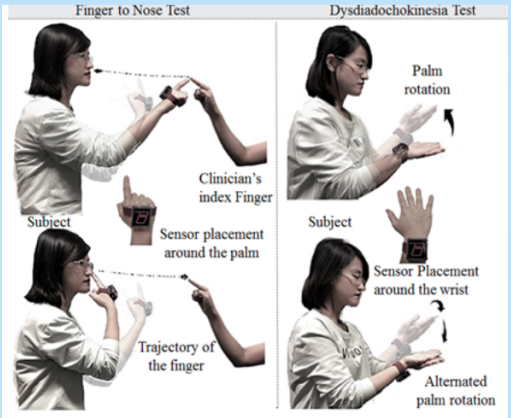
Investigation of free-water as a novel biomarker of disease progression and stage in Friedreich's Ataxia has found promising results in a small group of individuals. We aim to explore this further in a larger group.

WEARABLES FOR ATAXIA RESEARCH & DIAGNOSIS

ASSOC PROFESSOR DAVID SZMULEWICZ LEADS A GROUP OF RESEARCHERS WHO DEVELOP TECHNOLOGY TO AID IN THE DIAGNOSIS AND MEASUREMENT OF ATAXIA.

Ataxia measurement technology is important in not only identifying which cerebellar ataxia a person may be suffering with, but also in research to understand the way in which diseases progress over time. These devices also allow us to measure improvements in ataxia, which is critical to the success of treatment trials.

This technology includes devices that measure the characteristic eye movements seen in many cerebellar ataxias, as well as wearable devices that measure arm and leg movement, as well as balance.



The devices are now able to deliver, **in real time,** a score to the clinician or researcher that is more accurate than one obtained using traditional methods of assessing people with ataxia. These devices will be rolled out to a number of ataxia clinics for further testing.

ATAXIA RESOURCES

In this edition of the newsletter, we would like to highlight SCA-Source!

A website now run by the National Ataxia Foundation, SCA-Source is a go-to for easily digestible break downs on the most recent ataxia research world-wide. SCA-Source summarises scientific articles, explains ideas and concepts central to ataxia, highlights updates in gene discovery, and much more.

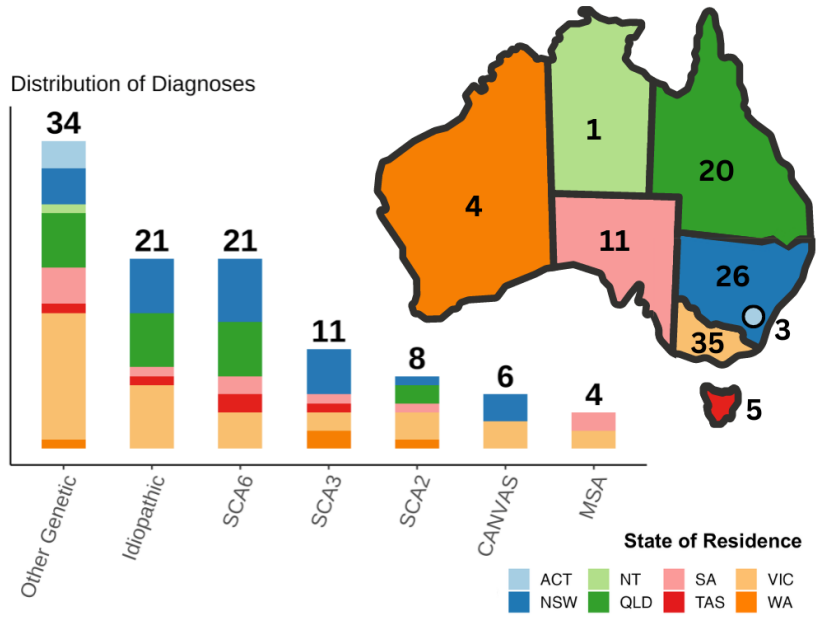
Check out some of CNRG's favourite SCA-Source articles:

Did Kayli Davies and Professor Lockhart's stem cell research pique your interest?
https://www.ataxia.org/scasourceposts/snapshot-what-are-induced-pluripotent-stem-cells-ipscs/

Everything you need to know about magnetic resonance imaging (MRI).
https://www.ataxia.org/scasourceposts/snapshot-what-is-magnetic-resonance-imaging-mri/

Want to learn about the cerebellum's role in ataxia?
https://www.ataxia.org/scasourceposts/decoding-the-language-of-cells-in-the-cerebellum-to-understand-the-progression-of-symptoms-in-sca3/

AUSTRALIAN CEREBELLAR ATAXIA REGISTRY (CARe)



Located in Australia and interested in Ataxia research? You should 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:
harding.lab@monash.edu