ISSUE 3
AUG 2023

TRACK-FA NEWSLETTER

TRACK-FA is a longitudinal natural history study that tracks brain and spinal cord changes in individuals with Friedreich's ataxia (FA). We have a team of researchers from Australia, USA, Germany, Brazil and Canada in collaboration with global industry partners. We are testing the sensitivity of neuroimaging biomarkers to provide a basis to include them in future clinical trials.

AT A GLANCE

Baseline recruitment has concluded!

TRACK-FA is closing for recruitment at the end of August 2023.

By the end of August 2023, across all study sites we will have enrolled over 272[1] participants, including over 177 participants with Friedreich's ataxia and over 95 matched control participants, whose ages range from 6 to 42 years old (Figure 1).

This means that overall, our baseline data set will contain over:

- 1062 clinical tests
- 272 blood samples
- 272 MRI sessions
- 657 cognitive and mood assessments
- 272 speech assessments

We thank everyone who continues to participate in TRACK-FA and contributes to the growing database to build our knowledge!

Our partners

[1] Final recruitment number may be higher, after the final assessments for TRACK-FA study visit 1 are completed in late August 2023.

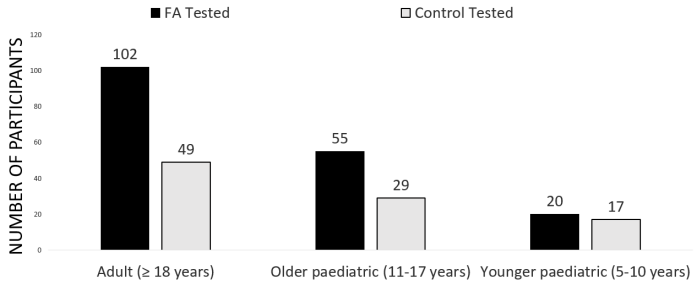

Figure 1 Recruitment summary (Aug 2023) by participant group and age.

Follow-up study visits are under way

We have finished assessing all participants for their first (baseline) study visit, and now we're keeping busy assessing TRACK-FA participants who are returning for their second (12 month) and third (24 month) study visits (Figure 2). As of August 2023:

- 115 participants have completed study visit 2
- 36 participants have completed study visit 3

After some early delays at the beginning of the study due to the pandemic, we are now on track to complete all data collection before the end of 2025.

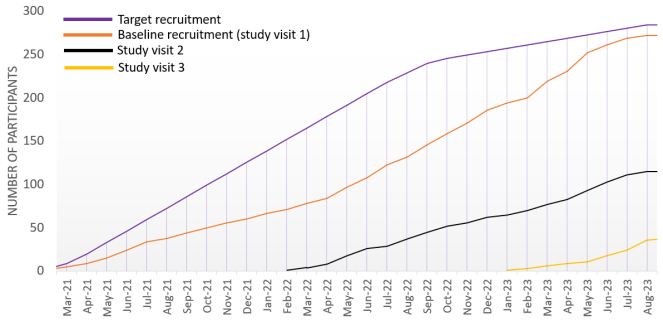

Figure 2 Cumulative study-wide recruitment (Aug 2023) for FA and control participants combined, for study visit 1, 2 and 3.

WHAT ARE WE DOING NOW THAT WE'VE COMPLETED BASELINE RECRUITMENT?

TRACK-FA baseline recruitment may be over, but we still have much to do! Besides completing follow-up study visits 2 and 3 for our returning participants, we're keeping busy analyzing our complete set of baseline data.

What regions are we analyzing in MRI scans?

We are investigating several regions in the brain (in particular the **cerebellum**) and **spinal cord** (Figure 3), which we know from previous studies are important for coordinating and controlling movement, and which play a central role in FA.

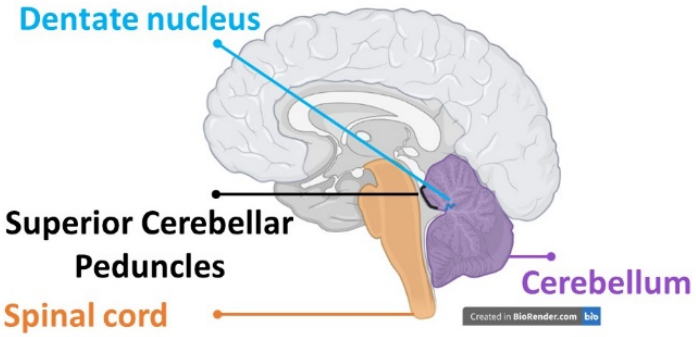

Figure 3 Major regions of interest in TRACK-FA

What are we measuring in the MRI scans?

TRACK-FA is a multi-modal neuroimaging study, which means that in each scan we are measuring many different characteristics of the brain and spinal cord.

We are investigating the **size**, **connections**, **iron levels**, and **neurochemical markers** in several areas where we expect to find differences between healthy controls and people with FA, as well as changes over time.

The table below summarizes the key measurements that we are taking for each region of the brain and spinal cord.

In Figure 4, you can see some of the images of these different regions that we have acquired for TRACK-FA.

SUMMARY OF REGIONS AND MEASUREMENTS OF INTEREST IN TRACK-FA

			Measurement			
Region	Sub-region	Location	Size	Iron levels	Connections	Neurochemicals
Cerebellum	Total cerebellum	Sits at the back of the brain	✓			
	Dentate nuclei	Sits deep inside the cerebellum	✓	✓	✓	
	Superior cerebellar peduncles	Connects the cerebellum to the rest of the brain	✓		✓	
Spinal cord	Cervical spinal cord	Connects the brain to the rest of the body	✓		✓	✓

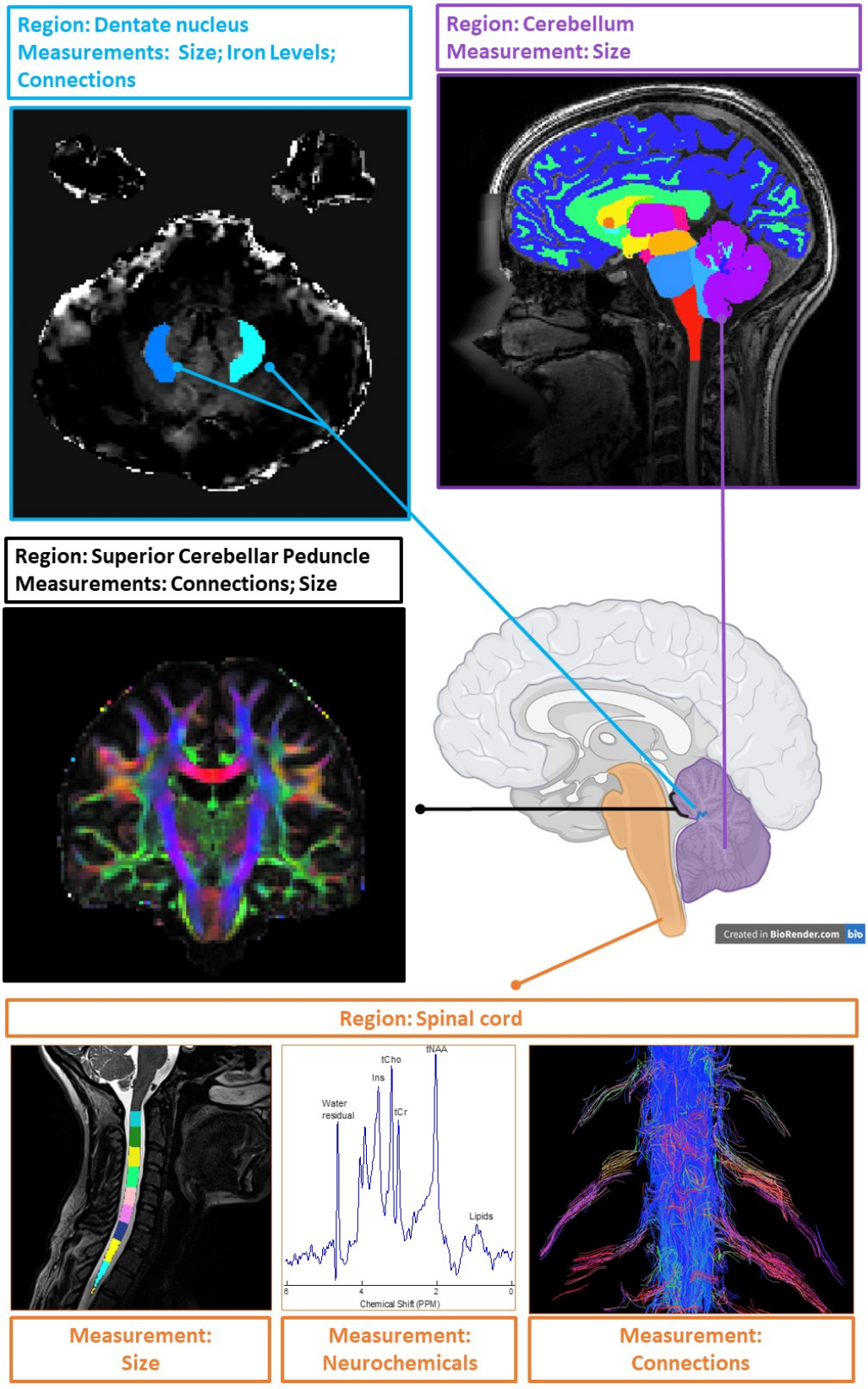

Figure 4 Examples of the images acquired for TRACK-FA for each region and each measurement.

Stay tuned for the next TRACK-FA newsletter in late 2023 when we will share some of our key findings so far!

MEET OUR TRACK-FA TEAM MEMBERS

In the next few TRACK-FA Newsletters, we'll introduce you to some of our team members around the world!

Name: Professor Nellie Georgiou-Karistianis

TRACK-FA Site: Monash University (Melbourne, Australia)

Meet the TRACK-FA Principal Coordinating Investigator

How did you get involved in FA research? I've dedicated my career as a cognitive neuroscientist to clinical research in rare neurodegenerative disorders such as Huntington's disease and Friedreich ataxia. Given that the medical profession still faces challenges in treating diseases like Friedreich ataxia, I'm inspired by the power of clinical research to contribute to improving outcomes for people living with neurodegenerative disease.

What's been the highlight of TRACK-FA for you so far? I'm proud of the significant global expertise that we bring together in TRACK-FA. It's truly an honor to collaborate with such an interdisciplinary team of world-leading experts. I look forward every month to our global team meetings to discuss the progress we have made on the data that we are collecting for TRACK-FA.

Name: Professor Christophe Lenglet

TRACK-FA Site: University of Minnesota (CMRR and Institute for Translational Neuroscience)

Meet a TRACK-FA Scientist

Job/Role in TRACK-FA: Co-PI; Neuroimaging co-lead with PG Henry

What are the highlights of TRACK-FA Study so far? Our TRACK-FA consortium and all participants have demonstrated impressive perseverance and determination to keep the study going despite the numerous challenges associated with the COVID-19 pandemic. Moreover, TRACK-FA is proving to be an outstanding source of high-quality neuroimaging data! I think it will likely continue to inform and power many important analyses (for instance using artificial intelligence), even beyond those initially planned, that will be critical to our understanding of FA and discovery of sensitive biomarkers!

What have you learned from being part of TRACK-FA? Multi-site collaborative studies like TRACK-FA are critical to identify the most promising targets for treatments in the brain and/or spinal cord. Not only do we need such large amount of data to learn what part(s) of the central nervous system are affected early-on in FA, we also must demonstrate that this data can reliably be used across institutions in trials. TRACK-FA put together a unique group of international experts that have all contributed to various aspects of FA research. It is exciting and humbling to test whether our previous own findings from smaller studies can be replicated and expanded in TRACK-FA!

What have you learned from TRACK-FA participants? Their dedication to research studies and clinical trials, and perseverance are always inspiring. They motivate us to do the best science we possibly can and to contribute towards finding treatments and a cure for FA!

How long have you been involved in FA research? I started getting involved in ataxia research (FA and SCAs) back in 2012 when I joined CMRR at the University of Minnesota. Several of my colleagues at the time (Drs. Oz, Iltis, Orr, Bushara) had already done a tremendous amount of work in this area for many years and so, it was natural and exciting to collaborate with them. Specifically, I was interested to see if the methods developed by my lab (centered on diffusion and anatomical MRI) could be helpful and complementary. Dr. Iltis and I were delighted to be awarded a "Kyle Bryant Translational Research Award" by FARA and this started our neuroimaging efforts in FA. Very shortly after, Dr. PG. Henry (TRACK-FA Neuroimaging Lead) joined our team and we have been working together since then!

What are your favorite pastimes? Rock climbing, biking and running.

Name: McKenzie Wells

TRACK-FA Site: The Children's Hospital of Philadelphia

Meet a TRACK-FA Study Coordinator/Genetic Counselor:

What's been the highlight of TRACK-FA for you so far? Meeting new patients who we would not normally get to meet and getting to work with other members of research study teams at CHOP (the TRACK FA team!).

What have you learned from being part of TRACK-FA? How to effectively coordinate across several different research teams.

What have you learned from TRACK-FA participants? As always, I am impressed with how motivated our patients are to participate in research!

How did you get involved in FA research? I was recruited by a former grad school classmate and coordinator.

What are your favorite pastimes? I like reading all types of books, typically on my train ride to work.... also spending time with my family and 2 dogs and traveling when I can.

Name: Alessandra Tomaselli

TRACK-FA Site: Monash University (Melbourne, Australia)

Meet a TRACK-FA Research Officer

What's been the highlight of TRACK-FA for you so far? Meeting the participants and learning about Friedreich's Ataxia from personal experiences. I have also enjoyed gaining experience in cognitive assessment performance and scoring and acquiring basic skills in image processing.

How did you get involved in FA research? I have an interest in neuroscience and FA is a disorder I knew nothing about so thought it would be a good challenge. It has been great learning so much about FA and FA research while completing the Graduate Diploma in Psychology at Monash University.

What are your favorite pastimes? In my spare time, I enjoy circuit training, mentoring and umpiring netball, immersing myself in the arts (whether it be art exhibitions, comedy or theatre shows), eating different cuisines and trying new things (I have recently taken up yoga). Although I am not a massive fan of horror, my favorite movie would have to be Suspiria (1977) due to the amazing production and innovative cinematic techniques for the time and genre.

SOME OF OUR PARTICIPANTS COMPLETING A TRACK-FA STUDY VISIT

SPOTLIGHT ON A TRACK-FA TEAM: CHILDREN'S HOSPITAL OF PHILADELPHIA (CHOP)

In the next few TRACK-FA Newsletters, we'll introduce you to our teams at TRACK-FA sites around the world. In this issue, we introduce you to the TRACK-FA team at the Children's Hospital of Philadelphia.

Left-to-right:

Back: Tim Roberts, Shana Ward, Peter Lam, Bill Gaetz, Rachel Golembski, Kellie Mcintyre, Medina Keita

Front: McKenzie Wells, Shivani Patel, Kyle Bryant, Jen Farmer, Charlotte Birnbaum

Inset bottom: Dave Lynch, Mina Kim, Lisa Blaskey, Victoria Kaufman

CHOP Research Assistants: Victoria Kaufman, Shana Ward and Charlotte Birnbaum

Getting to be a part of TRACK-FA has been a highlight of our time at CHOP. Our FA participants are awesome! We often discuss how impactful it is to meet our participants and their families since they are a huge part of what makes being involved in FA research so special. We admire the eagerness and willingness of our FA participants to lend their time to important research! Being involved in FA research has also allowed us to reflect on some of the accessibility inequities of everyday life. As able-bodied people, these things may not have been as salient in our minds before. We find ourselves often considering wheelchair accessibility and sidewalk infrastructure in and around the Philadelphia area which makes us grateful to have the opportunity to learn more about these topics, and to advocate for people with mobility challenges. We have learned an incredible amount getting to be a part of this study and look forward to staying involved in FA research! Victoria's simple pleasure is reading a good book on the beach. Her most recent favorite was Tomorrow, and Tomorrow, and Tomorrow by Gabrielle Zevin! Shana enjoys playing tennis and cycling in her free time or reading a good book on her Kindle. Charlotte likes listening to music on vinyl and collecting records! Her current favorite album is For Everyman by Jackson Browne.

CHOP Principal Investigators: Dr. David Lynch, Dr. William Gaetz and Dr. Timothy Roberts

It is a distinct pleasure to participate in this multicenter imaging study. Our work with TRACK-FA involves collaboration with imaging scientists and clinicians from around the world, and we are excited to help discover new biomarkers of clinical change in people with FA. The cutting-edge imaging methods used in this study are truly ground-breaking and innovative. We are extremely optimistic that our findings will provide new insight into the systems and processes affected across the varying stages of disease progression in FA and believe that TRACK-FA will serve as the definitive reference for advanced imaging in the evaluation of novel and emerging candidate therapies and interventions for FA.

TRACK-FA SITE TEAMS

University of Florida

L-R: Sub Subramony, Mackenzi Coker, Manuela Corti, Thomas Mareci

University Hospital RWTH Aachen

Top L-R: Imis Dogan, Kathrin Reetz, Shahram Mirzazade, Jörg Schulz, Ankica Grgic, Sandro Romanzetti. **Bottom L-R**: Stella Glasmacher, Ravi Dadsena, Sara Schawohl, Maha Sagar, Christina Krockauer, Katharina Hammers

University of Campinas

L-R: Alberto Martinez, Cynthia Silveira, Rachel Guimarães, Marcondes Franca, Fernanda Bittar, Juliana Ferreira,Thiago Rezende.

Monash University and The Murdoch Children's Research Institute

Top L-R: Nellie Georgiou-Karistianis, Louise Corben, Ian Harding, Martin Delatycki. **Bottom L-R:** Helena Bujalka, Susmita Saha, Alessandra Tomaselli

University of Minnesota

Back L-R: Young Woo Park, Christophe Lenglet, James Joers, Pierre-Gilles Henry, Thiago Rezende (visiting from University of Campinas), Pramod Pisharady, Isaac Adanyeguh. **Front L-R**: Diane Hutter, Gulin Oz, Shannon Smith, Katie Gundry. **Not pictured:** Dinesh Deelchand.

McGill University

Top L-R: Massimo Pandolfo, David Rudko. Dylan Sembinelli, Christian Rampal. **Bottom L-R:** Soheil M Quchani, David Costa, Ronaldo (Ron) Lopez, Julien Doyon

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For more information about the TRACK-FA Study, see our website:
https://www.monash.edu/medicine/trackfa