HUNTINGTON'S DISEASE TASMANIA

Providing a voice for people with Huntington's disease and their families

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Huntington's Tasmania

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Education, Advocacy, Support, Hope

From the President's Desk

Hello everyone,

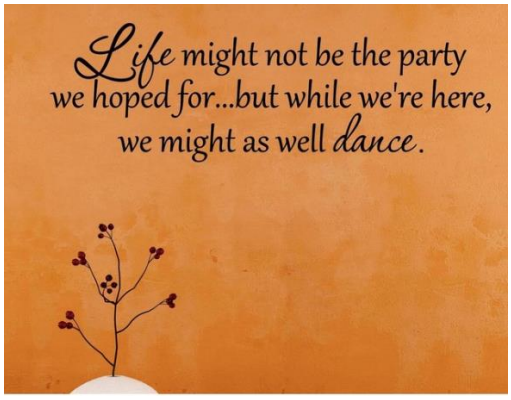
I hope you and your family are staying well and warm this Winter.

It is amazing that we are now more than halfway through 2020 and what a year it has been. We have never experienced a year like this, certainly challenging yet also inspiring at times. Right now, COVID-19 remains a key concern for many people. It has been difficult trying to be across all the latest information, as things seem to change day by day. The recent resurgent in Victoria keeps us on our toes, however we continue to meet the needs of our HD community here in Tasmania as best we can.

Unfortunately, our fundraising activities remain on hold for the foreseeable future.
We are hoping to make a HD Recipe book as a fundraiser, so if you have a special family favourite you would like to add please sent it to us.

I would like to say a special thank you to all who contributed to my Facebook birthday donation with all funds going directly to HD Tasmania. I feel extremely humbled by your generosity and support with over $1,200 raised. This money will go to support our families.

If you would like to become a member of Huntington's Tasmania, membership forms are available on our website or by contacting the association. Having a strong membership provides us with a unified voice when we approach Governments for increased financial support. Also, please contact our office if you have changed your address.



Don't forget that it is business as usual for us here at HD Tas. We are open and here to support and help any way we can. You are not alone – our HD Community is here for you.

Warm regards

Pam Cummings

From the Service Desk

Our North-west Case Manager Subha Perumal resigned in June, we wish her well as she returns to private practice as an Occupational Therapist. We welcome back Noel O'Connor who has taken over her role.

Thank you to our Case Managers who have continued to support our families during the difficult time.

Dancing at the Vatican

The final of two screenings of "Dancing at the Vatican" was shown on Friday August 14th, a wonderful Documentary, raising awareness, inspiring and emotional. Former NBC foreign correspondent and now global spokesperson, activist and gene carrier of HD, Charles Sabine, says 'what happened was the biggest moment in the history of the disease, the first time any major leader has recognised the existence of the disease.'

This is what one of our Tasmanian members had to say about the Documentary:

I wanted to say a huge thank you for organising the viewing of such a heart-warming documentary! Your efforts haven't gone unnoticed. Your support for us in Tas is appreciated! The comments from families with HD were so true. The opportunity to be together was so encouraging for them. "This is my family. We are all together in this battle" the boy's mother said after spending time with the HD community.

Charles Sabine is truly remarkable. So kind and brave to take on the challenge given his own genetic situation. A warm personable man with a big heart!

I was very touched by the families and those supporting the HD community. The speech in the Parliament & Vatican City by the Senator was filled with such emotion I cried too (One of the many times). What a beautiful woman who has put her heart and soul into HD research.

Brenda was so loveable. To see her joy at meeting Axle was touching. What a great outcome for the boy ostracised by his friends too! Football being the game changer. The dear mother & daughter team caring for their family in difficult circumstances was incredible. How delightful they got to travel and be supported. Amazing women. Everyone had a brave story....

My hope for a better future never wavers. Hope keeps us moving forward instead of giving up.

Staying Connected

We are looking for photos and stories to be included into our newsletter. It is a great opportunity for families to get involved and share with other HD families their photos and stories. Whether you're affected by HD yourself, a carer, family member or friend, we would love to hear from you.

An update on Huntington's disease research in Victoria

I'm a neuropsychiatrist and have had the pleasure of flying to Launceston from Melbourne to do Huntington's disease clinics for some years.

Research is extremely important to me as a clinician, and obviously also to the HD community in general. It helps us understand Huntington's disease, how it affects people and those around them, has led to the treatments that we currently have available, and has opened up the future prospect of disease-modifying drugs.

Huntington's research also goes beyond this. It has taught us a lot about the brain in general, and has provided insights that have led to a better understanding of other genetic and nervous system disorders.

Australia has a very strong history of contributing to Huntington's research, much of which is taking place a short hop over the Bass Straight. I've personally had the privilege of being involved in Enroll-HD, described below, and am currently putting together a project at the Florey Institute of Neuroscience and Mental Health using specialised brain imaging to detect free-radical-induced stress in the brain in Huntington's, which possibly might lead to new treatments.

The information below contains descriptions of some of the great HD work taking place in Melbourne. I have likely neglected to include some people, for which I apologise. I'd like to thank Dr Anita Goh, Prof Tony Hannan, Prof Nellie Georgiou-Karistianis, and Prof Julie Stout for describing their work below.
Dr Andrew Gleason

University of Melbourne / Royal Melbourne Hospital Neuropsychiatry Unit
Neuropsychiatry is the clinical unit of the Melbourne Neuropsychiatry Centre and is based at the Royal Melbourne Hospital. Professor Dennis Velakoulis is the Clinical Director.

We have been providing inpatient and outpatient assessment, diagnosis, and treatment of patients with HD since the early 1970s as part of the world's first HD clinic started by Emeritus Professor Edmond Chiu AM. We also run a Predictive Clinic that assesses individuals who have discovered that they are genetic risk of HD, and are interested in considering genetic testing options.

Current HD research

1. Clinical trial (drug) studies, including Roche's GENERATION HD1 and Wave Life Sciences' PRECISION-HD1 and 2.

2. Imaging studies (including looking at hippocampal subfields across three time points in the IMAGE-HD cohort).
3. Longitudinal biomarker studies in people with younger-onset neurocognitive disorders (BeYOND and MiND studies)
4. **The Enroll-HD study** - the world's largest observational study for Huntington's disease families. The purpose of Enroll-HD is to create a global database of people affected by HD to help the development of treatments. The study requires one visit each year and participants are tested on physical function, emotional state and thinking skills. There is an optional blood donation. More info: https://enroll-hd.org/participate/

We welcome interested potential participants to our HD research, particularly to participate in the Enroll-HD study. Participation in research is so important to help us increase our understanding of HD, improve the quality of life for the HD community, and also help to find treatments and a cure.

Who can participate in Enroll-HD?

Any member of a family affected by HD can take part, including:

- People who know they carry the expanded gene, whether or not they have any symptoms related to HD or have officially been diagnosed with it.
- People who haven't been tested to find out whether they carry the HD gene, but may be at risk based on family history. Even if participants don't want to know their gene status, they can still be part of Enroll-HD, we will not release this information.
- People who have a family history of HD but know they do not carry the expanded gene
- Spouses and partners (not blood relations) of people with a family history of HD
- Children under the age of 18 with clinically diagnosed juvenile HD may participate with the consent of a parent or legal guardian.

To register your interest in participating please contact
Dr Anita Goh
Email: goha@unimelb.edu.au

Florey Institute of Neuroscience and Mental Health, University of Melbourne – Hannan Lab

Professor Anthony Hannan and colleagues, at the Florey Institute of Neuroscience and Mental Health, are trying to understand what causes Huntington's disease (HD), right down to the level of molecules and cells. They are also trying to use this information to develop new approaches to delay onset of HD in gene-positive family members, as well as to slow down (and eventually stop) disease progression.

Professor Hannan's group are focusing on a preclinical model of HD. They not only study the brain, but also how the body is affected by HD. Two years ago his laboratory were the first to discover that the gut microbiota (the trillions of bacteria living in our gastrointestinal systems) is altered in HD. They are now working hard to determine whether this affects the onset and

progression of symptoms in HD, and how the gut and the brain communicate. This could lead to development of a new therapy for HD.

His laboratory also continues to follow up their previous discoveries that environmental factors including cognitive stimulation and physical activity can slow down onset and progression of HD. They are trying to working out how cognitive and physical activity are beneficial, and use this to develop new therapies. Furthermore, they are testing new drugs in their preclinical model of HD to try to identify new treatments, and hopefully eventually a cure, for this devastating disease.

More about Prof Hannan's work can be seen here:

https://www.florey.edu.au/science-research/research-teams/epigenetics-and-neural-plasticity-laboratory

Monash University – Georgiou-Karistianis Experimental Neuropsychology Research Unit, School of Psychological Sciences and the Turner Institute of Brain and Mental Health

The Georgiou-Karistianis Experimental Neuropsychology Research Unit (ENRU), Monash University, is headed by Professor Nellie Georgiou-Karistianis and has over 15 years of experience working on Huntington's Disease (HD). The lab uses brain imaging methods, as well as cognitive and motor assessments to better define how the disease progresses across the pre-manifest and manifest stages of HD.

Monash University has access to the largest HD database world-wide, which consists of over 4000 imaging, cognitive and clinical datasets acquired over 10 years across many different countries. Using this database, the lab is developing new cutting-edge scientific modeling methods to better track disease progression at different stages of disease. Outcomes from this work will allow us to inform drug companies of the type of patient that should be selected for clinical trials in order to make trials more efficient.

The lab also has a focus to further understand how different parts of the brain change over time and how they relate to the clinical presentation of the disease, as well as how cognitive training can be used to effectively preserve cognitive function and improve brain function. The lab has attracted over $14 million in grant funding, generated over 200 peer-reviewed publications, and trained over 25 PhD students. Our focus is on delivering improved outcomes for people living with HD in our communities.

Monash University – Stout Lab

Professor Julie Stout leads a research group in the Turner Institute for Brain and Mental Health that is 100% committed to Huntington's Disease. We are a team of about 15 people, and we are keen to meet as many people in Australia as possible who are affected by HD, and to put our efforts where they count for the Australian HD community!

Our major research efforts at this time include:

1. A large collaborative 5-year project, temporarily called the Australian Huntington's Disease Collaborative Initiative (AHDCI) until we come up with a more catchy name! The overall aim of the project build the collaborations and infrastructure across Australia that will enable:
    - Mapping all families and individuals affected by HD, ascertain their unmet medical, social, and financial needs;
    - Mapping available services and supports, including the activities of state associations like Huntington's Tasmania, HD specialty clinics, etc.;
    - Ascertaining unmet needs of people affected by HD;
    - Articulating the best model for HD care in Australia;
    - Laying the groundwork for Australian regulatory approval and PBS funding of novel treatments for Huntington's disease.

    We are building collaborations across the sector, which will encompass HD family members, state associations, clinicians and researchers, and we hope you and your family will join this effort!
2. The FOCUS-HD project: Our team is leading an international research project aimed at refining the tools used in HD clinical trials to measure cognitive functions and everyday activities for HD clinical trials. This project is in collaborative with the CHDI Foundation, in New York City, and we hope to start international data collection in 40 international research sites, including in Australia, in 2022.
3. Bringing clinical trials in HD to Australia: Our team is working with international partners and all HD specialist clinicians in Australia to bring clinical trials of new drugs for HD to Australia. Thus far we have been able to bring in one Roche trial and two Wave Life Sciences trials, and we continue to work to support and develop Australian clinics as clinical research sites in order to attract more trials that will give Australians with HD an opportunity to be a part of the teams that pave the way for new treatments.
4. Enroll-HD: Enroll-HD is in international registry of more than 20,000 people with HD, people with the HD gene, and their family members, which supports the efforts of researchers and treatment developers internationally. Melbourne has two Enroll data collection sites, one at the Calvary Health Care Bethlehem Hospital and Monash Uni, and the other Uni Melbourne's Royal Melbourne Hospital. We have some Tasmanian participants, and are eager to find ways to come to Tasmania to recruit participants and give as many Tasmanians as possible opportunities to participate in Enroll-HD. Professor Stout leads the international Scientific Oversite Committee of the Enroll-HD project.
5. With post-doctoral, PhD and doctoral researchers in our group, we have several more projects going on. Some of you may have participated in some of these, or may be invited to participate, including:
    a. Dr Yifat Glikmann-Johnston, who is studying the ability of people with HD to navigate or find their way in the environment;
    b. Brendan McLaren, who is testing an HD-specific mobile app;

c. Cory Wasser, who has conducted a 'poo' and probiotics study to look at gut functioning and treatment in HD;
d. Kelly Atkins, who has been studying apathy and motivation in HD, and how it links to exercise;
e. Hiba Bilal, who is studying depression in HD, and how it may link to the physiology of HD;
f. Emily Fitzgerald, who is studying how fluctuations in sleep might correlated with cognition and mood during the daylight hours.
g. Yuh-Shan Gan, who is studying what the needs are of young people from HD families;
h. Tayela Pritchard, who is conducting a project to find ways of measuring every day function; and,
i. Shi Wen Khoo, who is developing a survey for people affected by HD (individuals and their carers) to determine the unmet needs of people with HD.

6. The Stout Lab, together with Nellie Georgiou-Karistianis, have developed a registry of people with HD, people with the HD gene who don't have HD yet, and HD family members, who are interested in participating in research. Please feel free to volunteer to be part of this database by registering your interest at https://tinyurl.com/hrgvhdpr

Barbara's Beanies for HD

WE ♥ OUR volunteers

I would like to introduce to our amazing newest HD volunteer, **Barbara Sweeny**.

Barbara lives in Hobart, is 88 years young, and has a connection to Huntington's Tasmania. To support our organisation, she has been knitting the most amazing beanies, all colours, sizes and made from pure Bendigo wool.

She tells me that she used to knit jumpers, but now as they have become too heavy for her to hold, beanies seemed a good option. She warms my heart every time I speak to her for she is so excited to be helping.

They are on sale for $20 and can be purchased by ringing the Association or via our website shop. Barbara has a sister in her nineties who lives in Canberra and who may be interested in knitting us some nice warm scarves. What remarkable sisters they are.

This is a photo of my family who love theirs, even in the Brisbane weather.

Research:

HD Young Adult Study defines the sweet spot: symptom-free with measurable changes

We know that HD-related changes can occur many years before symptom onset, but how early do those changes begin? A team of researchers set out to determine that with a new comprehensive study in pre-manifest HD young adults.

By Dr Sarah Hernandez May 27, 2020 Edited by Dr Jeff Carroll Taken from HDBUZZ

A new study headed up by Dr. Sarah Tabrizi, a pioneer in HD research, assessed pre-manifest HD young adults many years from predicted symptom onset with a battery of clinical tests. The goal of this study was to identify a sweet spot – a time when HD participants weren't experiencing any observable symptoms, but when markers of disease progressing begin to show the earliest changes. This was a challenging task, but the HD researchers rose to the occasion!

Young Adult Study – assessing patients 24 years from predicted HD onset

As HDBuzz readers are undoubtedly aware, there is a bewildering array of trials of HD drugs planned and underway. A number of these drugs target the mutant HD gene, or the protein made from it, directly. To see if these approaches work, researchers need to find the right window of time in which to test their drugs.

The key question researchers are interested in understanding is: When is the best time to treat HD? Some researchers think that the best time to treat may be at the very earliest stages of HD – before any brain cells begin to die and before there has been any functional decline. But since we know emotional and psychiatric changes can occur even 10 to 15 years before symptom onset, no one was sure when the healthy baseline began to cross over into symptomatic onset – until now!

An team led by Dr. Tabrizi set out to try and identify the very earliest stages of HD – when patients are functioning at full capacity, but there's some measurable marker of decline. That last bit is super important. There needs to be some sort of measurable change so that when therapeutic strategies effectively improve HD progression, researchers will be able to measure improvement even in the very earliest stages of HD.

The name of Dr. Tabrizi's study is the Young Adult Study, or HD-YAS. This study examined over 130 young adults that included HD gene carriers as well as individuals without HD, that were on average 29 years old. The participants that carry the HD gene were predicted to be about 24 years from onset. That makes this one of the earliest comprehensive assessments of pre-symptomatic HD gene carriers ever.

All participants were assessed using many, many tests designed to assess both cognitive and psychiatric components of patients. A few of these tests included brain imaging, blood collection,

spinal fluid collection, assessment of cognition (planning, attention, memory), and psychiatric assessment (depression, anxiety, behaviour). So these participants were quite thoroughly examined!

Cognitive and psychiatric function are preserved, but NfL is increased

"This means that no matter how hard we look at people carrying the HD mutation this far from onset, there really is a time in which even the most sensitive tests don't reveal any changes, compared to people without the mutation "

The first major component of the study they described was the cognitive and psychiatric assessment. What they found was amazing: Of all the cognitive and psychiatric tests performed on HD gene carriers and individuals without HD (and there were lots of different tests), none of them showed any difference – wow! This means that no matter how hard we look at people carrying the HD mutation this far from onset, there really is a time in which even the most sensitive tests don't reveal any changes, compared to people without the mutation.

This study also examined the sizes of various parts of the brain to determine how early changes in these regions may be occurring. One of the primary areas of the brain affected by HD is the striatum, which is made up of two halves called the putamen and caudate. These areas of the brain shrink as HD progresses due to the loss of cells that occurs in these regions over time.

While there was no change in caudate size, there was a reduction in putamen size in the people carrying the mutation, called the **preHD** group. But this difference was small and didn't match with predicted years from onset in the preHD group, which means further study is needed to understand what this change means. No other brain regions that were assessed showed size differences.

The last major component of this study looked at biomarkers – measurable markers in samples from patients that change with disease progression. Identifying biomarkers in HD patients is critical for tracking disease progression and for measuring the effects of treatments.

Currently, one of the most reliable biomarkers we have for HD is changes in the levels of a protein called neurofilament light, or NfL. While it can be measured in blood plasma, examining levels of NfL in CSF appears to be more sensitive and accurate. We've written about NfL, and what role it might play in future HD trials here.

Happy HD-YAS participants providing invaluable samples - here, spinal fluid - to the HD-YAS study (photo courtesy of HDYO). HD-YAS found that NfL levels in both blood and spinal fluid were increased in the preHD group. Since NfL levels increase with injury to brain cells, this indicates that there is some level of stress on the brain occurring in the preHD group, even this far from symptom onset.

While this may seem like a negative finding, it's actually really good! Even though NfL levels are elevated, study participants aren't experiencing any cognitive of psychiatric effects because of it. This means that a timepoint has been established where HD mutation carriers have totally normal function, but there are biomarker tests that can still be measured to determine if therapeutics would be effective. This is exactly what HD-YAS set out to determine!

What do these findings mean for the field and future trials?

Overall, HD-YAS was able to conclude that NfL levels in the spinal fluid may be the earliest detectable event in HD before symptom onset. These researchers also found that movement, cognitive, and psychiatric function remain unchanged, even up to 24 years from predicted onset – amazing news!

When this study is combined with other large studies, like TRACK-HD, PREDICT-HD, and ENROLL-HD, a comprehensive, predictive map begins to take shape. Thanks to HD-YAS, and studies that came before it, we now know that the earliest, subtle, functional changes begin sometime between 24 to about 15 years from symptom onset.

"While we all hope that HD patients will regain functional capacity even after symptomatic onset, that's just not something we know based on the current data. But if we discover that HD patients need to be treated before symptoms begin to appear, we now know exactly when that is based on HD-YAS "

The findings from HD-YAS are an important discovery for the field, indicating the time at which a healthy baseline exists in HD individuals. If researchers learn that the best time to treat HD patients is prior to any sort of symptom onset, we now have an idea of when that time would be. This will be critically important for designing future clinical trials aimed at preventing HD, rather than treating it.

Have you missed the boat?

It's important to note that these results don't mean that lowering HTT after symptom onset won't have an effect. That question is still very much up in the air. The full set of results from the Phase III tominersen trials will help researchers understand if patients can regain cognitive, psychiatric, and motor function once they begin to decline. Following the progress of the brave trial participants as they continue to take tominersen will be critical in determining if follow-up trials are needed.

While we all hope that HD patients will regain functional capacity even after symptomatic onset, that's just not something we know based on the current data. But if we discover that HD patients need to be treated before symptoms begin to appear, we now know exactly when that is based on HD-YAS. This allows researchers to stay one step ahead and hit the ground running, saving valuable time.

Our Condolences

We send our love and support to the family of Jonathon Harper who passed away recently. The HD community is thinking of you at this difficult time.

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