HUNTINGTON'S DISEASE TASMANIA

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

Inside this Issue:

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Huntington's Tasmania

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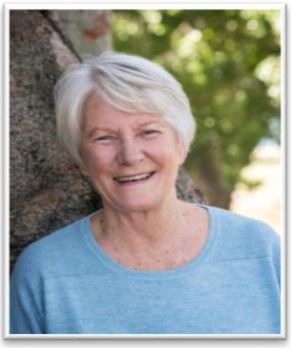
Education, Advocacy, Support, Hope

From the President's Desk



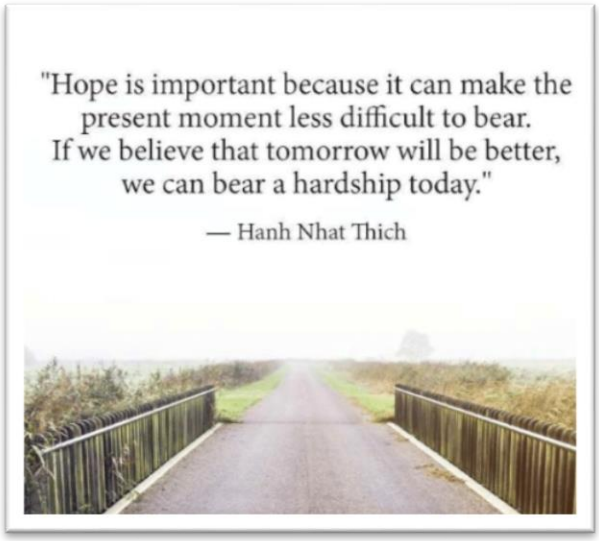
Hello everyone,

I hope you and your families are safe and well.

After the devastating bushfire season in Australia during Summer, we now find ourselves being challenged as we struggle through Covid-19. Our lives have been turned upside down as we learn to navigate this bizarre new world that we find ourselves in.

We are all living and working in challenging times but here at Huntington Tasmania we are still working to support our families. Although our office is closed, I am working from home. We are here to help so pleased give us a call. We are available 24/7 on 0417309818 or email huntingtontas@outlook.com.au.

Unfortunately, due to the restrictions we have had to cancel all of our fundraising and activities for the foreseeable future. This is a major blow for our organisation as most of our funds come from these events. However, I have a lot of hope for the future and Huntington's Tasmania will organise some fantastic events to both reconnect our families and fundraise when restrictions have eased.



I think that when the dust settles, we will realise, how little we need, how very much we actually have, and the true value of the human connection.

Please stay safe and well, we will come out of this stronger than ever.

Warmest regards

Pam Cummings

From the Service Desk

Welcome back from maternity leave to Subha who returned before Easter.

A big thank you to Noel O'Connor for supporting our families in the NW whist Subha was away, he developed a good rapport with clients and families and will be missed.

What does COVID-19 mean for HD families?

What does COVID-19 mean for HD patients and families?

A key question for many in the HD community right now is: Am I, or is my loved one, at greater risk for COVID-19 because of HD? The answer to that is – it depends. On its own, having the genetic mutation that causes HD doesn't make anyone more or less susceptible to COVID-19 than someone without HD.

What would make an HD individual more susceptible to COVID-19 is if they had any underlying conditions that put them in the "high-risk" category. Those can be as obvious as having asthma or being a smoker. But this can also include HD individuals who are symptomatic since we know that swallowing, clearing secretions from the lungs, and self-understanding of limitations can be impaired by HD.

Advice from various global HD organizations can be found here:

•https://www.hda.org.uk/getting-help/covid-19-information-advice
•https://hdsa.org/wp-content/uploads/2020/03/COVID-Statement-3-18-20-final.pdf
•https://www.huntingtonsociety.ca/novel-coronavirus-covid-19-and-huntington-disease-what-you-should-know/

"On its own, having the genetic mutation that causes HD doesn't make anyone more or less susceptible to COVID-19 than someone without HD. What would make an HD individual more susceptible to COVID-19 is if they had any underlying conditions that put them in the "high-risk" category. "

To stay safe and healthy we should all continue doing what the WHO recommends – wash our hands regularly for 20 seconds with hot water, clean surfaces with a disinfectant, and practice social distancing. Social distancing means only coming in contact with members of your household and only going out for essential things, like an essential job, grocery store run, or to get medication from the pharmacy. Everyone should also remain vigilant for the symptoms of COVID-19, which include fever, a dry cough, shortness of breath, and fatigue.

Some HD patients at particularly high risk may need to isolate themselves even more strictly. You should seek advice from the above sources and your health provider if you are concerned.

It can take up to 14 days after SARS-CoV-2 exposure to bring on COVID-19 symptoms, which is why many doctors are recommending a 14 day isolation period. However, we are now learning that a portion of the population may remain asymptomatic. This means they show no symptoms, but do have the virus and can pass it to other people. In fact, the asymptomatic portion of the population may be as high as 20 to 30%! This is why social distancing and staying at home when possible are critical for not spreading the virus – without widespread testing, we don't truly know who does or doesn't have the virus, so isolation is the key to staying healthy.

This too shall pass

This virus has undoubtedly brought a stressful and scary time for the entire world, but there have been a few bright spots. And while the pandemic will eventually fade away, we will be left with its silver lining. Many have been able to spend additional time at home with loved ones, even if that means having a computer on their lap. Scientific discoveries are being made at break-neck speed as the global research community comes together to fight a common goal. And last but not least, dogs around the world are rejoicing that their 2 legged friends are spending every night staying in. So stay safe and stay healthy, for this too shall pass.

Article taken from HDBUZZ

Exercise at home

We have been granted permission from Cardiff University to use their programme, Exercises for people with Movement disorders.
To use this programme, go to

https://vineo.com/289892489

https://vineo.com/289893681

HD short films to watch now

In 2019 HDSA (Huntington's Disease Society America) produced 3 powerful short films *Carol & Richard: A Love Story*. *The Hodgsons* and *The Vaughns*.

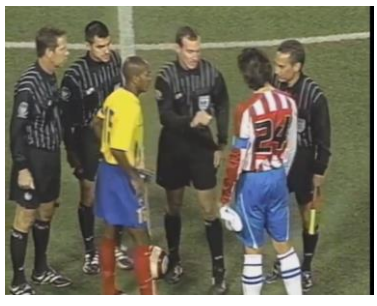
All were directed by Rae Maxwell.

The films are featured on HDSA You Tube Channel and each has received thousands of reviews."

The Hodgsons https://www.youtube.com/watch?v=rcEi3JYdxQ

Richard & Carol – A Love Story - https://www.youtube.com/watch?v=Kr6F4pTyfcU

The Vaughns - https://www.youtube.com/watch?v=aKSZ5tYtFO4



My battle with HD

Nancy Wexler has spent her life studying Huntington's disease—the disease that killed her mother, her uncles, and her grandfather. Now, Wexler for the first time has revealed that she, too, has the disease, Denise Grady reports for the *New York Times*.

A family history

Huntington's disease has always been a major part of Wexler's life, Grady reports. Wexler's mother, Leonore Wexler, was a geneticist working to find a cure for the disease, which had killed her three brothers and her father. At age 53, Leonore was diagnosed with the disease, as well. Each child of a Huntington's patient has a 50% chance of having the dominant gene that causes the disease, Grady reports. The disease itself is rare, affecting roughly 30,000 people in the United States with another 200,000 at risk of developing the disease, according to Grady.

After Leonore was diagnosed with Huntington's, her ex-husband and Wexler's father, Milton Wexler, who was a psychotherapist, established the Hereditary Disease Foundation in the hopes of finding a cure or treatment for the condition. Wexler, who had received a doctorate in psychology, also chose to dedicate her career to researching the disease.

Wexler helped care for her mother for the decade following Leonore's diagnosis. "As she became increasingly ill, I dressed her, carried her, helped her brush her teeth and go to the bathroom, fed her, and, mostly, held her and kissed her," Wexler wrote in a 1991 essay, "Her eyes still haunt me with their sadness and fear."

Leonore Wexler died in 1978 on Mother's Day. Both Wexler and her sister, Alice, knew they had a 50% chance of inheriting and developing the disease.

Wexler heads to Venezuela

In 1979, Wexler gathered a team and headed to Venezuela to study a large family affected by the disease that was first described by Americo Negrette, a Venezuelan doctor, in 1955. Researchers believe the family has the highest rate of Huntington's disease in the world.
Wexler believed that, to find the genetic mutation causing the disease, researchers would need DNA samples from as many of those family members as they could get—but members of the family had long been ostracized by their community, which feared the disease was transmissible. "Doctors wouldn't treat them," Wexler told Grady. "Priests wouldn't touch them."

Wexler told the family that she and they were similar, and that her family also had the disease. "I fell in love with them," she said.

Wexler returned to Venezuela multiple times over the course of 20 years, ultimately collecting 4,000 blood samples and tracing Huntington's disease through an extended family that spanned 10 generations and included more than 18,000 people.

Anne Young, former chief of neurology at Massachusetts General Hospital who made 22 trips to Venezuela with Wexler, told Grady that the trips were "a real testament to how an individual can take a team and get absolutely water out of a brick."

Young added that Wexler "was just totally charismatic, and when you walked into the room she would hug you and look you in the eye and listen to everything you said. She never thought about herself. She was always thinking about what she could learn from the other person. People became totally devoted to her. Everybody felt like they'd take a bullet for her."

Four years after Wexler's first trip to Venezuela, Wexler's team in 1983 found a stretch of DNA that served as a marker for the disease and, ten years later, Wexler and her team found the gene associated with the disease—a landmark finding that allowed for the development of a test that could detect whether at-risk patients would develop Huntington's.

Scientists say that discovery would have never happened had it not been for Wexler, Grady reports.

A 'ticking' clock

Despite years of research and knowing their risk, neither Wexler nor her sister were tested for the genetic mutation, Grady writes. Wexler told Grady, "I don't think I could have lived with that knowledge. I think I assumed I wouldn't get it, because I was fine."
Wexler said it was easier to live not knowing whether she'd develop Huntington's. "Denial is important."

As Wexler got older, people became concerned about her and Alice's risk of developing Huntington's. "Everybody watched me like a hawk," Wexler said.

NIH Director Francis Collins, who has worked with Wexler on Huntington's researcher, told Grady, "We knew the clock was ticking for her and Alice." He said, "It was a matter of watching [Wexler] all the time and wondering if she's escaped the curse or is it going to fall on her, too."

Eventually, Wexler began exhibiting symptoms of the disease and she started noticing them when she saw herself in the mirror or on video. "Every time I saw myself on video, I looked a little bit worse," she said.
While Wexler preferred not to speak about her condition, her sister encouraged her to publicly acknowledge having the disease, and Wexler eventually announced her diagnosis.

"I think that one thing her coming out about it will show is that getting a diagnosis of Huntington's disease is not a death sentence," Alice Wexler told Grady. "It's something people can live with for a long time, if they have the right medical care and social services. She has been living her life in a productive way, and still will."

Wexler said she hopes that her announcement will help destigmatize the disease. "I think it's important to destigmatize Huntington's and make it not as scary," she said. "Of course it is scary. Having a fatal disease is scary and I don't want to trivialize that. But if I can say, I'm not stopping

my life, I'm going to work, we're still trying to find a cure, that would help. If I can do anything to take the onus off having this thing, I want to do it."

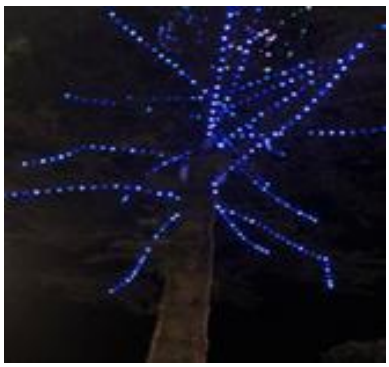
Wexler is still working, reviewing grant applications, fundraising for Huntington's research, and going to scientific conferences. "Enjoy life while you can," she told Grady. "Find what gives you some pleasure and go for it. Don't get kidnapped by this" (Grady, *New York Times*, 3/10).

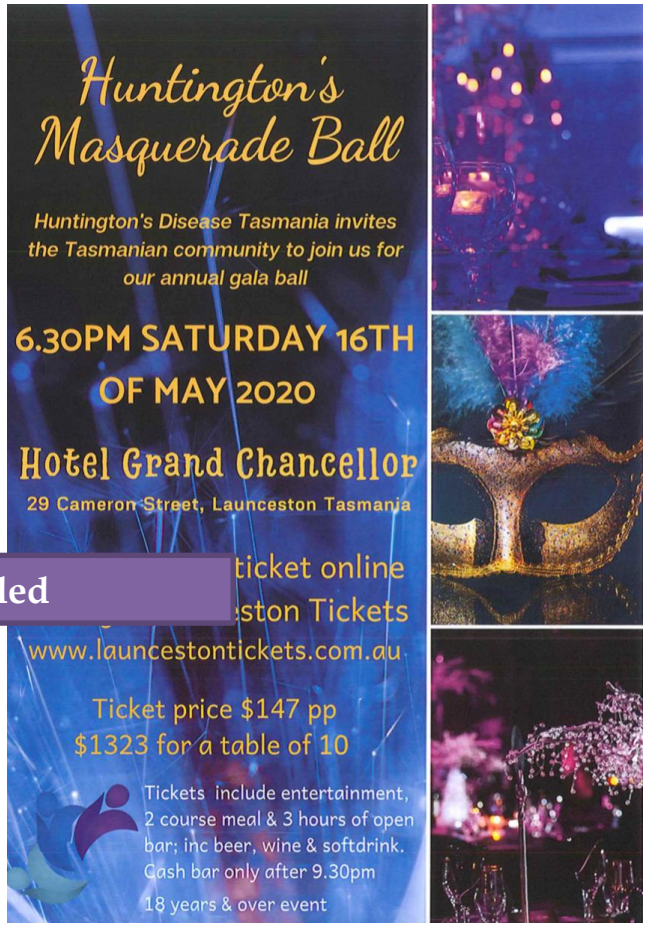
Taken from : Advisory.com

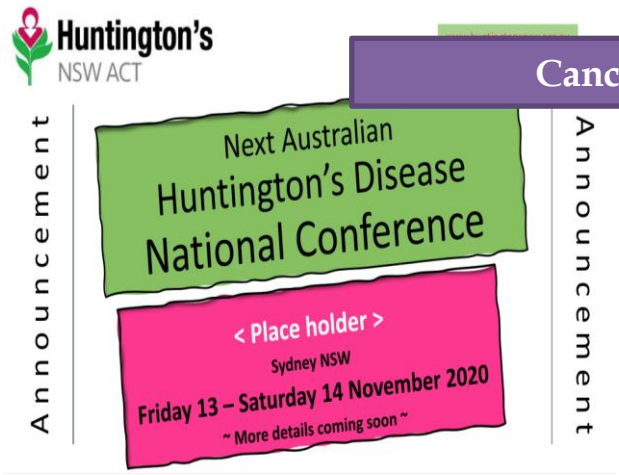
Events Cancelled

Unfortunately, COVID-19 and associated restrictions have forced the cancellations of HD Awareness month events this year. Our HD Masquerade Ball will not go ahead, but we will make it a bigger, better ball next year. The HD National Conference is also cancelled this year.

We will still have many venues across the state lighting it up for HD! Hopefully many buildings and trees across our state will still be lit up in Blue and Purple. Locations will be on our Facebook page, please send us your photos to spread our Awareness message. Please help us to get our message out.







Status of current HD trials in Australia

In 2019, the HD community in Australia welcomed three new international clinical trials from the sponsors Wave Life Sciences and Hoffman-La Roche. These trials are all planned to continue for some time, at least into 2021. The trials are very important because they are testing novel drugs in people with Huntington's disease (HD). All three trials have been progressing well in terms of recruitment and participant activity.

We wanted to inform the community of necessary changes to the trial activities due to the COVID-19 pandemic. The doctors and site staff for all three HD trials in Australia are following the guidance of the trial sponsors regarding how to manage the trials during the COVID-19 outbreak. In addition, they must follow requirements in the states and hospitals where these trials are taking place to minimise the risk of exposure to the virus for trial participants and staff.

Specific changes in trial activities vary site to site due to differences in site policies and guidelines. Importantly, sites will continue to remotely monitor the health and safety of all trial participants currently enrolled in these trials.

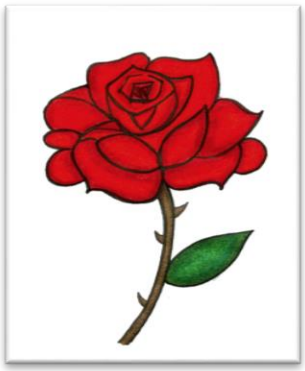
If you are a participant in one of these ongoing trials, the site staff will keep you informed about changes to scheduling or temporary suspensions of trial visits.

We are in close contact with the sponsors responsible for these trials and the governance officials at each site where these trials are conducted. They will inform us when it is safe for the trials to recommence. When this happens, trial participants will be contacted regarding next steps in their trial participation.

We trust that you understand that this important decision has been made to protect the health and safety of all trial participants and staff, as well as the wider community.
We hope you remain safe and healthy during these uncertain and times.

Julie Stout & Alison O'Regan

Our Condolences



We send our thoughts and love to the family of Ingrid Fairbrother who sadly passed away. Ingrid was a beautiful, clever and inspiring young woman. She will be missed dearly.

RESEARCH

New Molecule can reverse the HD mutation in lab models.

A collaborative team of scientists from Canada and Japan have identified a small molecule which can change the CAG-repeat length in different lab models of Huntington's disease.

By Dr Michael Flower April 06, 2020 Edited by Dr Rachel Harding Originally published on March 13, 2020

CAG repeats are unstable

Huntington's disease is caused by a stretch of C, A and G chemical letters in the Huntingtin gene, which are repeated over and over again until the number of repeats passes a critical limit; at least 36 CAG-repeats are needed to result in HD.

In fact, these repeats can be unstable, and carry on getting bigger throughout HD patients' lives, but the rate of change of the repeat varies in different tissues of the body.
In the blood, the CAG repeat is quite stable, so an HD genetic blood test result remains reliable. But the CAG repeat can expand particularly fast in some deep structures of the brain that are involved in movement, where they can grow to over 1000 CAG repeats. Scientists think that there could be a correlation between repeat expansion and brain cell degeneration, which might explain why certain brain structures are more vulnerable in HD.

But why?

This raises the question, what is it that's causing the CAG repeat to get bigger? It seems to be something to do with DNA repair.

We're all exposed continually to an onslaught of DNA damage every day, from sunlight and passive smoking, to ageing and what we eat. Over millions of years, we've evolved a complex web of DNA repair systems to rapidly repair damage done to our genomes before it can kill our cells or cause cancer. Like all cellular machines, that DNA repair machinery is made by following instructions in certain genes. In effect, our DNA contains the instructions for repairing itself, which is quite trippy but also fairly cool.

"What is it that's causing the CAG repeat to get bigger? "
We've known for several years that certain mouse models of HD have less efficient systems to repair their DNA, and those mice have more stable CAG repeats. What's more, deleting certain DNA repair genes altogether can prevent repeat expansion entirely.

But hang on, isn't our DNA repair system meant to protect against mutations like these?? Well normally, yes. However, it appears a specific DNA repair system, called mismatch repair, sees the CAG repeat in the huntingtin gene as an error, and tries to repair it, but does a shoddy job and introduces extra repeats.

Why does this matter?

There's been an explosion of interest in this field recently, largely because huge genetic studies in HD patients have found that several DNA repair genes can affect the age HD symptoms start and the speed at which they progress. One hypothesis to explain these findings is that slowing down repeat expansion slows down the disease. What if we could make a drug that stops, or even reverses repeat expansion? Maybe we could slow down or even prevent HD.

So what's new?

Chris Pearson's group in Toronto have developed a compound called naphthyridine-azaquinolone, which we'll just refer to more easily as 'NA', which binds CAG repeats and could prevent repeat expansion.

Using cells from HD patients in a tissue dish, NA was shown to successfully slow, and possibly even lead to a small reduction in CAG repeat length. Pearson showed that blocking transcription, the process in which genes are used as templates to make proteins, prevents repeat expansion. This suggests that during transcription, the huntingtin repeat might be bent into an abnormal shape, which mismatch repair machinery in the cell recognises and then tries to repair. However, precisely how NA works in this process remains unclear.

Pearson's team injected NA into one side of the brain of an HD mouse model. They targeted the striatum, a region known to show lots of CAG expansion. Compared to the untreated side, NA prevented expansion and even caused some shrinkage of the repeat number.

Next, they showed NA reduced the build-up of clumps of toxic huntingtin protein in the mice's cells. It is not clear yet whether the treated mice have improved symptoms or increased lifespan. This will be important for scientists to work out before deciding whether preventing repeat expansion has potential as a therapy for people.

What's the catch?

A huge obstacle to making new drugs is getting them into the cells that most need them; in the case of HD, that means throughout deep regions of the brain. NA is able to freely enter different cells once in the brain, but this current version of the molecule has not yet been shown to cross the blood-brain-barrier. Scientists might need to modify and improve the NA molecule to avoid needing to be directly injected into the brain.

Fiddling around with DNA repair, one of our body's major defence systems, could be dangerous, and there's the potential for major side effects like cancer. Pearson showed that NA didn't affect the core function of mismatch repair, which is to remove DNA bases when they get put in the wrong place. The researchers carefully analyzed the rate of mutations across the whole genome, and there was no detectable increase in the rate at which they were found, compared to controls when they were treated with NA.

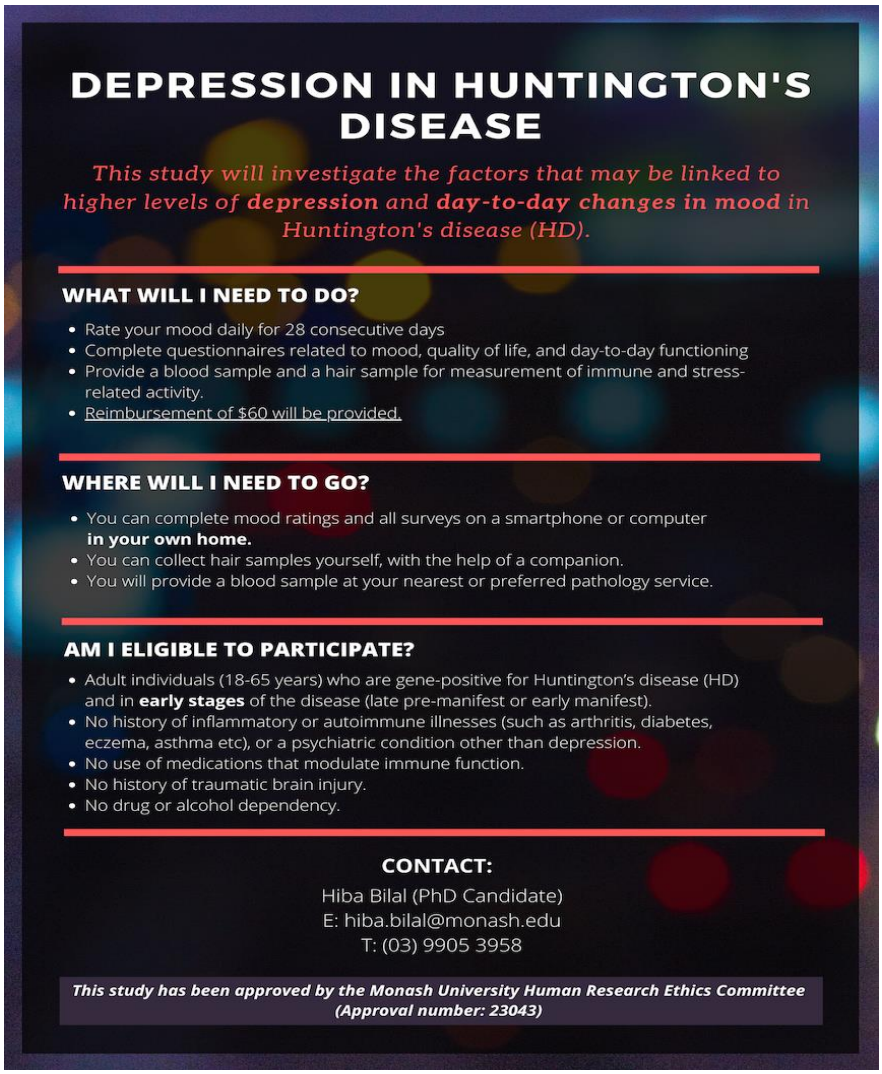
It is possible to imagine treating HD patients at an early age, before they develop any symptoms; this might stabilise the CAG repeat and could prevent or at least delay the onset. CAG

repeat shrinkage in their sperm or eggs could even mean they wouldn't pass the disease on to their children.

However, for NA there is still a lot of work to do. For starters, we would need to show that preventing CAG expansion slows down the disease, we would then need to come up with a way to get NA into the deep regions of the brain, and finally we would need to be sure it is safe with limited side-effects. Early treatment could also mean being exposed to risks like cancer for even longer, so there's clearly a lot to be worked out.

In summary, NA is an exciting research compound, but there is still a long road ahead before something like it might be a drug that could be taken by people to preventor.

Can you help?



Hiba Bilal is currently studying her PhD in clinical Neuropsychology at Monash University, under the supervision of Professor Julie Stout with a focus on factors linked to depression and day to day changes in mood in Huntington's disease.

Hiba is seeking those with HD who are in the pre-manifest or early manifest stages of this study, as well as their carers or partners.

For further 7information, please contact Hiba Bilal on hiba.bilal@monash.edu or phone (03) 99053958.

Huntington's Tasmania receives funding through the Department of Health and Human Services Tasmania.

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