HUNTINGTON'S DISEASE TASMANIA

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

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Help us to help you and we'll raise awareness together.

FOR MORE INFORMATION:

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Huntington's Tasmania

hunt_4_a_cure

Education, Advocacy, Support, Hope

From the President's Desk

Welcome back everyone. I hope you all had a well-deserved and relaxing break.

It has been a difficult start to the year for many people across mainland Australia as bushfires devastated many communities. As we watched with great sadness our thoughts were for those affected, the brave firefighters and the many volunteers who have worked tirelessly over many weeks. Our thoughts are especially for the many Huntington's families who may have been impacted by these disasters.

It is with pleasure that I introduce Ruth Forrest MLC who has agreed to become our new Patron. Ruth was born and educated in Tasmania. She is the mother of four adult children and grandmother to one grandson. She lives in North West Tasmania with her partner Rob. Ruth was first elected to the Tasmanian Parliament in 2005.

From 1979-1982, Ruth completed her General Nurse training in Tasmania and went on to completed an Intensive Care Course in 1983 and Midwifery training in February 1984. She worked as a nurse and midwife since 1982, primary as a midwife, a caseload model of care that she and a colleague established in Tasmania in 1989.

In May 2005, Ruth was elected to the Legislative Council of Tasmania as an Independent Member, representing the rural and remote electorate of Murchison. She was re-elected in May 2011 and again in 2017. In 2018 she was elected Deputy President and Chair of Committees in the Legislative Council. Currently she is a member of several Parliamentary standing, select and sessional committees, holding the position of Chair for a number of these. Ruth maintains a strong interest in health policy and service delivery. She advocates strongly for social justice and the rights of women, girls, marginalized groups and vulnerable or disadvantaged communities. In October 2019 Ruth was named one of "The Australian Financial Reviews 100 Women of Influence" in the category of Public Policy. We are honoured to have her as our Patron and look forward to working with her.

With 2020 now well underway myself and our board are looking forward to a busy and exciting 2020 with lots happening across the state.

Warmest regards

Pam Cummings

Understanding HD
Communication in Huntington's Disease

When we talk about the symptoms of Huntington's, we tend to talk about physical and movement changes, cognitive changes (difficulties with planning and thinking) and behavioural changes. All of these have an impact of the way someone with Huntington's communicates.

- **Physical Changes** – people with Huntington's can't control the muscles used for speech as well as they could before. You might notice that their speech is a little slurred, or they are struggling with volume control.
- **Cognitive changes** – changes in the brain usually mean that people struggle to put their thoughts into words. Often, they find it hard to start a conversation. They may become focused on one topic and not be able to move on from it (this is particularly common if there is a change to the normal daily routine e.g. if there is an appointment and they are worried about getting there). They may repeat certain words that seem important to them.
- **Emotionally** – they may become more apathetic; they simply don't have the same 'get up and go' anymore, and this can affect their communication skills. If someone feels anxious or depressed, whether due to Huntington's or another reason, it's also likely to have an impact on their communication. They may find it hard to be in a group of people which may mean they avoid social situations, start to withdraw and feel socially isolated. This can create a cycle of decreasing communication.

When we break down the issues affecting communication like this, it can help us think about how we can support people to communicate.

Key tips around communication are:

- Talk about one thing at a time. Keep it simple and don't overload the person you're caring for with information. Sticking to a single topic helps people with Huntington's to process information and respond. Use short sentences and even pictures or visual cues, such as showing them an item you're offering them.
- Give more time. Remember it takes time for people with Huntington's to process information and form a response. Ask a question, then wait for an answer – don't interrupt the thought process by repeating your question or putting it another way.
- Avoid distractions. Try and focus on the conversation. Get the person's attention and then tell them what you would like to say. Avoid talking to someone if the TV is on. Where possible, keep them away from noise when talking to them. Don't expect them to walk and talk or eat and talk at the same time. This can be hard as we are used to using meals as a time for conversation. It may take a bit of time to see what works best for them: they may, for example, enjoy going for a coffee and a cake but want to chat

first, then have a quiet time to eat and drink, then the conversation can be picked up again.

- Limit choices. Ask closed questions (i.e. ones that require a 'yes' or 'no' answer) so they don't have to search for the answer. This may feel counterintuitive as we think of choice as being empowering, but for people with Huntington's making a choice can often feel difficult and stressful. It's the same for most of us; we would prefer a multiple-choice test than having to write an essay - it's much easier to respond when the answer is already there.
- Listen. It can take a lot of effort for people with Huntington's to speak, so try to listen to what they're saying. This can become tricky if there is a lot of repetition.

A speech therapist can also help with difficulties with communicating, as well as eating, drinking or swallowing. You can get a referral to a Speech Therapist through your GP or a specialist Huntington's clinic.

Research News:
The third dimension: using minibrains to understand brain development changes in HD

Researchers show that highly expanded CAGs in the HD gene can cause early developmental changes using 3D brain models called organoids. What'd they find?

By Dr Sarah Hernandez February 06, 2020 Edited by Dr Jeff Carroll

A new publication used tiny 3D brain models created from human cells to show that the mutation that causes HD could lead to early changes in brain development. However, it's clear that HD patients can, and do, develop fully mature brain cells that maintain normal function, in most cases, for decades. So let's put these findings into context and dig into what these developmental changes that have been discovered using human cells in a dish might mean for HD patients.

Getting human brain cells without collecting brain samples.
Even though HD is unique to humans, most organisms have a version of the gene that is mutated to cause HD – *huntingtin*, or *Htt* for short. A variety of organisms can be used for studying HD and each model can inform different aspects of how the disease works. For example, if a scientist wants to know if an experimental treatment could benefit HD, they could use fruit flies or even worms to get those answers.

While flies and worms are quite different than humans, they have very short lifespans (about 14 days for fruit flies) so scientists can get their answers quickly. If they want to know what

will happen in a more complex brain, scientists often choose mice. But to understand the effects that their work will have in humans, scientists need to test their ideas in humans - or at least human cells.

In 2006 two separate scientists showed that you can reverse the biological timeline of a skin cell, priming it to turn into any other cell type in the body. More recently, blood cells have even been used. These primed cells are called "induced pluripotent stem cells", or iPSCs.

If scientists are interested in studying a brain disease like HD, they can then turn those iPSCs into the cell types of interest, like neurons. And even better, if the skin or blood cells are from an HD patient, scientists then have everything they need to study the neurons of that patient without having to take a brain sample. Not only super cool science, but also great news for HD patients, who would like to hang onto their brains!

Usually, cells are grown on the flat surface of a Petri dish, but recently researchers have devised a way to coax iPSCs to grow into 3 dimensional balls of cells - which resemble a little brain at an early stage of development. These 3D structures are called **brain organoids** and are akin to a tiny model of a brain.

Growing these cells in 3D allows researchers to study the way that they organize as the organoid grows, informing very early events in development within the brain. But while these tiny brain-like structures seem to have similar early developmental patterns to a human brain, it's not a working replica and they don't possess the capacity for cognitive function.

You are a beautiful and unique snowflake

In a recent study, these brain organoids were used to investigate the impact that the mutation that causes HD has on their development. They did this using 4 different cell lines that are identical in every way, except one: the HD gene. But, wait. How can 4 different cell lines be identical and different?

Everyone has unique aspects to their DNA. By using cell lines that are identical in every way except the CAG expansion in the HTT gene, researchers can be sure any changes they observe are due to HD.

You can think of people as snowflakes – we're all unique in our own way, not just with obvious physical differences, like different hair colour or eye shape, but also at the genetic level. Everyone has a slightly unique makeup in the code of their DNA that makes them different. So while 2 people may have the genetic code necessary for hands, one may have very long fingers and another may have short fingers.

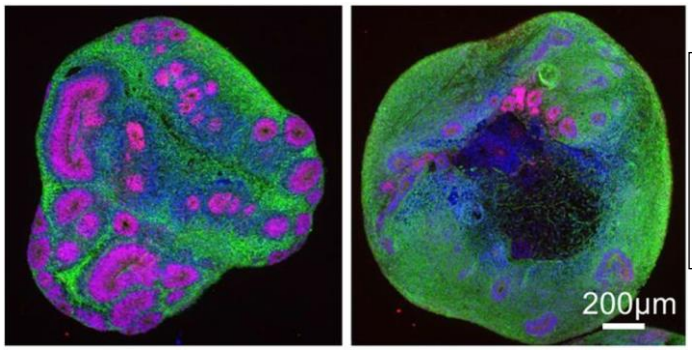
If researchers take cells from 2 people, one with HD and one without, their cells will not only contain the different CAG lengths of that person's HTT gene, but will also contain all the other genetic differences that make them uniquely them! This can confuse results a bit though because researchers won't know if any changes they measure are because of

differences in their HD gene or if they're because of another unique alteration in that person's DNA.

So back to those identically different cells – to prevent any confusion in their study about whether the results are from different CAG lengths in the HD gene or some other unique DNA code a person has, researchers used a series of cell lines originating from a single cell line that has been genetically altered only within the HTT gene so that it contains CAG repeats of different sizes.

In this case, the CAG repeat tract was increased from 30 (to represent someone without a risk for HD) to 45, 65, or 81 (representing adult-, adolescent-, or juvenile-onset HD, respectively) while all other genes in these cells remained identical. So now the researchers can be sure that any differences they observe between these cell lines are explicitly due to the changes they induced in the HD gene. Pretty clever!

Early-onset juvenile HD may not be a purely degenerative disorder



Recent advancements have allowed scientists to grow neurons in 3D, modelling a minibrain. In this study, juvenile-onset HD minibrains (right) were found to have fewer and smaller internal structures, shown here in pink, compared to organoids representing someone without HD (left).

When using all 4 cell lines to create organoids, the first thing the researchers noticed was that even though organoids from all 4 lines were the same size, the HD organoids developed smaller internal structures that developmentally lead to the formation of important brain cells called neurons, suggesting that brain development is blunted. However, this was only observed in organoids that correspond to adolescent- (CAG of 65) and juvenile-onset HD (CAG of 81), while the organoids that represents adult-onset HD (CAG of 45) were similar to the organoids representing someone without HD.

So what does this mean? The authors interpreted their findings to mean that the mutation that causes HD, particularly in cases of juvenile-onset, stunts brain development. However, an alternative idea is that the mutation that causes HD may just delay development.

To test this, the authors examined older organoids – they measured the difference between the organoids that have 30 and 81 CAGs and found that they still had smaller internal structures, even at this later time point. So it appears that, at least for juvenile-onset HD cases, brain development in these organoids is not just delayed, but rather stalled. However, the adolescent- and adult-onset organoids weren't included in this specific experiment.

Another key finding from this study suggests that the juvenile-onset organoids develop into neurons more quickly than the organoids without the HD mutation. But if you've been

staying up-to-date on your HD organoid literature, you may find this a bit confusing because a paper that came out about a year ago found the exact opposite – that HD organoids derived from iPSCs develop into neurons more slowly than organoids without HD.

So does this mean that one study is right and the other is wrong? No. Even though the 2 studies found opposite effects in the speed of HD organoid neurodevelopment, each study was performed slightly differently, using different cell lines and measuring effects at different time points.

What both studies agree on is that the mutation that causes HD leads to early changes in neurodevelopment. But, just because results suggest early changes in development doesn't mean that these changes can't be compensated for. In fact, the authors of the more recent study identified a drug with the ability to partially restore the lower measurements they observed in the juvenile-onset HD organoids!

"What both studies agree on is that the mutation that causes HD leads to early changes in neurodevelopment. But, just because results suggest early changes in development doesn't mean that these changes can't be compensated for. "

But what about the organoids that represent adolescent- and adult-onset HD? If you're a stickler for details, you may have noticed that most of the findings of this study just focus on organoids that represent juvenile-onset HD, which represent about 5-10% of the HD patient population. This means these experiments are assessing a rare form of an already rare disease. However, the authors of this study are diligent about interpreting their findings in the context of what their data represents, saying, "Overall, these findings suggest that HD, at least in its early-onset juvenile forms, may not be a purely neurodegenerative disorder and that abnormal neurodevelopment may be a component of its pathophysiology".

Hot off the presses

One thing to note about this study is that it's currently published in a repository called BioRxiv (pronounced "bio archive"). BioRxiv is a phenomenal resource because it publishes data ahead of print and is available to everyone. While this gets data out to the masses sooner, it also means that it hasn't undergone the scientific process of "peer review", which is an unbiased evaluation of the work by other scientists in the field who are unconnected to the project.

Peer review is critical for maintaining the rigor of scientific studies and provides the authors of the work a thoughtful outside perspective from other experts in their field. Because this study hasn't yet undergone peer review, reviewers might request additional work prior to publication to clarify some of the results or even request further examination of the organoids that represent adolescent- and adult-onset HD.

So you can think of this study like an unfinished book at the moment – we'll have to tune back in after its final publication to get the full story.

Do these developmental changes ever normalize?

While the organoids are very cool because they can tell us about HD-related changes at the cellular level that occur early in development using human cells, we really need data from patients to interpret the effect that any changes may or may not have on a fully developed human.

Another study did just that and examined the sizes of different brain structures of children and adolescents (age 6 to 18) with and without the adult-onset form of the HD mutation using MRI. These are kids with no symptoms of HD, whose parents have agreed to allow them to participate in research to better understand the very earliest changes caused by the HD mutation.

The organoids that represent juvenile-onset HD develop neurons more quickly and show stunted development compared to organoids that represent someone without HD, adult-, and adolescent-onset HD, suggesting altered brain development specifically in cases of juvenile-onset

This study reported a larger striatum (one of the primary brain regions affected by the mutation that causes HD) in HD mutation-carrying kids early on, from age 6 to 11, while HD gene-negative kids have a larger striatum later, from age 11 to 18. So it seems that the gene-positive kids have more rapid neurodevelopment, at least of the striatum, but that gene-negative kids eventually catch up and end up having a larger striatum at the ages examined in this study. However, this difference appears to be quite modest, with only about a 1mL swing – about ¼ of one gummy bear for perspective.

Studies like these that use non-invasive methods capable of detecting very small changes are exactly what's needed to assess the contribution that HD has on brain development. They will help interpret findings from studies that represent very early development, such as the organoid study in a dish, in the context of human patients.

Ultimately, research demonstrating brain developmental changes resulting from HD is new, and while biologically interesting, researchers don't yet know what it all means in the context of the disease. However, it's important to remember that researchers are also working discovering mechanisms that can compensate for any brain developmental changes they report.

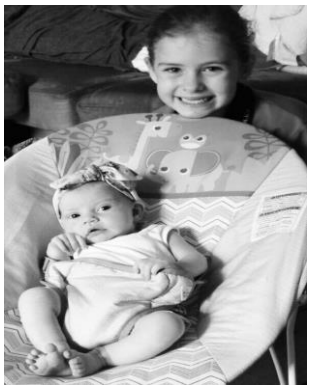
Article taken from HDBUZZ

HD Happenings

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 or family member we would love to hear from you. Here are what some of our members have been up to recently:

Bus Group Fun

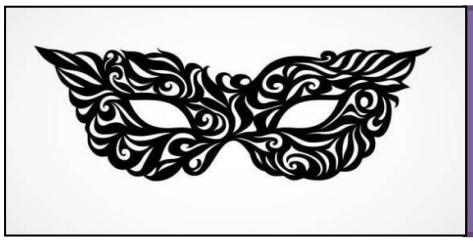
In December the participants of the Tuesday bus group with, families and carers attended a Christmas Lunch at Bridport.
The venue had a lovely view to the beach and the owner made everyone feel very welcome. The meal was delicious with a good range of suitable food choices.
It was a great day and a wonderful way to celebrate the end of the year.



Congratulations

We were very excited to hear of the safe arrival (all though a little late) of Amanda and Jeremy's baby, Annabelle Vicky, born 29th January. Our loving thoughts and best wishes from all our HD Tassie families.

National Conference - Information to come



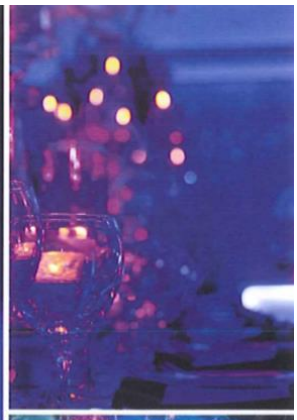
Save the Date Masquerade Ball 2020

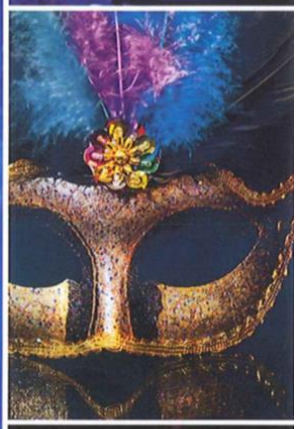
Excitement is mounting for our Gala Masquerade Ball to be held May 16th this year.

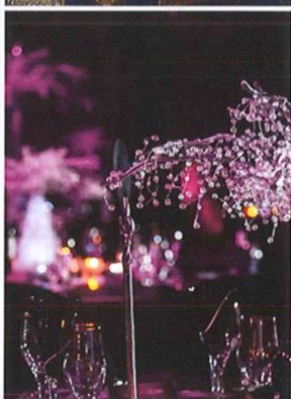
Come along to the Grand Chancellor in Launceston for a wonderful night of fun and entertainment.

Bring your friends, maybe get a table of 10.

It is the major fundraising for Huntington's Tasmania so please come along and support us.





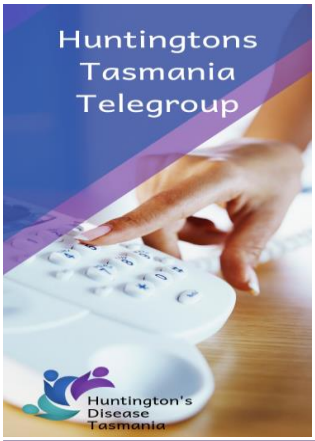


Light it up 4 HD

This year our Light it up 4 HD will coincide with out Masquerade Ball. We will have as many venues around lite up to spread the HD Awareness in Tasmania.

If you know of a venue /bridge/church or building near you that you would like to see lit up in Blue/Purple, please let us know and we will contact them.

HD Telegroup



Our monthly Telegroup continues on the 2nd Wednesday of every month from 6-7pm.

All are welcome. Contact the office 64313403 or 0417309818 for details.

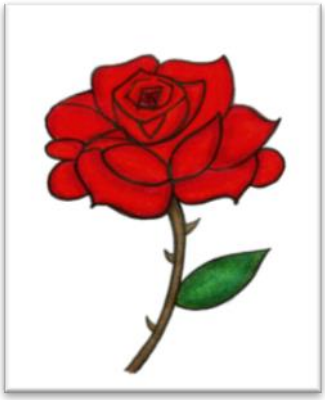
HDYO
International Young Adult Congress 2020

This is the inaugural International HD Young Adult Congress. A three-day event filled with education, support, connection, motivation and fun. Young people (18-35ish) from around the world are invited to convene in Glasgow May 9-11 2020.

Expressions of interest are still open. Please contact the office if you would like any more information.

Our Condolences

We send our thoughts and love to the families of Margaret Castles and Sandra Harding who sadly passed away recently.



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