



Gateway

News from Huntington's New South Wales

Volume 18 No 1

Autumn 2015

Huntington's NSW 1975—2015

This year marks the 40th anniversary since the founding of the NSW Huntington's Disease Association. Through the dedication and commitment of many people we have come a long way since those early days and although we still don't have a cure for HD we are able to provide meaningful support to families impacted by HD. I do hope you will be able to join me and the Board at some of the various events planned for the year—it promises to be a very exciting one culminating with our Walk4Hope on Sunday 27th September. Thank you for supporting us on our journey and remember it's better to light a candle than to curse the darkness.

*In friendship
Robyn Kapp*

The Inheritance Documentary

An intimate story of a courageous family



Sydney Premiere Screenings

"Truly one of the most moving and inspirational stories I have ever witnessed on the big screen."
Cathy Stephenson—DomPost

To be introduced by Associate Professor Clement Loy, Director and Neurologist, Huntington Disease Service, Westmead Hospital.

Followed by a Q&A with the filmmakers, Director/Producer Jeff McDonald, Editor/Narrator Bridget Lyon & Robyn Kapp, EO, Huntington's NSW.

Tuesday 24 March – Dendy Opera Quays

6:30pm for 7:00pm start

\$25 tickets: Film + Q&A

\$40 tickets: Film + Q&A + Post-Screening Drinks

Buy Tickets: <http://www.trybooking.com/GYWA>

Wednesday 25 March – Parramatta Events Cinema

10:00am for 10:30am start

\$25 tickets: Film + Q&A

Buy Tickets: <http://www.trybooking.com/GYWI>

Carers' Support Group

Huntington's New South Wales and
Huntington Disease Service – Westmead Hospital

*invite you to
come along to our*

CARERS' SUPPORT GROUP

*for a get together with other carers who, like
yourself, are caring for a partner, a family
member or a friend with HD.*

*Come along and join us as we share our chatter,
laughter, tears and experiences.*

Sessions will be held at
Huntington's NSW Offices
21 Chatham Road, West Ryde NSW 2114

2015 Sessions

18 March, Wednesday, 10.30am
15 April, Wednesday, 10.30am*
13 May, Wednesday, 10.30am
01 July, Wednesday, 10.30am*
19 August, Wednesday, 10.30am
23 September, Wednesday, 10.30am*
28 October, Wednesday, 10.30am
27 Nov or 04 Dec, Fri, Year-end Get-
Together (TBC)

* Denotes School Holidays

To RSVP and for further information, please
contact either: Jet Aserios or Cecelia Lincoln, SW
Department, Westmead Hospital on 9845 6699 or
Robyn Kapp, Huntington's NSW on 9874 9777

Simple Sensational Soft

Simple Sensational Soft is a new cookbook especially for people with swallowing difficulties, and shows how everyday food such as pizza, lamb shanks and lamingtons can be recreated for modified diets.



All recipes have been reviewed by a speech pathologist and given the tick of approval for people on modified diets.

In her forward to the book, Dr Patricia Kailis, AM, OBE, MBBS writes "This is an inspiring cookbook. Not just because of its recipes – carefully tested and beautifully presented – but because of the love and care that triggered its creation. Its roots are in Brightwater Kailis House (Belmont WA) home to six people living with Huntington's Disease. Respect and joy and a spirit of loving family are the foundations of this wonderful cookbook. If someone you love can only eat softened, modified food, you will find lots of tempting delights to give them pleasure. "

Retail Price \$30.00 (includes \$5 postage & handling). To purchase go to
<https://www.brightwatergroup.com>

Catching up with our local member

Brian Rumbold and Robyn Kapp recently caught up with our local member, Victor Dominello, the Member for Ryde in the NSW Government. The meeting provided the opportunity for Victor to hear more about Huntington's Disease and the work of the Association and for Brian and Robyn to thank him for his support through the Community Building Partnerships Program.

This program provides valuable funds which allow us to maintain our property in West Ryde. We'll soon be embarking on our next project which is repainting the interior of "Elsie Court Cottage" and replacing the carpet.



From left: Victor Dominello MP,
Robyn Kapp & Brian Rumbold

We did it!!

\$10,000 from the Dick Smith Foods Foundation

With the help of all our wonderful members, their families and friends, who sent in photos of Dick Smith products we have received \$10,000 from the Dick Smith Foods Foundation.

Huntington's NSW was represented at the presentation of cheques in Martin Place, Sydney by our President, Brian Rumbold; Secretary, Amanda Dickey; Fundraising Consultant, Pauline Keyvar and EO, Robyn Kapp.

A special thank you to all who supported us in this venture and a very special thank you to Dick Smith and his Foundation for their generosity in donating \$1million to 75 charities around Australia in 2014.



Brian Rumbold receiving the cheque from Dick Smith



Brian Rumbold, Dick Smith & Amanda Dickey



Robyn Kapp, John Williamson, Pauline Keyvar and Amanda Dickey



It's for real!



Save the date...

Mad Hatter's Tea Party
Friday 22nd May 2015

Intercontinental Hotel

cnr Phillip & Bridge Sts Sydney

5.30pm-9.00pm

*More information and details of how to purchase tickets will soon be available on our website
www.huntingtonsnsw.org.au and our Facebook page*



Bike Riding 'Round Australia for HD



*With Tammy Gardner,
CEO of Huntington's
Victoria*

A few years ago Maddison Spence started a list of things he wanted to do in 10 years, three of those were to travel around Australia, bike ride from Brisbane to Melbourne and donate to charity. So he decided why not combine all three and bike ride around Australia for a good cause. Huntington's Disease was not something he knew much about until close friends had been affected. Mad Dog (as he's more widely and affectionately known) believes it's so refreshing and morally stimulating that he has the opportunity to lend a hand to those with HD, those who are at risk. He says he has always wanted to donate a large amount of money to charity but always had that mindset 'is my donation going to make any sort of difference'. Although Huntington's NSW is a smaller organisation and whether the donation be big or small, he is confident that it will be put to significant use to assist those impacted by HD.



*A warm welcome from Ann
Jones, IHA President, in Perth*

Mad Dog has received 102 donations since he began The Great Australian Bike last December and to date the donations received total \$11,791.72. You can show your support by making a donation to help him reach his goal of \$20,000 for Huntington's NSW at <https://give.everydayhero.com/au/mad-1>



Maddison and his trusty bike

Research Grant: Predicting the course of functional decline in HD

The Board of Huntington's NSW recently approved funding of \$55,000 from the Association's Research Fund to fund a research project "Predicting the course of functional decline in HD" that is being undertaken by Dr Govinda Poudel, Professor Nellie Georgiou-Karistianis, Professor Gary Egan and Associate Professor Alex Fornito at Monash University in Melbourne.

Professors Georgiou-Karistianis and Egan have integrated cutting-edge multimodal neuroimaging methodologies to significantly enhance biomarker discovery in HD (via IMAGE-HD study). Assoc Prof Fornito is the world leader in network and computational analysis of brain imaging data and Dr Poudel is an early career computational neuroscientist with more than four years of postdoctoral research experience.

Proposed research focus: People with Huntington's disease suffer from significant cognitive and psychiatric impairments including decreased executive function, reduced working memory capacity, depression, irritability, apathy, and inflexibility. These deficits contribute to profound functional decline and a gradual loss of independence in activities of daily living. Other researchers including research at Monash have identified the brain changes associated with cognitive and psychiatric dysfunction in HD. However, none of this research has been able to predict its potential course of decline. In particular, being able to identify those who are highly vulnerable to a rapid progression of cognitive and psychiatric dysfunction can be of immense value for clinicians. This research will remedy this gap in Huntington's disease care by developing brain imaging based biomarkers that can predict the progression of cognitive and psychiatric dysfunction in people with HD. Building on their Australian based IMAGE-HD study data and their expertise in computational methods in HD brain imaging, this team will develop machine-learning based tools to predict the potential trajectory of cognitive and psychiatric decline in people with HD from multimodal brain imaging data. They envisage that the tools developed from this research will be valuable to clinicians and researchers for investigating patient-specific therapeutics and interventions for arresting the progression of HD.

Key benefits:

1. The neuroimaging-based biomarkers to be developed in this research will allow the team to make quantitative predictions about individual patient's likelihood of rapid progression in cognitive and psychiatric decline.
2. A software platform (i.e., set of software tools) to be developed will be highly valuable for researchers/clinicians for assessment of each patient's multimodal neuroimaging data and quantitative prediction patient-specific functional decline.
3. This project will identify most relevant brain regions that may be potential targets for future intervention to arrest the progression of cognitive and psychiatric decline in HD. Clinicians will be able to use brain-imaging data to better inform the development of patient-specific interventions and care.



Dr Govinda Poudel



*Professor Nellie
Georgiou-
Karistianis*



Prof Gary Egan



*Assoc Professor
Alex Fornito*

Huntington's Disease in Popular Culture: A Brief Historical Perspective

Alice Wexler, PhD

In Ruth Rendell's 1988 London mystery *House of Stairs*, the narrator suggests a startling sea change in the world of Huntington's disease (HD). "The news-papers and television and magazines have been full of Huntington's lately," she observes. "Huntington's has become a fashionable disease, displacing multiple sclerosis and even schizophrenia in the public's curiosity." [1]. She refers, no doubt, to the publicity surrounding the discovery of a genetic marker for HD in 1983 and the beginning of presymptomatic genetic testing three years later [2]. The start of the Human Genome Project in 1990 and the identification of the expanded Huntingtin gene in 1993 drew further attention to HD [3].

Considering that many people get their medical information from popular culture, it is useful to consider how HD has been portrayed on television and also in novels such as *House of Stairs* [4]. Why did the disease suddenly start to appear at this time when it was largely absent before? What aspects were emphasized? How accurate were fictional and dramatic portrayals? What societal attitudes toward the disease were revealed? How did presentations of HD differ from those of other neurological, psychiatric, and/or genetic disorders? Did representations change over time as biomedical knowledge of HD advanced?

Prior to the 1980s, characters with HD or at risk rarely appeared in fiction or in television dramas. When they did, they were minor figures, portrayed inaccurately, like Tony Polar in *Valley of the Dolls* (1966) [5]. Or they were patients in a single episode of a medical drama, as in *Marcus Welby, M.D.* (1970) [6].

But starting in the 1980s, persons at risk began to appear as protagonists in stories and TV series that often portrayed them with considerable empathy and realism. Unlike other diseases such as Alzheimer's disease that were shown through characters living with the illness, HD was distinctive in appearing primarily through a character at risk. Many of these at risk characters struggled with anxiety, depression, and the dread of becoming ill, as for example in *House of Stairs*: "Huntington's chorea were words I repeated to myself if not every day of my life, almost as often," the narrator Elizabeth Vetch tells us. Anytime she stumbles or drops something, "the feeling is always inescapable

that this may be it, this time it is no ordinary tiredness but the early warning in itself [1]."

Not surprisingly, the presymptomatic gene test loomed large in a number of TV dramas and novels, with two television series featuring major characters trying to decide whether to learn their genetic status. "Everwood" (set in a small Colorado town in the early 2000s), shows high school senior Hannah, whose father has HD, going by herself (not standard practice) to see a social worker (not a genetic counselor, as would typically be the case). In this episode the social worker nicely explains the complexity of the testing process and the profound consequences of the choice though another episode subtly trivializes the impact by equating it with a much less significant discovery (i.e., with Hannah's best friend learning that her boyfriend has got another girl pregnant) [7].

In perhaps the most well-known and complex television depiction of a character at risk, the medical drama "House" showed "Thirteen" (Dr. Remy Hadley) as a secretive, sardonic, but talented young staff physician working under Dr. Gregory House at a Princeton, New Jersey hospital. A number of episodes involve a verbal tug of war over the genetic test between Thirteen and the brilliant but sometimes abusive House, whose behavior on this issue goes against all accepted protocols. Suspecting Thirteen may be developing HD symptoms, House taunts her with being "in denial" and afraid to get the genetic test, which Thirteen resists, saying "when you run out of questions, you run out of hope." But Thirteen also violates rules when she eventually tests herself and, all alone, learns she carries the abnormal gene. More realistic is her (temporarily) reckless behavior after getting this result and her guilty memories of her HD-affected mother. Still, through many twists and turns of the plot, House continues to respect Thirteen as a physician no matter what else is going on in her life. She may be fatalistic, but she is also feisty. "You want to make sure your life



Alice Wexler (right) with her sister, Nancy Wexler

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matters," she tells one of her patients. "I don't want to be just tightening bolts and following instructions. I want something to be different because of me [8]." Above all she is a complicated, sometimes contradictory figure whose behavior and personality cannot be reduced to the disease.

Set in Paris rather than Princeton, Emilie Hermant's 2009 *Reveiller l'aurore* [Awakening the Dawn] features a narrator, Alice Rivieres, who unlike Thirteen felt obliged to get the test from the moment it became available. The novel beautifully portrays her fury and depression on learning she carries the expanded gene, not so much because of this result as because of the closed narrative of "deterioration" in which it is framed. After months of complete withdrawal and grief, Alice begins a series of healing conversations with Tahitidouche, her container of bath gel whom she imagines as her interlocutor. Eventually the piano music of Schumann, coming over the radio, breaks through her paralysis, opening up "miniscule points of light that flicker slightly in the night, signaling a far off city at the edge of the sea." Together with "Tahiti," she embarks on a journey, both figurative and literal, toward a place of creativity and hope [9].

As in *Reveiller l'aurore*, the social stigma surrounding HD is a theme effectively woven through many portrayals, typically conveyed through the at risk character's feeling of being devalued and the fear—and sometimes experience—of rejection. For example, when Isabel da Costa in Erich Segal's 1985 novel *Prizes* learns she is at risk for HD, she suddenly feels like a "leper," a woman with "an appalling heritage" whom no rational person would want to marry [10]. Alice Rivieres mourns that "no one could love a girl like me. I am not normal, I am going to disappear." The female narrator in Joanna Scott's 1994 short story "Tumbling," states straightforwardly that "the few men I dated after my daddy's death were tourists since the locals wouldn't have me." As she puts it, "give a decent girl two-to-one odds [not correct] that she is carrying a time-bomb, and even the most desperate romantics will keep their distance [11]."

In fact, a number of female characters at risk are portrayed as alone or involved in difficult romantic relationships while their male counterparts usually have supportive partners. In some stories, the protagonist herself rejects love out of a desire to avoid putting a partner in the position of seeing her "deterioration" and having to care for her through a long illness, as in Jennifer duBois's *A Partial History of Lost Causes*, published in 2012 [12]. In others,

her choices turn out badly, as in *House of Stairs*. Or she engages in promiscuous behavior, as in "House," although Thirteen eventually forms a satisfying relationship with another woman. And Isabel da Costa's boyfriend sticks by her despite her feelings of being "a genetic time bomb."

Secrecy and the difficulty of talking about HD in the family—or even learning much about it—is another salient theme, often presented as an important cause of the main character's unhappiness and sense of isolation. In many stories HD is at the heart of a family mystery, as in Nancy Werlin's 2004 young adult novel *Double Helix*, which addresses the themes of kids overhearing parents discussing HD and the difficulties of disclosure to friends as well [13]. Steven T. Seagle's 2004 graphic novel *It's a Bird* also centers around the efforts of the protagonist, a writer for Superman comics, to talk about HD with his parents, who tried to protect their children by keeping the disease hidden and who struggle with shame and guilt themselves [14]. Sometimes secrecy is shown as a strategy of self-protection, especially in relation to marriage and childbearing: the von Kleist brothers in Kurt Vonnegut's 1985 sci-fi novel *Galapagos* keep their risk secret out of a desire to protect both their relatives and themselves. For "if it had been generally known that the brothers might transmit Huntington's to their offspring, all the von Kleists would likely have found it difficult to make good marriages..." [15].

How accurate were portrayals of HD symptoms and etiology? Fiction and television dramas tended to emphasize the horrors of HD—"one of the real 'nasties'"—no doubt as much for dramatic effect as for an attempt to be realistic [10]. Most correctly noted the 50-50 risk (some spelled out autosomal dominant inheritance) and the fact that HD is a "disease of the brain" that affects behavior and causes involuntary movements, described variously as "dancing," "jerking," "twitching," "spasms," "fidgeting," "lurching" and so forth. Some authors also alluded to atypical symptoms such as "hallucinations" and "delusions," using popular language such as "going crazy" or becoming "insane" or "madness" to describe cognitive and mood disturbances although these terms are inappropriate. In its portrayal of the thuggish Baxter, a man with the slight choreic movements of early HD, Ian McEwan's 2008 bestseller *Saturday* plays on familiar stereotypes of the person with HD as violent and destructive and the person with disabilities as a villain. As Nancy Wexler and Michael Rawlins have shown, the surgeon-narrator

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in this novel, Henry Perowne, views Baxter almost as if he were a monster, reducing him to the sum of his symptoms and implying that all his bad actions can be attributed to his HD [16–18].

Nonetheless, as medical knowledge has advanced and HD and disability awareness have increased, the portrayal of HD has generally become more realistic and multifaceted, with characters who respond proactively despite the frequent mantras “untreatable and incurable” and “nothing to be done.” For example “House” shows Thirteen enrolled in a clinical drug trial. Pierre Tardival, the protagonist of Robert Sawyer’s 1997 sci-fi mystery *Frameshift*, attends an HD support group. A genetics researcher at the University of California, Berkeley, Tardival is a man with 79 CAG repeats (which should have given him juvenile HD actually). He marries and has a child through in vitro fertilization and preimplantation genetic diagnosis. He also fights genetic discrimination while uncovering a conspiracy against people with disabilities. Even as his symptoms emerge, he does genetics research for as long as he is able [19].

The American protagonist of *A Partial History of Lost Causes* also goes on a quest inspired by her awareness of carrying the aberrant HD gene. After her chess-playing father dies with HD, she decides to pursue his haunting question: “how one proceeds in the face of catastrophe, how one gracefully executes the closing moves of a doomed game...” In St. Petersburg, Russia in 2006, she becomes the confidante of a former chess champion turned opposition political leader, an idealistic man who runs for president against Vladimir Putin with no hope of winning and whose life, under constant death threats, helps her find value in her own [12].

If *A Partial History* and *Frameshift* employ the motif of racing against time before catastrophe strikes, Octavia Butler’s sci-fi short story “The Evening and the Morning and the Night” challenges the notion of “catastrophe” altogether. It is also one of the earliest HD stories, published in 1987 by the only African American author in the group. In this tale, the young protagonist Lynn carries two copies of the gene for what Butler calls Duryea-Gode disease or DGD, a fictional disorder that combines features of HD, PKU, and Lesch-Nyan disease. Lynn knows it is “only a matter of when: now or later.” However in Butler’s vision, “DGDs” have talents favorable to aesthetic creation, if only they can live in a supportive community that constrains their self-destructive tendencies. When Lynn and her boyfriend, another double DGD, visit such a

community, they see the possibilities. As a female double DGD, Lynn learns she has additional gifts that make her especially sought after as a resident [20]. In this story, according to literary scholar Gerry Canavan, the disease “need not be understood solely as a tragic, ultimately meaningless fall from grace, but [as part of] a fully human life that can retain its own dignity and vitality despite hardship” [21]. It is interesting that Butler was one the few writers to imagine a scenario in which HD could be prevented or cured. In her 1988 trilogy *Adulthood Rites*, she describes one character inducing in another “an enzyme that turned off the Huntington’s gene,” much like the process of gene silencing today [22].

In conclusion, these stories and TV dramas offer a window onto popular perceptions of HD disease during the years of the Human Genome Project and the decade after. They suggest both the persistence of eugenic assumptions and the emergence of new ways of thinking about disability. Above all, by speaking about HD, they help dispel the silence and shame that have long added to the suffering caused by this disease. The fact that HD is now well enough known to be part of the backstory for the award-winning twenty-first century TV series “Breaking Bad” suggests how much has changed [23].

Hopefully in the future we will see more accurate portrayals of genetic testing for HD and a greater diversity of HD characters (most of the current ones are of predominantly European ancestry and live in North America or Western Europe). We will see characters managing the illness in the way that, say, the actor Michael J. Fox manages his Parkinson’s disease; stories illuminating the social conditions that add immeasurably to the burdens of HD and dramas that imagine new social environments to enhance lives with HD. By opening up conversations about HD, these forms of popular culture offer a valuable addition to the physician’s armamentarium and an important resource for medical and science students, clinicians, HD families, and the general public alike.

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Drug Improves Huntington's Symptoms in Mice – and Their Offspring

HD drug changes DNA folding across generations

By Dr Melissa Christianson, Edited by Dr Jeff Carroll

In Huntington's Disease, one of the many problems arising from the disease mutation is that DNA gets folded incorrectly. A new study in mice reveals that a drug changing the way DNA folds may have beneficial effects in Huntington's – even for the untreated offspring of treated individuals. This discovery could affect how we think about drug therapies for Huntington's Disease.

Science's Big Rivalry

Everyone loves a good rivalry – Microsoft versus Apple, Coke versus Pepsi, Hector versus Achilles – and scientists are no exception. For scientists, one of the biggest rivalries of all has to do with how we become the people we are. Are we born into the world pre-determined to be what our genes and DNA tell us, or are our selves – along with the health we enjoy and diseases we suffer – determined by the environment we experience? In other words, which is more important: nature or nurture?

As in many rivalries, both the DNA side (nature) and the environment side (nurture) both have strong support in their camps. However, it's becoming clear that the answer won't be black and white but instead an in-between shade of gray. New research shows that nurture can sometimes even affect nature, and at the root of it is DNA.

Know When to Fold 'em

DNA, the body's genetic code, is the longest instruction manual on Earth. If you were to take all of the DNA from just one cell in your body and stretch it out straight, it would be about two meters long. Since you can fit about 10,000 average human cells on the head of a pin, this means that those two meters of DNA must be folded up really tightly to make them small enough to fit inside of a cell.

DNA folding is doubly important, because it also allows different cells in the body to receive different genetic instructions from the same DNA instruction manual. Have you ever wondered

how a cell in your toe knows how to be a toe cell and not an eye cell? In part, it comes down to DNA folding and the resultant covering (or uncovering) of specific genetic messages. Even though every single one of the cells in your body has the same DNA, different cells with different jobs have their DNA folded differently.

You can think of DNA kind of like a square of paper that you'd fold up when making an origami flower. To make a flower, the paper must be folded in a very precise way, such that some parts are hidden inside the flower and other parts are visible once the flower is made. If you had written down instructions on the paper before folding it, only some of the original writing would be visible once you finished folding up the flower. The others would be hidden inside the flower's folds.

In just this way, only some of the genes (instructions) in DNA are visible at any given time to a cell in your body.

On the Mark

As you might guess, this DNA folding is a well-honed process. DNA has special chemical marks on it that mean the equivalent of "fold here" or "unfold here". Following these different folding directions leaves different pages of the genetic instruction manual free for reading.

These marks, and the resulting folding/unfolding of DNA and gene expression, are called "epigenetic". Just like your DNA (which you receive at the moment of conception from your mom and your dad), epigenetic marks can get



Each cell of the body has a massive amount of DNA to keep track of. Cells fold and organize this genetic information in a very careful way, like a perfectly folded origami flower.

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handed down from parent to child. Unlike your DNA, though, the epigenetic marks can also move around or change. Things like stress, diet, and toxins affect the marks, and so these same things can affect DNA folding and, ultimately, the genetic instructions that get read from your DNA instruction manual.

Altered DNA Origami in HD?

So, what does all of this DNA origami business have to do with nature versus nurture and Huntington's Disease? In Huntington's Disease, we know that one tiny section of the DNA instruction manual gets repeated too many times. This change falls into the "nature" realm; correcting it at the DNA level would be really hard, since this would require altering the DNA makeup of each of the trillions of cells in a human body.

However, scientists think the Huntington's mutation also messes with the DNA folding process. Even a small change in the folding instructions could cause major problems. As anyone who has ever tried to make a paper crane knows, doing just one step out of order virtually ensures that you won't have a properly folded crane at the end. Similarly, if the markers telling the DNA where to fold get changed, then the DNA won't be folded in the right way. The wrong genes will be visible at the end of the folding, and this could lead to disease.

However, this DNA-folding problem is approachable in a way that the straight DNA problem isn't. Since we know that things in the environment (i.e., those in the "nurture" category) affect DNA folding, maybe we can use these to correct the DNA folding problem.

Can We Re-Fold DNA?

With this idea in mind, scientists have started searching for ways to reset the DNA folding markers in Huntington's Disease and other diseases. If they could do this, they think they could potentially re-fold DNA and correct the genetic instructions available to cells of the body.

One way to change these markers is by using drugs known as HDAC (pronounced h-dack) inhibitors. HDAC inhibitors are all the rage in Huntington's (and, more generally, neuroscience) research right now: in several animal models of

Huntington's, they can alleviate symptoms and even prolong lifespan. There are already a number of early stage clinical trials ongoing to determine if HDAC inhibitors are safe in humans.



When DNA is stored and folded incorrectly, cells have a difficult time finding the genes they need. This seems to be happening in brain cells in HD, and fixing the problem might go some way to helping brain cells in HD stay healthy.

Putting It to the Test

A group of scientists at the Scripps Research Institute has been trying to figure out exactly how and why HDAC inhibitors improve models of Huntington's disease in the laboratory.

These scientists took male mice with a mutant human Huntingtin gene and treated them with a HDAC inhibitor, one already known to be beneficial in animal models of HD, for a month. As they expected, drug treatment changed the folding marks (and thus the genetic instructions being read) in the cells of the male mice and delayed the onset of Huntington's-like symptoms.

Then, the researchers did something really cool.

Since they knew that folding marks can get passed down from parent to child (just like DNA), they allowed the drug-treated male mice to mate. Excitingly, the offspring of the treated mice had a delayed onset for their HD symptoms, with improved motor function and cognition. These improvements were particularly pronounced in male offspring. Further, the offspring, none of whom had ever been treated with the drug, even had some of the same DNA folding patterns as their treated fathers.

All of these changes occurred without altering the DNA code, just by changing the pattern in which it was folded!

The Bottom Line: What Does This Mean for HD?

Scientists are still figuring out what this very new information means. In theory, this work is exciting because it's the first example of an

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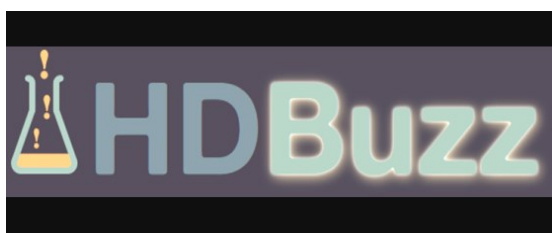
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improvement in symptoms across generations due to moving about the DNA folding markers.

Whether this type of cross-generational effect would happen in humans (who are way more complex than mice) and in both genders (only male mice were treated in the study) remain to be determined, as does whether such improvements could persist through more than one generation. More importantly, this work is still very early-stage, so scientists don't yet understand how altered DNA folding patterns actually improved the Huntington's symptoms in the mice. All in all, translating this work to humans is still some time away.

However, this research is really interesting, because it gives us new ways to think about a class of drugs that are just beginning to be used in human patients. Although it's still in its infancy, this type of treatment could lead to better understanding and better development of future drug treatments for HD.

Acknowledgement: www.hdbuzz.net



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AHDA (NSW) Inc

The Australian Huntington's Disease Association (NSW) Inc is a not-for-profit organisation established in 1975.

Our Mission

The energies and resources of the Australian Huntington's Disease Association (NSW) Inc are directed towards satisfying the needs of people with or at risk for Huntington's Disease and their families in NSW and the ACT by providing and/or facilitating delivery of a range of quality services.

Our Philosophy

People with Huntington's Disease and their families are individuals with equal value to all other members of Australian society, with the right to treatment and care by knowledgeable professionals and care givers, the right to appropriate support services and the right to have the best quality of life possible.

Our Services

These include education and information; advocacy; counselling and referral; holiday programs; family support; rural outreach and client services.

Our Board

President: Brian Rumbold
Vice President: Deb Cockrell
Treasurer: Richard Bobbitt
Secretary: Amanda Dickey
Member: Felicity O'Neil

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