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FIVE MINUTES with Baroness Greenfield

### NEWS IN BRIEF:

 Summit to end Parkinson's

• Nature, nurture and the brain

> • A new path for schizophrenia treatment

# ASK a Researcher:

How does hearing loss influence dementia?

Lifting the lid on chronic traumatic encephalopathy (CTE)

# Mind over pain:

Could understanding our emotions be the key to unlocking chronic pain?



#### Letter from the CEO



As we near the halfway mark of 2024, it brings me great pleasure to reflect on two significant achievements for NeuRA so far in this year. These particular milestones

are examples of our commitment to advocacy and policy-informing research, reinforcing our vision to not only continue making strides in science, but ensuring that our discoveries lead to real-world impact.

Dr Claire Shepherd and the Sydney Brain Bank team recently made headlines, demonstrating NeuRA's dedication to research that resonates beyond the scientific community. Dr Shepherd's work on chronic traumatic encephalopathy (CTE) in former rugby players not only made waves in national media, but gained international traction, while offering critical insights that will steer public discourse and policy on sports safety well in to the future.

Earlier this year, Professor Carolyn Sue AM took on the role of Chair at the National Parkinson's Alliance's Summit in the nation's capital. The Summit united a diverse group, from parliamentarians, clinicians and researchers to individuals with lived experience of Parkinson's disease. Together, they worked towards a shared aim: to amplify the conversation on Parkinson's disease and to champion the development of a National Parkinson's Action Plan. It is our priority to continue playing a part in driving these critical efforts to align research insights with the direction of public policy.

I continue to be deeply grateful for the support that you, our donors and supporters, bring to our mission. Your support is the bedrock of our progress.

As we look ahead to the second half of the year, I am confident that we will continue to go from strength to strength. We are on a path to making brain health a priority in public policy and individual wellbeing, and I look forward to continuing this journey with you.

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Matthew Kiernan AM CEO, Neuroscience Research Australia



From left: NeuRA researchers Professor Sylvia Gustin and Ms Nell Norman-Nott,

and Ms Nell Norman-Nott, explore the power of emotional regulation in tackling chronic pain on page 4.

# Welcome to the Autumn edition of NeuRA Mag!

# We invite you to discover our latest advancements and scientific updates.

In this issue, we delve into the perennial debate of 'Nature vs nurture', featuring the latest research from NeuRA's Centre for Wellbeing, Resilience and Recovery. We also share a promising avenue for personalised medicine in schizophrenia treatment, focusing on the potential of the drug raloxifene.

Our main feature, 'Mind over pain', explores the power of emotional regulation in tackling chronic pain. NeuRA researchers Professor Sylvia Gustin and Ms Nell Norman-Nott have led this fascinating area of chronic pain research, where they discovered psychological resilience to be a vital tool in chronic pain management.

We also hope you enjoy an exclusive Q&A with our special guest this month, world-renowned neuroscientist, Baroness Susan Greenfield CBE, as she shares her insights on neuroplasticity, the impacts of digital technology on young minds and the future of Alzheimer's treatment.

We hope this issue offers valuable insights into our research and as always, we look forward to your feedback. •



# Professor Carolyn Sue chairs Summit to End Parkinson's in Canberra

Renowned clinician scientist, Professor Carolyn Sue AM, was recently invited to Chair the National Parkinson's Alliance's Summit to End Parkinson's at Parliament House in Canberra.

Bringing together more than 100 parliamentarians, clinicians, researchers, community representatives and people with lived experience, the Summit was held to raise awareness of the immediate and critical needs of Australians with Parkinson's disease and seek government support for developing a National Parkinson's Action Plan.

"With increased investment and coordinated research effort Australia has the potential to make major contributions towards the development of preventative treatments, and ultimately a cure, for people living with Parkinson's disease," said Professor Sue, Kinghorn Chair, Neurodegeneration at NeuRA. •



# A new path for schizophrenia treatment

Could raloxifene, a drug that acts on oestrogen receptors in the brain, be the key to better treatments for schizophrenia? Hope is on the horizon, according to NeuRA researchers Sophie Debs and Dr Tertia Purves-Tyson, who recently published a study in *Brain, Behavior, and Immunity,* indicating that raloxifene changes gene expression related to the neurotransmitter dopamine and modifies dopamine-influenced behaviour in a way that varies by gender. This ongoing research opens new possibilities for improved symptom management in schizophrenia, paving the way for more personalised treatment approaches.



## Nature vs nurture

Scientists at NeuRA's Centre for Wellbeing, Resilience and Recovery have gained new insight into how the brain handles emotions and cognition, identifying a complex interplay of genetic and environmental factors.

Using functional magnetic resonance imaging (fMRI) scans on twins, the study, featured in the journal Human Brain Mapping, demonstrates that our brain function is shaped by both our genetic makeup and life experiences.

"Knowing what areas of our brain function are linked strongly to our environment can help us develop personalised intervention approaches to promote higher mental wellbeing," said Associate Professor Justine Gatt.

This intricate analysis of twin data provides a deeper understanding of the 'nature vs nurture' impact on brain activity. Mind over pain: Could understanding our emotions be the key to unlocking chronic pain?

The adage "mind over matter" is often used in the context of overcoming pain or discomfort, but new research led by Professor Sylvia Gustin, Senior Principal Research Scientist at NeuRA & UNSW Science and clinical researcher Ms Nell Norman-Nott, has found there is in fact, a scientific basis to this age-old saying.

he study, published recently in the European Journal of Pain, suggests that emotional regulation could play a more important role in managing chronic pain than previously thought.

Chronic pain is not just a condition of physical discomfort; it is deeply intertwined with emotional and psychological health. Individuals suffering from chronic pain frequently experience escalating and uncontrollable levels of worry, fear, sadness, anger and guilt. This emotional burden significantly affects their quality of life and complicates the management of their condition.

According to the Australian Institute of Health and Welfare, compared with individuals who do not suffer from chronic pain, those who do are 2.5 times more likely to experience mental health problems. This statistic underscores the complexity of chronic pain, which affects 30 per cent of the global population. Traditional approaches to managing chronic pain have focused on physical treatments and pain medications, many of which can carry unwanted side effects. However, the potential to alleviate pain through managing our emotions was a relatively untapped area of research – until now.

Professor Gustin's and Ms Norman-Nott's work into understanding the psychological aspects of pain found that psychological interventions focused on regulating negative emotions can significantly decrease pain intensity.

"By changing how we manage negative emotions, we may be able to change the experience of pain itself," said Ms Norman-Nott. "We found this not just to be a temporary relief but to have the potential for long-term improvement in quality of life for those affected by chronic pain." This finding implies a profound connection between the health

### Cracking the code to chronic pain

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of our emotions and the experience of physical pain, highlighting the role of emotional resilience as a pivotal component in chronic pain therapy.

The study, the first of its kind to aggregate decades of research in a systematic review and meta-analysis, identified that





Australians aged 45 and over are living with persistent, ongoing pain. Individuals who live with chronic pain are **2.5 times more likely to experience poor mental health** than those who don't.



incorporating emotional-focused skills to manage stress, anxiety and low mood – such as resilience building and enhanced emotional expression – can lead to a sustained reduction in pain levels.

Specifically, analysis of eight rigorously conducted trials involving over 900 participants revealed that patients who underwent interventions that included emotion regulation skills experienced a notable decrease in pain intensity, a benefit that persisted over time.

Following these interventions, patients reported an improvement of 10 points on a 100-point scale for measuring pain intensity observed both immediately after intervention and at subsequent follow-ups. Not only is this improvement statistically significant; it is potentially life-altering. "For an individual experiencing chronic pain, a decrease of 10 points on the pain scale can significantly alter their daily experience, potentially transforming a day dominated by pain and isolation into one that is productive and enjoyable," said Professor Gustin.

The implications of these research findings are clear: altering our emotions about pain may change our actual experience of pain. To translate these findings into practice, Professor Gustin and Ms Norman-Nott have developed the Emotional Recovery Program, an innovative, internet-delivered intervention aimed at equipping patients with the necessary skills to regulate their emotions and, by extension, their pain.

You can find out more or express your interest in participating, here:



### Under the microscope



Centre to right: Microscopic images without CTE and with CTE.



Dr Claire Shepherd.

# Australian-first case series from the Sydney Brain Bank finds CTE in former rugby code players

Research from the Sydney Brain Bank at NeuRA has shed new light on chronic traumatic encephalopathy neuropathologic change (CTE-NC) in former rugby league and union players, and brings to the fore neuropathologies that often co-exist with CTE-NC.

TE is characterised by the presence of abnormal accumulations of a protein called tau in the brain. To diagnose CTE, an individual must display tau protein within brain cells around blood vessels in the folds of the brain known as sulci. Diagnosis can only occur at autopsy.

Published in the Journal of Neuropathology and Applied Neurobiology, the Australianfirst case series saw researchers analyse the brains of six former professional rugby code players in life and death, in collaboration with the University of Sydney, Alfred Health and Harvard Medical School.

The researchers found mixed neurodegenerative pathologies, including CTE-NC, were common across the group of players, who all had extensive exposure to collision sport and exhibited progressive cognitive impairment during life.

CTE-NC was identified in four out of the six cases. One additional case exhibited some characteristics of CTE-NC, but did not meet the full diagnostic criteria. Study lead and Director of the Sydney Brain Bank, Dr Claire Shepherd, said this research finding "adds to the growing body of evidence showing CTE is more commonly seen in individuals who have been exposed to repetitive head impacts".

Intermediate or high levels of Alzheimer's disease pathology were detected in four cases, and hippocampal sclerosis was seen in two of the six cases. Limbicpredominant age-related TDP-43 encephalopathy (a type of pathology that has been associated with problems with memory and thinking) was observed in all cases.

Dr Shepherd explained that the level of co-existing neuropathologies found in this cohort "clearly shows that more must be done to understand more about the relationship between head injury and – not only CTE but – all forms of neurodegenerative disease".

"While a growing awareness of CTE is incredibly important, it's also vital that clinicians keep an open mind to other neurodegenerative diseases Dr Shepherd explained that the level of co-existing neuropathologies found in this cohort "clearly shows that more must be done to understand more about the relationship between head injury and – not only CTE but – all forms of



neurodegenerative disease".

that may also be at play when individuals who have had high exposure to head impacts present with progressive cognitive decline or impairment. This is particularly important as other conditions, such as Alzheimer's disease or Lewy body disease, may benefit from treatment, whereas there is currently no treatment for CTE."

Dr Shepherd said Sydney Brain Bank researchers were incredibly grateful to the players and their families who were part of this case series, and the broader Former Elite-Level Athlete Brain Health Research Program.

"Their involvement contributes to the growing body of scientific knowledge of CTE-NC, as well the relationship between co-existing pathologies and repetitive head impacts. Every brain donation helps us to understand a new piece of the puzzle." •





Neuroscience luminary Baroness Susan Greenfield CBE joins us at NeuRA this May. Dive into our exclusive interview to explore her insights on neuroscience and the future of brain health.

During your career, you have often spoken about the concept of brain plasticity. Could you share how your research into neuroplasticity has reshaped our understanding of learning and memory?

Research into neuroplasticity has long been a focus for neuroscience. My own work has highlighted how environmental enrichment can effect transient coalitions of brain cells that in turn relate to levels of consciousness. More specifically, we know that when brain cells are stimulated, they grow branches (dendrites) which increase the surface area, thereby enabling the potential to make more connections. I have suggested that by making connections, we can personalise the brain to have an individual "meaning" to events, people and objects around us.

#### You've previously raised concerns about digital technology on brain development. Given our digital world, what key risks do young people face?

Given the plasticity of the brain, where neurons have less established connections, young minds have less 'sales resistance' to incoming stimulation and less ability to evaluate those stimuli in the context of previous events. Hence, young minds are particularly vulnerable to the perils of a world of two dimensions with only sound and vision. In turn, such a scenario will lead to a greater emphasis on supersensory stimulation, perhaps less wellbeing given a reduction in direct social interaction, and all that might result from a distancing of the real world.

As the founder of Neuro-Bio and a pioneer in exploring novel therapies for neurodegenerative diseases, could you share the breakthroughs on the horizon for Alzheimer's that you're most excited about, and how your research is contributing to these advancements?

Our research at Neuro-Bio differs from most mainstream approaches, in that it is based on an empirically validated narrative of how the neurodegenerative process occurs: we are thus able to develop a novel means of detecting the key toxin molecule driving the process as well as devising a means of intercepting it. I'm therefore very excited that in the not-too-distant future, this work could lead to (a) a biomarker that detects Alzheimer's before the symptoms appear, along with (b) a therapeutic that stops any more cells dying. The combination of (a) + (b) would lead to an effective treatment for the first time.

On the other hand, it could be that the popularity of neuroscience ensures that the brightest and best take up careers in this sector with inevitably exciting results.

#### As a female scientist who continues to have a successful and long-standing career in science, what changes have you witnessed in terms of gender equality within the scientific community?

Sadly, I have not witnessed as much change as is needed. However, over a career of some 45 years, I'm delighted that certain male chauvinistic attitudes are not as tolerated nor assumed to be as normal as when I started in science. Moreover, various schemes ensuring gender equality have again started to move the dial. That said, I still feel that female scientists can be at a disadvantage, not only because of prevailing attitudes of others but of a lack of confidence in themselves.

#### In your opinion, how do you envision the future of neuroscience evolving in the next decade?

It may be that the current increase in enthusiasm for big data overrides original thought: Karl Popper famously asserted that all science should be prompted by a falsifiable hypothesis, and I fear that it may become harder to suggest novel ideas that may actually eventually be wrong. On the other hand, it could be that the popularity of neuroscience ensures that the brightest and best take up careers in this sector with inevitably exciting results.





NeuRA (pictured left), answers a question from one of our supporters.

### How does hearing loss influence the development or progression of dementia, and could hearing aids help protect against it?

Hearing loss has been associated with increased dementia risk but researchers don't yet understand the causal mechanism for this. It could be due to the possibility that the factors which cause hearing loss may also cause dementia. Or there may be an increased risk due to lack of sensory stimulation that reduces neuronal connectivity, eventually leading to brain atrophy.

What remains unclear is the extent to which intervening in people with hearing loss will have a benefit for their future cognitive health. There have been mixed findings on this topic with some studies showing a benefit and some not.

A recent Randomised Control Trial led by a world expert Professor Frank Lin found no effect of hearing intervention in reducing cognitive decline in people with hearing loss, but sub-group analysis found that in those at risk of cognitive decline, there was a benefit. But in high functioning adults without risk of cognitive decline, there was no benefit. This is the first published large trial on this topic so I think that over the next few years we will get more evidence to guide clinical advice on this topic.

In the meantime, it's important to speak to your doctor if you notice changes to your hearing. •

### **Include NeuRA** in your Will

Including a gift to NeuRA in your Will is a powerful way to accelerate research that will transform people's lives. A gift of just 1% of your estate will allow us to deliver worldfirst clinical trials, effective treatments, early interventions and crucial research that we simply could not do otherwise.

With your gift, we will help people lead happier and healthier lives for longer and we will shape the future of neurological wellness for generations to come.



NeuRA's Bequest Officer, Lauren Moore, is available to help you to organise a gift in your Will and keep you up to date with NeuRA's research. Please feel free to phone Lauren directly on 02 9399 1093 or email bequests@neura.edu.au



**NeuRA** (Neuroscience **Research Australia**) ABN 94 050 110 346

Margarete Ainsworth Building, 139 Barker Street, Randwick NSW 2031 Australia Tel 1300 888 019

If you wish to update your preferred communications from NeuRA, please call 1300 888 019.



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