



## Centre for Healthy Brain Ageing (CHeBA) Sydney Centenarian Study

NEWSLETTER | April 2021

### Co-Director's Message

Dear Study Participant,

Greetings from the Sydney Centenarian Study team. It is my pleasure to write to you once again to thank you for your contributions to this study. While the study was making great strides toward the beginning of 2020, the onset of the COVID-19 pandemic forced us to suspend all our assessments. We were therefore not able to include many keen centenarians and could not follow up some of you already in the study. Your health has been paramount in our minds, and we hope that you have all come through this period with the optimism and resilience that centenarians like yourself are renowned for.



**Scientia Professor  
Perminder Sachdev AM,  
CHeBA Co-Director**

Even though we would like to continue this study indefinitely, we have had to suspend it as our funding finished at the end of 2020. There is still much work to be done with the data as well as the blood samples and brain scans that you have provided, and this will continue over the coming years. We are hopeful that we will soon secure funding once again to resume this work, as we think it is of the utmost importance to help secure the health of future generations.

In the meantime, on behalf of the team and indeed everyone in the Centre, our very best wishes to you for a healthy and joyful post-pandemic period.

Warmly,

Perminder Sachdev  
Chief Investigator, Sydney Centenarian Study  
Co-Director, Centre for Healthy Brain Ageing



Centre  
for Healthy  
Brain Ageing

# Study Coordinator's Message

Greetings from the team at the Sydney Centenarian Study (SCS). We hope this newsletter finds you in good health. We would most importantly like to thank you, our wonderful participants and informants, for the generous gifts of time and energy that you have given to the study.

In this newsletter, you will find a brief summary of a recent publication involving data from SCS, as well as "sneak peeks" of some centenarian research currently in progress by staff and students here at the Centre for Healthy Brain Ageing (CHeBA).

As reported in the accompanying message from Professor Sachdev, at this time SCS will be going into a hiatus for the foreseeable future. 2020 was an eventful year for the SCS, as indeed it was for Australian society and the world. At the beginning of 2020 we started our biggest recruitment effort to date. We invited eligible individuals aged 95 and over to join the study from three local government areas in the eastern suburbs of Sydney. We were delighted to receive an enormous response, with more than 60 individuals expressing interest in joining SCS. Throughout February and early March, it was an absolute pleasure to meet some of these newly recruited participants.

However, our recruitment effort was stopped in mid-March by the coronavirus pandemic, which shaped the remainder of 2020 for the study and for society as a whole. We could unfortunately no longer meet our new participants face to face. However, we were determined to continue to follow up our existing participants for their regular six-monthly follow-ups, and thus undertook phone interviews with as many as possible. We are incredibly grateful to the participants who were able to speak with us over the phone, or completed written questionnaires, throughout 2020. We also talked to many close family members and friends of our participants who gave us further perspectives about their life.

In October we farewelled our previous Study Coordinator – Dr Catherine Browning - who led the study through the challenges of the pandemic and was well-liked and respected by our participants. We wish Catherine well in her future endeavours. I stepped into the Coordinator role to steer the study through its final months. I was privileged to at last provide our participants newly recruited in 2020 with the opportunity to enrol in the optional components of SCS. These include the collection of blood or saliva samples to obtain genetics data, and MRI brain scans. In December we farewelled our Research Assistant Julia Riches, who had been an absolute delight to work with and helped the study accomplish so much during its final months.

The study has now been suspended, but if funding becomes available in the future, we will carry on from where we stopped. Meanwhile, we plan to work actively with the data we have collected so that the findings of this study can be communicated to all. Thank you so much again to all our participants and informants for your support and contributions to the study throughout 2020 and prior years. From all the staff at the Sydney Centenarian Study and the Centre for Healthy Brain Ageing, we wish you and your family a very happy and healthy 2021.



Fleur Harrison

Acting Study Coordinator,  
Sydney Centenarian Study



# Brain Donation

In our quest to understand and promote healthy brain ageing, discovering what differentiates a healthy brain from one with a disease like dementia is essential and requires examination of brain tissue. Like organ donation, donating brain tissue after your death can leave a legacy for future generations by providing the resource that researchers need to understand how the brain works and how to fight dementia.

The Centre for Healthy Brain Ageing collaborates with the Sydney Brain Bank and participants in the Sydney Centenarian Study are able to donate their brain to this program. By comparing observations from brain tissue with the huge volume of information we have collected over the course of our study, we hope to gain new insights into the neurobiological basis of ageing and dementia.



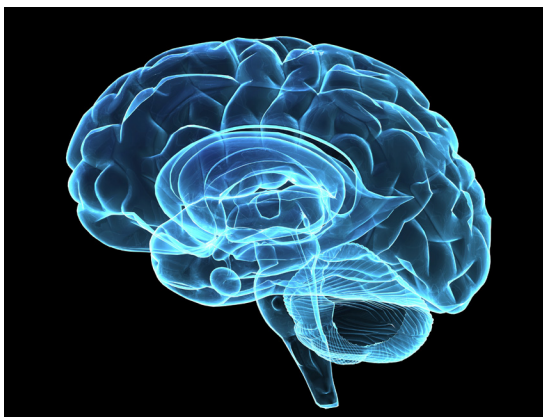
If you would like more information about brain donation or would like to register as a donor, please contact study staff on **(02) 9385 0433**.

## Research Highlights

### Sulcal Widening

Our brains have wrinkly folds. These folds are called gyri and grooves are called sulci. The reason our brains have these morphological features is to increase the capacity to house a larger surface of outer layer of the brain in a limited space of the skull than is possible in a smooth-surface. The outer layer of the brain is called cortex, and the cortex of our brain is responsible for higher cognitive processes like memories, language and consciousness.

The brain shrinks with increasing age and there are changes at all levels from molecules to morphology. The shape and size of brain folds change as well in ageing process. The shrinking cortex will give rise to sulcal shallowing and widening.



However, how the folds of the brains of centenarians respond to the ageing process had never been investigated due to the difficulties of obtaining MRI scans of this population. Using MRI scans of Sydney Centenarian Study participants, we found that most of the examined sulci significantly widened with increased age and the centenarians were no exception.

However, the rates of sulcal widening were lower in the centenarians in comparison with young old individuals (between 76 and 84 years), which meant that the shrinkage in this group of exceptional longevity participants was not happening as fast as the younger ageing population. How do we explain this interesting finding? Is this because to reach exceptional longevity you would need to have exceptionally 'good' genes in the first place and these 'good' genes give centenarians an edge in slowing ageing process? It seems that we have more work to do...

A slower rate of sulcal widening in the brains of the nondemented oldest old, *NeuroImage*, 2021.

DOI: <https://doi.org/10.1016/j.neuroimage.2021.117740>

# Upcoming Research



## Whole Genome Sequencing of Centenarian Samples Completed

### Dr Karen Mather

Longevity has a strong genetics component as shown by family and twin studies. For example, siblings of centenarians have an increased probability of reaching 100 compared to those without a family history of longevity. In the hope of finding genetic variants and molecular pathways that promote healthy ageing and longevity, we are interested in describing the genetic features of centenarians.

Although the minimum age for recruitment into the Sydney Centenarian Study (SCS) is a young 95 years of age, the study now has had at least 197 participants who have reached 100 years or older. We have recently completed whole genome sequencing of DNA from 101 centenarians, which provides us with detailed information about the genetic makeup of these long-lived SCS participants. Seventy-four percent of the sample sequenced were women, which reflects the gender difference in reaching 100 years and over. This newly acquired data allows us to look at different types of genetic variants, including genomic repeats - sections of DNA that can vary in their copy number and to estimate telomere length.

Telomeres are the DNA caps found at the ends of our chromosomes that have a protective function, which shorten as we age. Our preliminary results suggest that centenarians have shorter telomeres compared to younger individuals aged in their 70s. Future work will continue to compare the variation in centenarian genomes with individuals who have not survived to a great age. We will also evaluate the similarities and differences between different ethnic groups of centenarians from around the world, such as Japan. This exciting work puts us at the forefront of centenarian genetics research.



## A Longevity and Gene Expression Study

### Dr Mari Kondo

At CHeBA, we want to understand all aspects of the ageing process in order to help people to live healthily for as long as possible. The Sydney Centenarian Study (SCS) has been an extremely valuable source of data. As a researcher at CHeBA I want to tell you how much I appreciate your participation in the SCS. The project that I am working on is one of many that have been enabled by the data collected from the SCS.

In the CHeBA Genetics and Epigenomics laboratory, our aim is to understand the genetics and epigenomics of successful ageing. Epigenomics is one way genes can be turned on or off, and up or down, by many factors including our interaction with the environment we live in, the quality of our social life and cognitive stimulation, our diet, and our physical activity levels. By identifying the genes that are over- or under-expressed (ie turned up or down) in very long-lived individuals, we will be able to better understand what's happening in the body to facilitate successful ageing. The study I am currently working on aims to identify differences in gene expression between long-lived individuals (95 - 103 years of age) and people in their late 70s.

The long-lived group is comprised of SCS participants, while the late 70s group is from CHeBA's Sydney Memory and Ageing Study. RNA (ribonucleic acid), which tells us which genes are being expressed, has been extracted from donated blood samples. The levels of the different RNAs are being compared between the long-lived and the younger groups using a combination of cutting-edge and gold standard molecular biology techniques. The study is designed to detect gene expression differences between the groups and uncover whether these differences map to specific biological pathways that may be involved in living to an exceptional age.

# Meet Our Researchers



Dr Catherine Browning

**Did you experience a ‘defining moment’ which led you to this field?**

My interest in memory research was particularly sparked when I was studying cognitive science at university. I had an incredible lecturer and mentor who inspired a love for cognitive science that has stayed with me until today. My much-loved grandmother died in her 90’s with fully intact cognition but frail physical health, while I observed otherwise healthy young people close to me experiencing cognitive challenges. This all contributed to me deciding that I wanted to learn more about the complexity of memory, the brain, and how it ages.

**What are you currently researching?**

Now that I have left CHEBA, I would like to extend my own research. My PhD work investigated prospective memory, which is essentially remembering to do things in the future. Paying bills, keeping appointments, taking medication, buying milk and all the many things we are required to remember to do throughout our daily life are prospective memory tasks. All people struggle with this type of memory throughout their lifespan but if it declines, it is something that may determine whether you can live independently or not. The thing

about prospective memory that makes it so interesting is that it does not rely on memory alone. It involves other cognitive processes and regions of the brain. This is mostly the frontal region, which is involved in planning, initiating activities, and paying attention to your environment. When you need to remember to buy milk, many complex “executive” processes are required in addition to just memory. So, when we complain that our memory is poor because we forget to do the things we need to do, it is not just memory that we are talking about! Importantly, it is predicted that difficulties in prospective memory - which are not captured in our standard memory tests - might foreshadow later cognitive decline. I would like to demonstrate this in my future research.



***Dr Browning with her son James, husband Graeme, and daughter Emma***





Fleur Harrison

**What are you currently researching?**

I'm currently working on my PhD on how to assess apathy, in particular, how do we differentiate between apathy, depression, and fatigue? There are commonly used questionnaires for depression which include questions about apathy and fatigue, which could be used for accurate assessment and to guide diagnosis. However, there is very little research indicating whether using questionnaires to differentiate the three is valid or clinically useful.

I've also added a biological aspect to my research. There is a fast-growing area known as biological psychiatry, which investigates whether conditions considered a "mental health disorder" have underlying biomarkers. There is strong evidence that the immune system is linked with our mental health, although our understanding is still limited to fairly broad-brush strokes. For my research, I'll be looking to see whether apathy is linked to higher levels of markers of inflammation, known as cytokines. This would provide insight into a possible underlying cause for apathy, and also how it may potentially be treated.



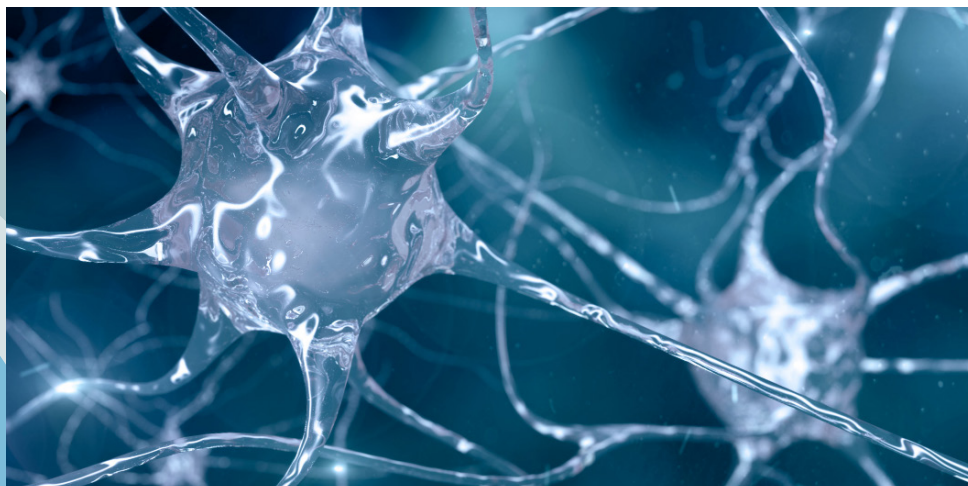
*Fleur, who loves horse riding, is pictured here with 'Menzies'*

**Why is your research important?**

Little research has been completed on apathy. It's a complex yet under-researched topic, which has a profound impact on an individual's function and ability to live a fulfilling life. Apathy is at the intersection of a number of academic fields, such as psychiatry, geriatrics, psychology and immunology, which means my research may potentially have a positive impact on people with many health conditions.

**What do you love about working for CHeBA?**

In my work on the Sydney Centenarian Study, I really just adore speaking to our participants, having a human connection with them, and learning about their fascinating lives. And more broadly, CHeBA has just so many talented people working with such a diverse range of methodologies – neuroimaging, genetics, epidemiological cohort studies – it's very exciting!





**Julia Riches**

**Did you experience a ‘defining moment’ which led you to this field?**

During my undergraduate studies I was unsure about my future path, but after working in my first research role at UQ, I discovered I was interested in the area of ageing. Meeting the Sydney Centenarian Study participants is a highlight of my role at CHeBA - especially experiencing firsthand the extremely valuable contributions older adults can make to research. When I finally got to meet CHeBA’s study participants I knew this was where I wanted to stay.

**Do you have any personal interests or activities which are protective behaviours against cognitive decline?**

I like to read a lot and taught myself how to crochet through YouTube videos. I have been crocheting a lot in lockdown – I finally finished a project I have been working on for a long time. At this stage I have only completed blankets, but I have just purchased a pattern to make a jumper for my next project. I hope learning new things keeps my brain active.



***Booties crocheted by Julia for a soon to arrive niece or nephew***

**Why is your research important?**

I think that, unfortunately, the value of older adults is often underestimated in the community. However, the contributions this group can make to research is enormously significant. I think it is important to learn as much as we can from older Australians. The more we understand about successful ageing and the health care requirements of this group, the better we can prepare for our future with an ageing population.



***Queenie, one of the lovely Sydney Centenarian Study participants, celebrates her 103rd birthday during the COVID-19 lockdown***

# StepUp for Dementia Research

One of the biggest challenges for dementia researchers is finding the right people to participate. As such, CHeBA has been a StepUp for Dementia Research 'Organisation Champion' since November 2020. Organisation Champions play a vital role in supporting the development of this free online, postal and telephone service that connects people interested in dementia research with researchers conducting studies into dementia prevention, diagnosis, treatment, care and cure.



Anyone aged 18 and over – both with and without dementia – can register their interest. Based on volunteers' characteristics such as age, location and diagnosis, they will be matched to any studies for which they may be eligible. StepUp for Dementia Research will improve recruitment into research studies, which has the potential to save millions of dollars and fast-track dementia research. Importantly, StepUp will give the public a voice and help them contribute to the future of dementia research. Ultimately, without research participants research cannot take place.

For more information and to register visit the StepUp for Dementia Research website: <https://www.stepupfordementiaresearch.org.au/>

## Stay Connected

### Join Our Mailing List

To stay up-to-date with the latest CHeBA research, news and events, subscribe to the CHeBA newsletter by emailing [h.douglass@unsw.edu.au](mailto:h.douglass@unsw.edu.au).

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