Seasons greetings from the Older Australian Twins Study! We hope this newsletter finds you in good health. We would like to take this opportunity to share some updates about the study and highlight some of our recent research findings with you, our participants and your relatives and friends.

The Older Australian Twins Study began in 2007 when the team received its first large grant for this longitudinal study from the National Health and Medical Research Council. Since then, over 350 twin pairs have assisted the Study team with their research, some participants on up to four occasions. The study’s history in numbers is shown overleaf.

Most recently, we have collected data, including beta-amyloid PET scans, from 207 twins. High levels of beta-amyloid detected in the brain are associated with Alzheimer’s Disease. On page 3 we describe how the PET data will allow us to determine the extent to which genetic and environmental factors contribute to accumulation of beta-amyloid.

Next year, the Older Australian Twins Study will be inviting our existing as well as new participants to contribute to the next stage of our study. To be able to extend our invitation beyond metropolitan regions, and to make the most of our resources, we will use an online computerised survey and assessment of cognition, and involve regional pathology services in collection of blood samples for genetic analysis.

Thanks to your generous participation in our research, the Older Australian Twins Study team have accumulated a mammoth amount of data on all aspects of ageing including memory and cognition, physical health, genetics, brain structure and mortality. These data have led to the publication of over 30 scientific papers in respected, international medical journals. Some of our recent findings are detailed on Pages 3-6. A complete list of our published research can be found on our website:

https://cheba.unsw.edu.au/project/older-australian-twins-study

To all of our participants and your relatives and friends that have contributed to our research, thank you for all the time you have given us thus far. We wish you a happy and healthy holiday season and we look forward to working with you for many years to come.
**Progress to Date**

**Wave 1**

Baseline assessment 2006 - 2012
n = 623 (23 siblings)

- Blood Tests n=553
- MRI n=417
- MZ twins n = 330
- DZ twins n = 266
- MZ triplets n = 3
- Unknown n = 1

**Wave 2**

Wave 2 assessment 2009 - 2013
n = 450 (1 sibling)

- Blood Tests n=399
- MRI n=293
- MZ twins n = 257
- DZ twins n = 192

**Wave 3**

Wave 3 assessment 2012 - 2016
n = 390

- Blood Tests n=349
- MRI n=237
- MZ twins n = 220
- DZ twins n = 170

**PET**

PET sub-study assessment 2012 - 2017
n = 207 (104 new participants)

- Blood Tests n=198
- MRI n=179
- MZ twins n = 125
- DZ twins n = 82

**Planned for 2018: Online assessment**
- Recent medical history
- Current medications
- Cognitive assessment
- Physical & social activities
- Mood
- Social cognition
- Blood test (optional)
- MRI scan (where feasible)
- Informant interview

**OATS Online**

**THANK YOU!**
Since 2007, over 350 twin pairs and 700 informants have assisted the OATS team with our research on up to four occasions.
What are the genetic and environmental contributions to amyloid “plaques” in older adults measured using brain scans?

Over the last five years, 207 of our Older Australian Twins Study participants have undergone a special type of brain scan (PET scan). The PET scan, sometimes referred to as a “PiB-PET” or a “NAV-PET” scan, reveals the presence of amyloid “plaques” (see images below). These plaques were previously only detectable by staining slices of brain tissue from deceased individuals. While still not well understood, the presence of amyloid plaques predicts memory decline and are a hallmark of Alzheimer’s Disease. However, some individuals have increased levels of amyloid in their brain without any apparent symptoms or memory problems.

Using the PET scan data we have acquired, we can now look for the presence of amyloid plaques and compare this information to the data we have collected in the participant interviews. While changes in certain genes are already known to increase the risk for amyloid accumulation in the brain and onset of Alzheimer’s Disease, many environmental exposures and lifestyle factors also contribute to a person’s risk of (or protection from) later developing Alzheimer’s Disease. Using the data from our PET study, we will be able to quantify the relative contributions of genes and environment to increased levels of amyloid plaques and to the symptoms of Alzheimer’s Disease.

The scanning of participants in this study was performed in Melbourne and Sydney. Unfortunately, the tracers (PiB and NAV) that are used to label the amyloid plaques so that they can be detected by PET scan are very unstable and must be used on the day they are prepared. At the time of commencing this study, Sydney did not have a facility capable of preparing the tracer. The tracer therefore had to be synthesised at Austin Health in Melbourne, and then rapidly transported to the PET scanners for use on the same day. We thank our participants for their time and for their forbearance as we worked around the logistical issues this presented.

In July 2017, Professor Sachdev presented preliminary results from this first large-scale study of amyloid imaging in monozygotic and dizygotic twins at the Alzheimer’s Association International Conference in London. Our team is currently busy analysing the final data and preparing articles describing the results for publication in medical journals.
In the media

“It’s a twin thing” - the Older Australian Twins Study featured on ABC’s Catalyst program.

A number of Australian twin research studies were featured on ABC’s Catalyst program in October 2017 (“It’s a twin thing”: www.abc.net.au/catalyst/), including the Older Australian Twin Study. The program highlights the complex interplay between genes and environment in determining physical traits and disorders, personality and brain health.

In the Catalyst program (~45 minutes in), Professor Sachdev discusses advances in identifying risk factors for dementia, including for Alzheimer’s Disease. While it was previously thought that inherited genetic traits present the greatest risk for Alzheimer’s Disease (~70%), new research suggest it may be much less, in the order of 35-40% of the risk. Professor Sachdev highlights three modifiable environmental factors that may decrease the risk of dementia. These are:

1. regularly performing complex mental activity
2. maintaining social engagements
3. doing regular physical activities

Many twins featured in the Catalyst program commented that having a twin meant they always had a mate or best friend, always had company and were never lonely. The close social bond and supportive relationship that typically exists between twins has previously been suggested to contribute to the longer life-span of twins relative to non-twins. But whether you are a twin or not, being mentally, socially and physically active is something we can all benefit from.

As part of our next assessments, the Older Australian Twin Study will be taking a closer look at how our ability to perceive, process and interpret social information impact on well-being in older age. This aspect of our work is funded by an Australian Research Council grant to Professor Perminder Sachdev and Dr Karen Mather.

Do you know any twins aged 65 years or older?

As well as inviting our current participants to continue their contribution to our study, the Older Australian Twin Study is seeking new research participants aged 65 years and above to help us discover the secrets to healthy aging.

Participation involves completing online questionnaires and assessments including answering some questions about your history, health, diet, memory and lifestyle. There is also the option to provide a blood sample and, if feasible, undergo a brain scan. Any older twin pairs from around Australia are invited to participate.

If you are interested in learning more, please contact the Older Australian Twins Study on 1800 818 946 or twins@unsw.edu.au
**Student and staff milestones**

**Depression in older age under the microscope**

The long road towards PhD completion is coming to an end for two students investigating genetic factors involved in late-life depression.

In her work, Ms Ruby Tsang found that genetic factors account for only a moderate amount of variability in late-life depression. She also found that genes regulating the generation of new neurons have altered patterns of DNA methylation (which control levels of gene activity) in individuals experiencing late-life depression. Ruby Tsang’s PhD studies at the University of New South Wales are supervised by Drs Reppermund and Mather and Professor Sachdev. Ruby was supported by the Viertel PhD Scholarship from Alzheimer’s Australia Dementia Research Foundation, and received a travel scholarship from Twins Research Australia in 2017 to present her findings at the 13th World Congress of Biological Psychiatry in Denmark and at the annual conference of the International Society for Affective Disorders in the United Kingdom.

Ms Liliana Ciobanu’s project utilises blood samples from elderly individuals to identify changes in gene expression networks and pathways associated with late-life depression. The observed changes were linked to variations in the genetic code of the same participants. Liliana Ciobanu’s PhD studies at the University of Adelaide are supervised by Professor Baune and Dr Toben. Liliana presented aspects of her work to the World Congress on Psychiatric Genetics in Jerusalem in 2016.

**Goodbye and good luck**

This year, the Older Australian Twins Study farewelled two long-standing team members. Many of our participants have met Christel Lemmon and Tanya Duckworth over the last seven years, as they travelled across Victoria and New South Wales interviewing twins about their life experiences and current health. Christel and Tanya truly appreciate the warm welcome they have received on their travels and are unanimous in having thoroughly enjoyed getting to know our twin participants and hear their interesting life stories. “Getting to know lots of interesting people, such as champion boxers, holocaust survivors, an actor, an anthropologist, a bishop, a professional tennis coach and an ex-flying doctor was a highlight of my work with the study” says Christel. Tanya adds that having started work on the study as an administrative assistant, then doing an Honours student project with the team and at the end working as a research assistant, she is grateful for the opportunities the study has afforded her in developing her research and clinical assessment skills.

Christel is still based at the National Ageing Research Institute in Melbourne. Her new role focuses on the experiences with aged and end-of-life care by elderly people, their loved ones, and the staff providing the care. Tanya was recently accepted into a Joint-Award PhD program through the University of Adelaide and the Technical University of Denmark in Neural and Complex Systems. She will be looking at the effects of creativity on neuroplasticity and cognition in adults with Post-Traumatic Stress Disorder, in partnership with Copenhagen Institute of Neurocreativity.

We wish Tanya and Christel all the best with their study and work.
Research Highlights

International collaboration to solve the enigma of genetic influences on brain structures

This year, data collected by the Older Australian Twins Study has contributed to the ENIGMA (Enhancing Neuro Imaging Genetics through Meta Analysis) Network’s research investigating the influence of genes and lifestyle factors on an important brain structure, the hippocampus.

The first ENIGMA study (published in *Nature Communications*) analysed genetic and MRI data from 33,536 individuals. The analysis identified 4 commonly occurring genetic variations that influence hippocampal volume. Three of the implicated genes are known to be important for neuronal cell migration, suggesting this is an important factor in determining hippocampal volume.

In the second study, analysis of data from the Older Australian Twins Study and four other twin studies demonstrated that while important, genetic factors account for only ~20% of the variability in hippocampal volume changes in adults. The flip-side to this is that modifiable lifestyle and environmental factors play a large role in determining changes in hippocampal volume.

This is important as a shrinking hippocampus is an indicator of conversion from normal ageing to impaired cognitive function and dementia. Using larger hippocampal volume as an indirect measure of good hippocampal function, below are some of the modifiable positive and negative factors affecting the hippocampus.

<table>
<thead>
<tr>
<th>Positive factors</th>
<th>Negative factors</th>
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<tbody>
<tr>
<td>Physical exercise</td>
<td>Obesity</td>
</tr>
<tr>
<td>A diet high in omega-3 fatty acids</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Treatment of vascular risk factors</td>
<td>Hypertension</td>
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<tr>
<td>Stress reduction and meditation</td>
<td>Clinical depression</td>
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<tr>
<td>Challenging yourself to learn new skills</td>
<td>Head trauma</td>
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The Centre for Healthy Brain Ageing (CHeBA) at UNSW Sydney has partnered with Kensington Public School to support Kids4Dementia (K4D), an education program improving students’ understanding of the condition to help create a more dementia-friendly society.

Dementia is the single largest cause of disability in older Australians (aged 65 years or older) and the third leading cause of disability burden overall. The number of Australians living with dementia is projected to almost triple from 413,000 now to 1.1 million by 2050.

The impact on children of having a family member with dementia is often overlooked and community knowledge of the disease remains poor, with significant social stigma attached to the illness. Currently, a third of young people know someone living with dementia, a figure set to increase rapidly.

K4D is an innovative, classroom-based program designed to improve young peoples’ social awareness by learning that a person with dementia is “still a person”, and not someone to ignore, fear, or laugh at.

Kensington Public School’s Year 6 students took part in the K4D program in early 2017. Students learnt about what causes dementia, how it feels to have dementia, how to keep the brain healthy and what happens in an aged care facility.

Thirteen teams of kids, parents, grandparents and friends participated in the Sydney Running Festival on 17 September 2017. They raised an incredible $15,000 which will go towards rolling the program out across 30 NSW schools.

Schools interested in implementing the K4D education program can contact Dr Jess Baker at kids4dementia@unsw.edu.au
Brain Donation

Brain imaging technology has improved markedly over the past few decades. However, even the most sophisticated imaging techniques cannot answer all our questions. To understand cellular changes in both healthy and disease-affected individuals researchers need to examine brain tissue.

The Centre for Healthy Brain Ageing collaborates with the Sydney Brain Bank and the Victorian Brain Bank. Participants in the Older Australian Twins Study are able to donate their brain to these programs if they wish. By comparing brain tissue to the huge volume of information we have collected over the last 10 years, 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 brain donor, please contact our friendly staff on 1800 818 946.

Meet the team

Suzy Forrester, Administrative Assistant (left)

Suzy has been an integral part of the Older Australian Twins Study team for 5 years, assisting with the administration and logistics of participant assessments. She very much enjoys her conversations with participants and appreciates the time they generously give to our study. Suzy is also studying for a Bachelor of Psychological Science at University of New South Wales.

Vibeke Catts, Study Coordinator (above, right)

Vibeke has a PhD in Biomedical Science from the University of Queensland. Prior to joining the Older Australian Twins Study in 2017, Vibeke performed molecular research studies to identify the underlying neurobiology of schizophrenia at Neuroscience Research Australia (NeuRA) in Sydney. She enjoys her new role as study coordinator and looks forward to seeing the research findings translate into the best possible quality of life for older Australians.

Researchers working on the Older Australian Twins Study spent a sunny day in November 2017 discussing our progress thus far and planning for the future.

WANT MORE NEWS?
Phone 1800 818 946 or E-mail twins@unsw.edu.au and ask to be put on the mailing list for the CHeBA Chronicle, distributed monthly via e-mail.