

Centre for Healthy Brain Ageing (CHeBA)

Older Australian Twins Study

NEWSLETTER | December 2021

Season's greetings from the Older Australian Twins Study (OATS)! We hope this newsletter finds you well. 2021 has been another challenging year with the COVID-19 pandemic. While we have become more used to the infection control measures, the restrictions on travel locally and overseas have prevented many of us from seeing those near and dear to us and being together to celebrate important life milestones. We hope the end of 2021 affords us all an opportunity to reconnect. We would like to take this opportunity to share with you some updates from OATS and highlight some of our recent research findings.

Since OATS began in 2007, we have been assisted by the participation of over 350 twin pairs along with their friends and family ("support persons"). Most recently, many participants braved the move to an online assessment. We know for some this has proven challenging, even frustrating, as you were forced to engage with the computer more intensively than would be normal for most people. Thank you for being open to accepting the challenge and for your ongoing commitment to our study. The silver lining of moving OATS Online has been that our study is resilient to the impact of COVID-19, and we hope the funding bodies will appreciate this unique aspect of our study when they review our current funding application.

As part of preparing our application for funding for OATS online, we sought detailed input on the proposal from a number of OATS participants. All participants and their support persons have also had the opportunity to provide feedback on their study experience during the questionnaire completion. We'd like to thank you for taking the time to tell us what you think. One suggestion was to provide a Certificate of years of service to the OATS study. If you'd like such a Certificate to include in your memorabilia or put on display, please let our Study staff know and we will arrange to have one mailed to you.

This newsletter features updates on some of the research based on OATS data that has been published in scientific journals in 2021. Many of our participants underwent a PET scan as part of their OATS participation and the key manuscript describing our findings, authored by Rebecca Koncz

has finally been accepted in *The Journal of Neurology, Neurosurgery & Psychiatry*. You can read more on page 4.

A PhD student, Abdullah Alqarni, has published an analysis of risk factors that contribute to the presence of vascular disease markers in MRI brain scans in the journal *Neurobiology of Aging*. Abdullah found that some risk factors appear to be unique to either men or women and some are common to both sexes. Abdullah's findings are featured on page 4.

A junior medical student, Siddharth Raj, published the results of his research project investigating the genetics of odour identification ability in the journal *Genes*. Siddharth found that the inability to identify the smell of chocolate is associated with higher genetic risks of being a smoker, of having Parkinson's Disease, and with the genetic risk for the presence of vascular disease markers in MRI brain scans. You can read more about this fascinating research on page 5.

We are very proud of our talented students and the contribution they make to our research, and feel privileged to be able to train them in research skills using data from OATS.

On behalf of the OATS team, our sincere THANK YOU for the contributions you have made to our study thus far. We wish you, your families and friends, a safe, peaceful and joyful festive season.



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

Scientia Professor Perminder Sachdev AM

OATS Online Journey One is Complete

Our first round of data collection for OATS Online, Journey One, is now concluded. The move from face-to-face to online assessments could not have come at a better time, with our first enrolments occurring during the first wave of COVID in June 2020.

Between then and July 2021, we enrolled 308 participants into the study, of whom over 250 completed their journey. During this time, we gave participants the option of completing either online or paper surveys. Over half of our participants opted to participate online, with 144 completing all activities online and 112 returning paper surveys. On average participants who completed their journey online spent around 8 hours doing the activities. This is a generous contribution of time to our study and we want to thank all our participants for their continued support. It is very much appreciated.

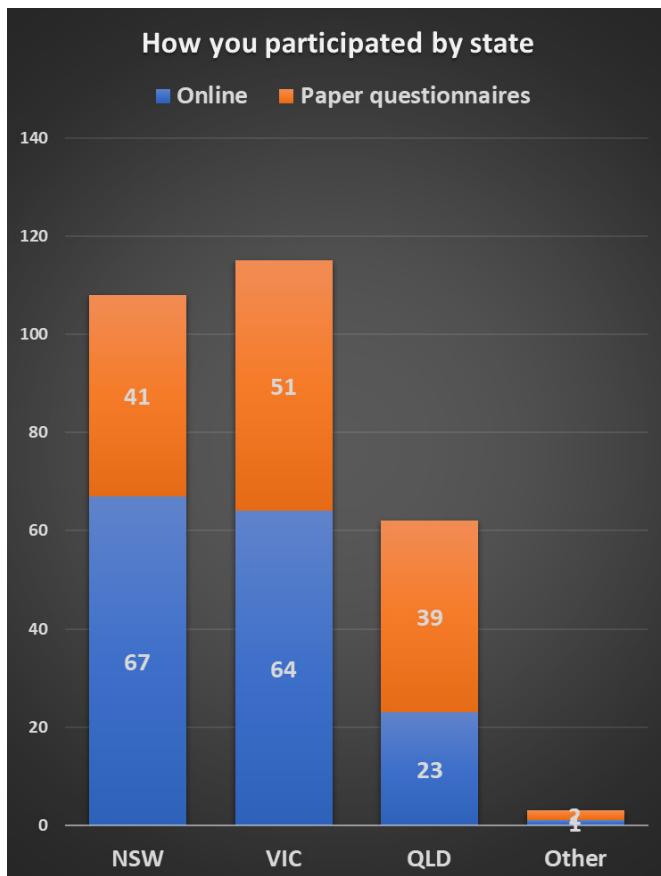
The change of format brought with it new cognitive assessments and the addition of measures of social cognition. These were met with mixed feelings by participants. Many missed the social aspect of face-to-face assessments and found the online assessments impersonal and less engaging. However, other participants preferred the flexibility of completing the assessments online. We want to thank all participants and informants for bearing with us during teething issues with the new system and the technical issues that some of you experienced.

Social cognition was another new component of OATS Online. The OATS team added two measures of social cognition because it is affected by cognitive decline and dementia. Reading the Mind in the Eyes, part of the Recent Mood and Personality survey, involved recognising emotions from images of eyes alone. The online Emotion Recognition Task involved identifying the emotions of short videos of faces. These tasks measure the ability to recognise and make judgements about other people's emotions.

Many participants found these tasks challenging. However, the results will provide valuable insights into social cognition and ageing. We look forward to sharing the results from these tasks with you in the future.

Unfortunately, because this is the first time we have used online tests, it has taken us longer than usual to give participants feedback on their cognitive performance. We want to thank you for your patience with this and assure you we are working to complete the feedback as soon as possible.

OATS Online Journey Two, which begins around 18 months after Journey One, commenced in November 2021 and will continue until December 2022. If you completed your Journey One online, you will receive an email when it is time to start Journey Two. If you completed Journey One by paper survey, you will receive a phone call from us to confirm that you are willing and able to participate in the Journey Two. If you have any questions or concerns, you are always welcome to contact us by phone, letter or email. We look forward to contacting you again for Journey Two!



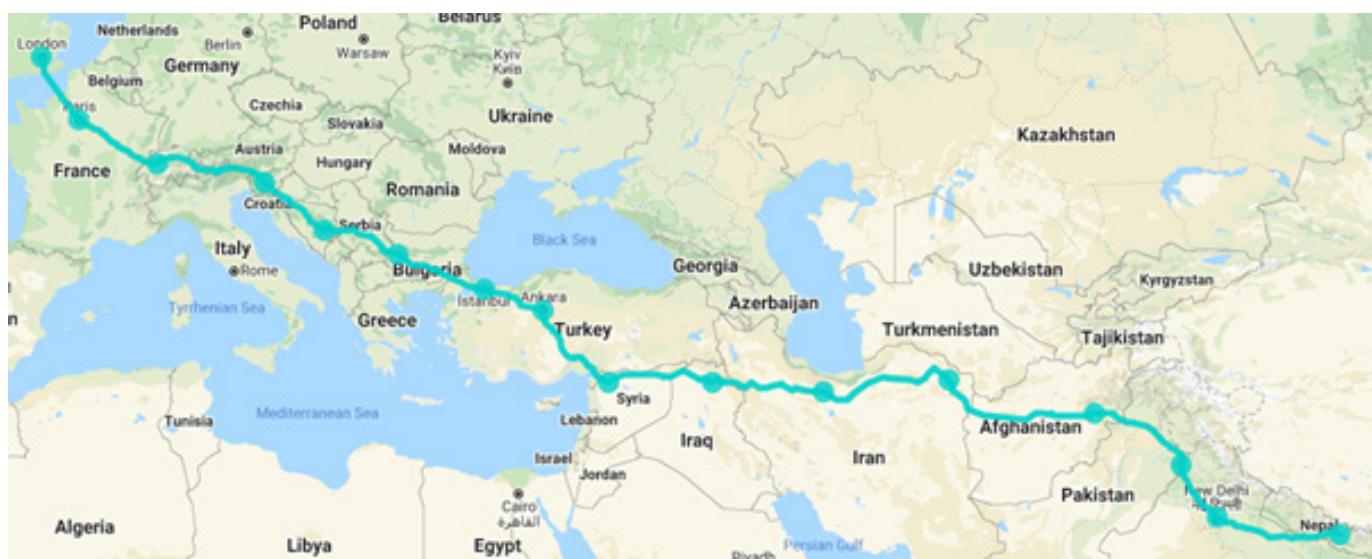
10,000kms During World Alzheimer's Month – CHeBA Lockdown Challenge

Through the month of September, CHeBA staff - including Dr Vibeke Catts, Amanda Selwood, Juan Carlo San Jose and Professor Perminder Sachdev from the OATS team - united virtually to clock more than 10,000 kilometres (nearly 15 million steps) from London to the Himalayas to promote the significance of social connectedness and physical health during Sydney's lockdown.

The ambitious virtual distance, commencing at the start of World Alzheimer's Month on 1st September, is a tribute to CHeBA's leaders, Professor Henry Brodaty AO and Professor Perminder Sachdev AM. In the early 1970s the system in New South Wales was that trainees for specialist training in psychiatry were required to spend their first year in a rural placement. As a young 26-year old, Co-Director Henry Brodaty chose London and as such, his first job as a psychiatry trainee was in the Academic Department of Psychiatry, Middlesex Hospital.

CHeBA's staff and students made their way across Paris, Switzerland, Slovenia, Sarajevo, Istanbul, Turkey, Syria and more all the way to the foothills of the Himalayas, in dedication of Co-Director Perminder Sachdev, who grew up in a small town near Shimla, the capital of Himachal Pradesh. Professor Sachdev completed his schooling at St Luke's School in Solan, just 1,000kms away from Kathmandu where this virtual walk concluded.

With evidence indicating that lockdowns can take a toll on our physical and mental wellbeing, the CHeBA Lockdown Challenge promoted the benefits of physical exercise and social connectedness, and raised more than \$6,000 for our Centre's research into early diagnosis, treatment and care for those with dementia, but also its prevention, and the promotion of positive ageing for the future.



Dr Vibeke Catts and Dr Amanda Selwood

Research Findings in 2021

Environmental Factors Significant in Alzheimer's Pathology

The question of the relative contribution of genetic vs environmental influences on brain ageing plays a major role in research. OATS researchers have revealed new insights into one of the hallmarks of Alzheimer's disease – amyloid plaques – by looking at the brains of identical and non-identical twins.

The study, led by OATS PhD student Dr Rebecca Koncz and published in *The Journal of Neurology, Neurosurgery & Psychiatry*, used a special type of imaging called amyloid PET, or 'position emission tomography' to quantify what proportion of amyloid accumulation is determined by genes, and what proportion is determined by environmental, or modifiable, risk factors such as high blood pressure and high cholesterol.

"Amyloid is a protein that accumulates in the brain very early in the development of Alzheimer's disease," said Dr Koncz. "It is a hallmark feature of the condition that starts to accumulate decades before memory problems become apparent."

The researchers discovered that the heritability of amyloid is moderate – meaning genes play only a moderate role in determining the variation in amyloid build up in the brain.

"This is significant, because it tells us that whilst genes are important, there is actually a major environmental contribution that may respond well to intervention" said Dr Koncz.



"With respect to modifiable risk factors, we examined whether vascular risk factors such as hypertension, diabetes, high cholesterol, or a history of heart disease were significantly associated with amyloid burden or had any shared genetic basis," said Dr Koncz.

While the study did not find a statistically significant association between vascular risk factors and amyloid, studies with larger sample sizes are required.

"Identifying modifiable risk factors will lead us to interventions that reduce the risk of amyloid accumulation – and ultimately risk reduction of developing Alzheimer's disease," said Professor Perminder Sachdev.

Men and women have different risk factors for brain changes

White matter hyperintensities are defects in the nerve fibres connecting different brain regions and the spinal cord. Generally, women tend to have more white matter hyperintensities than men. Health and lifestyle factors such as smoking, high blood pressure, obesity, and diabetes increase our risk of developing white matter hyperintensities later in life.

Mild white matter hyperintensities are common and can be asymptomatic. However, when they are severe, they can be associated with conditions such as vascular dementia and other forms of cognitive decline.

Abdullah Alqarni, a PhD student at CHeBA, used the brain imaging data from 179 OATS participants along with 432 participants from the Sydney Memory and Ageing Study to study the risk factors that contribute to white matter hyperintensities in men and in women. Are they the same risk factors or do they differ across the sexes?

His study, published this year in *Neurobiology of Aging*, found that having a high body mass index (BMI) increases the risk of developing white matter

hyperintensities in men only. However, women's risk of developing white matter hyperintensities was the same regardless of their BMI.

Other risk factors, including older age and high blood pressure, had the same effect on white matter hyperintensities in both men and women.

Alquarni's study opens up the possibility of preventing brain deterioration by moderating different lifestyle factors for men and women.



The Genetics of Smell

The ability to identify odours decreases with normal ageing. However, impaired odour identification can be associated with a diagnosis of Parkinson's Disease or Alzheimer's Disease, as well as other conditions. For this reason, OATS participants completed the *Brief Smell Identification Test (BSIT)* as part of the face-to-face cognitive assessments conducted in previous Waves. In the BSIT, participants identify 12 different scratch-and-sniff odours, such as cinnamon, turpentine, lemon, smoke, and chocolate.

Siddharth Raj is a UNSW Medicine student who completed a year-long Independent Learning Project on the genetics behind our sense of smell with OATS investigators Karen Mather and Anbupalam Thalamuthu in 2019. His paper examining the genes associated with performance on the BSIT was published in April this year in the medical journal, *Genes*. Five hundred and fourteen OATS participants were included in his study alongside 881 participants from CHeBA's Sydney Memory and Ageing Study.

He examined the association between odour identification and SNPs, which are tiny variations in DNA code between individuals. Raj found no SNPs associated with general odour identification ability. However, different SNPs may be associated with identifying particular odours.

Raj also investigated whether odour identification was associated with a person's genetic risk of conditions including Alzheimer's Disease, white matter hyperintensities, and Parkinson's Disease, as well a risk of being a tobacco smoker.

Genetic risk is the likelihood of developing a disease or pathology based on someone's DNA alone, not considering age, lifestyle factors, gender or other forms of risk. He found that general smell identification ability was not associated with the genetic risk of any of the included diseases.



However, participants who could not identify the smell of chocolate had a higher genetic risk of being a smoker, having Parkinson's Disease, or white matter hyperintensities. Interestingly, the inability to identify any of the other smells was not associated with the genetic risk of diseases examined.

Raj's study is one of the first to examine the links between genes and specific smell identification and adds to our understanding of the relationship between odour identification and ageing.

OATS Online Launch

A 15-year study investigating the impact of genetic factors compared with environmental factors on the brain health of twins, has taken advantage of technology by reaching twins residing outside of metropolitan areas.

The move to an online platform will not only enable the inclusion of 1/3 of Australian twins living outside major cities but will also facilitate the study of differences in access to specialist health care, health seeking behaviour and other potential contributors to the shortened lifespan of people living in regional and rural areas.

The Older Australian Twins Study, a major collaboration led by [UNSW Sydney's Centre for Healthy Brain Ageing \(CHeBA\)](#), has yielded important research in the world's quest for answers to the question of the role of 'genetics vs environment' in risk of medical conditions, including those associated with brain ageing.

Commencing in 2007 to investigate genetic and environmental differences and how they are related to either healthy brain ageing or age-related neurocognitive disorders, the study takes

advantage of the fact that identical twins share 100% of their genetic code, whereas non-identical twins share only approximately 50%. This means that twin studies provide a unique opportunity to identify which specific factors contribute, and which contribute the most, to health outcomes in older age.

The study has brought together geneticists and researchers in neuropsychiatry of older adults to examine key issues in cognitive ageing and dementia. It measures many behavioural and environmental factors, in particular lifetime physical and mental activity, physical and psychological trauma, losses and life events, early-life socio-economic environment, alcohol and drug use, occupational exposure and nutrition.

Since the study launched it has also measured blood biochemistry and collected genetic data.

Many features of the Older Australian Twins Study distinguish it from other investigations, including its longitudinal design, comprehensive neuropsychological assessments, brain imaging measures and links with a brain donor program.

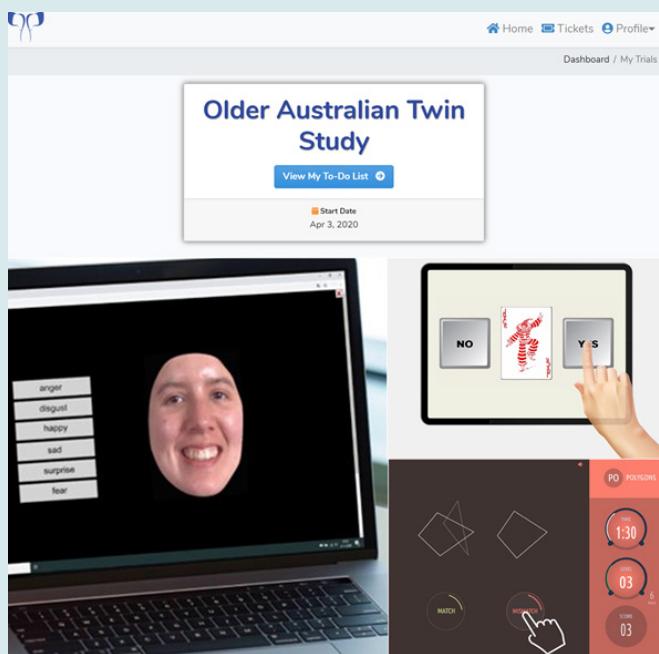
OATS Coordinator and Research Manager at CHeBA, Dr Vibeke Catts, said that advances in information technology – particularly the refinement of computer administered cognitive tests - now allows the researchers to carry out comprehensive and valid neuropsychological assessments with twins in their own home, using an online computer environment – something that was not feasible when the study first launched.

“In 2007, just over 50% of households without children under 15 had internet access at home,” said Dr Catts. “Today this has risen to over 80% with 91% using desktops or laptops to access the internet at home.”

“Partnering with twins across Australia, we trust that the advancement to an online study will be fruitful in furthering our understanding of the determinants of the ageing process and of age-related degenerative disorders,” said Dr Catts.

The twin study design is the best method for providing the strongest possible evidence for cause of disease from an observational study. We are aiming to include a younger group of twins and retain their participation as they age. Being able to acquire contemporary data through an online platform – rather than relying on participants’ recollection of their circumstances and health in midlife – strengthens the reliability of data obtained. An additional focus of the online study including a younger age group is to showcase that various interventions aimed at reducing risk factors earlier in life are likely to provide benefits across the individual’s remaining decades.

According to Professor Perminder Sachdev, Co-Director of CHeBA and Project Leader of the Older Australian Twins Study, “the depth and breadth of data collected in combination with the very large twin sample envisaged as part of taking the study online makes it unique in Australia and internationally.”



“Being able to include twins residing outside of cities on the Eastern seaboard of Australia will help us further identify which personal characteristics or circumstances contribute to healthy brain ageing compared with Alzheimer’s disease or other dementias.”

Professor Perminder Sachdev

“Given we know the deposition of a marker of Alzheimer’s pathology in people without dementia is only moderately determined by genetics, it suggests there may be many modifiable risk factors for this common type of dementia,” said Professor Sachdev.

Converting to an online platform will also lead to policy change and improvements in health care.

Since studies by the Australian Institute of Health and Welfare have shown that regional and remote populations are less likely to have convenient access to a General Practitioner, they are also much less likely to have local access to medical specialists. In contrast, populations in outer regional and remote areas have a higher rate of hospital admissions.

“Poorer access to local health care reduces the chance of early disease diagnosis and treatment, resulting in increased economic cost through higher rates of potentially preventable hospital admission and increased human cost associated with greater mortality – which in some cases would be preventable.”

Dr Vibeke Catts

“By studying the health seeking behaviour in twins across Australia, including twin pairs where one twin lives in a regional or remote area and the other twin in urban areas, our online study can investigate the relative contribution of risk and protective factors for healthy brain ageing – such as diet, exposure to suspected environmental risk factors for disease, health conditions, family history, occupation, income, educational attainment and employment opportunities – and ultimately better support the health and welfare of older Australians,” said Dr Catts.

The online version of the Older Australian Twins Study will retain a longitudinal design – which is a critical component in mapping progression to disorders of older age such as dementia - with

planned neuropsychological assessments at each assessment, as well as the collection of detailed lifestyle, mental activity, physical activity and dietary information. It will also continue to examine genetics.

While it will no longer focus on quantifying brain volume and other brain scanning measures associated with previous assessments in the Older Australian Twins Study, the amount and depth of data collected online will allow the researchers to assess multiple difference outcomes.

Older Australian Twins Study Online is targeting 1000 twin pairs with most participants to be healthy individuals living in the community.

"This large sample of twins will enable examination of risk and protective factors as well as outcomes that differ within each twin pair."

Dr Vibeke Catts

"We anticipate this online study will lead us to advances in research outcomes unseen before in relation to health and disease," said Dr Catts.

Thank you to OATS II Study Advisors

In August, OATS researchers submitted an application for a Clinical Trials and Cohort Studies Grant with the National Health and Medical Research Council to launch OATS II. If successful, we propose to recruit an additional 1000 twin pairs, extend the age range from 65+ to 50 years and above, use digital and blood-based biomarkers (biological indicators of disease), examine stool samples, and have a long-term longitudinal time frame that extends from OATS I (Fig 1). OATS II will be fully online and have a truly national reach that OATS I could not attain.

The digital platform recently used as part of OATS Online will be used again in OATS II.

To ensure OATS II was as good as it could be, we invited current OATS participants to be volunteer study advisors. We asked them to review the OATS II proposal from the perspective of an older adult in the community and an existing OATS participant. We are extremely grateful for the feedback we received from the thirteen study advisors we interviewed.

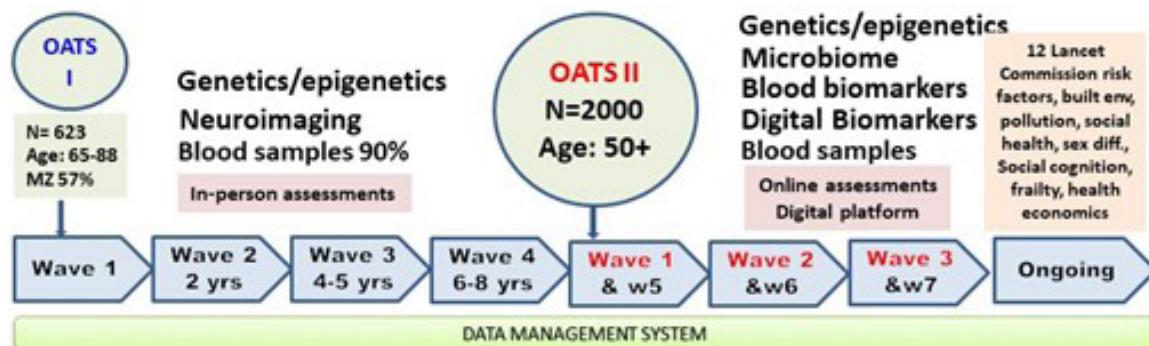


Fig 1: Flow chart of OATS II and its predecessor, OATS I.



OATS Online

In November OATS launched an online platform, which will not only enable the inclusion of 1/3 of Australian twins living outside major cities but will also facilitate the study of differences in access to specialist health care, health seeking behaviour and other potential contributors to the shortened lifespan of people living in regional and rural areas.

Visit the site: www.bit.ly/OATSONline



Stay in Touch

While we have mostly been working from home during the COVID-19 pandemic, you can still reach us using the study contact details below.

Write to us at:

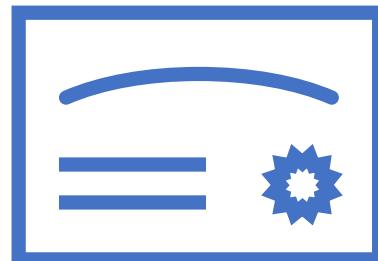
Older Australian Twins Study
Centre for Healthy Brain Ageing (CHeBA)
UNSW Medicine, School of Psychiatry
Level 1, AGSM (G27)
UNSW SYDNEY NSW 2052
Our toll-free number is 1800 818 946 and
you can e-mail us at twins@unsw.edu.au

Would you like a certificate for your years of service to OATS?

Many of you have been valued OATS participants since the study first began in 2006-2012, and a large proportion joined us in 2015-2017.

Your participation has allowed for the publication of over 60 scientific papers and nearly 20 student theses.

We are enormously grateful for your ongoing contributions to OATS. Therefore, we would like to offer you a certificate acknowledging your years of service to the study. If you would like to receive one, please phone or email us using the contact details at the end of the newsletter.



DID YOU CHANGE YOUR CONTACT DETAILS?

Please phone or email us and let us know.

WOULD YOU LIKE MORE NEWS?

In addition to the annual OATS Newsletter, you can opt-in to receive the CHeBA Chronicle, distributed monthly via e-mail. Just phone or email us and let us know.

You can also follow the Centre for Healthy Brain Ageing (CHeBA) on Facebook and Twitter.

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