UNSW SYDNEY | Australia's Global University

Centre for Healthy Brain Ageing (CHeBA)

COSMIC: Cohort Studies of Memory in an International Consortium

NEWSLETTER | June 2019

Dear COSMIC colleagues,

As we move well into the second year of the NIH grant, Darren and I are pleased to present to you an update of the various projects and activities within COSMIC. The growth has been exponential, and we are confident that the collaboration has reached a stage that it will begin to make a major impact on the field. The forthcoming paper in PLOS Medicine, which took nearly two years to complete, is a major milestone. It has already created a rich database for further exploration.

We would like to welcome you all at the brief session on July 16 in Los Angeles. If you are attending the AAIC, please do try to attend. You are welcome to bring any colleagues who have an interest to be part of the consortium.

On behalf of the Sydney team (Dr John Crawford, Dr Anbu Thalamuthu, Dr Steve Makkar, Dr Nicole Kochan), we want to thank you profusely for your generous contribution of data and time to make COSMIC such a vibrant endeavour. We think we are building a global community in the epidemiology of ageing and dementia.

Scientia Professor
Perminder Sachdev AM
(Co-Director, CHeBA)

Dr Darren Lipnicki
(Study Co-ordinator, COSMIC)

CHeBA Healthy Brains Positive Ageing

Highlights

Publication

"Determinants of cognitive performance and decline in twenty diverse ethno-regional groups: a COSMIC collaboration cohort study" accepted for publication in PLOS Medicine.

- Abstract below.

Including "COSMIC" in paper titles and by-lines

To increase the visibility of COSMIC and help with grant renewal applications, can authors of COSMIC manuscripts or presentations please include:

- "COSMIC" in the title (eg, …: a COSMIC study)
- "COSMIC collaborators" in the author by-line.

COSMIC Scientia PhD Scholarship

Applications are open for a PhD scholarship at UNSW working on COSMIC data

https://www.scientia.unsw.edu.au/scientia-phd-scholarships/risk-factors-and-biomarkers-dementia-and-brain-ageing

AAIC 2019

1. COSMIC presentations: oral (project #6) and posters (#3 and #8).
2. COSMIC meeting 6-8pm, Tuesday July 16; Intercontinental Los Angeles Downtown, 900 Wilshire Blvd. Room: Hancock Park East.
   - Followed by dinner (location to be determined).
   - Agenda items:
     i. Introduction (Perminder Sachdev)
     ii. Current projects (Darren Lipnicki)
     iii. General discussion
        1. Improving procedures to limit demands on members and avoid confusion. Data up-front? Data dictionaries?
        2. Journals to target
        3. Other funding opportunities
        4. Thinking of next NIH application.
        5. Any other matters?
   - Please advise if interested in attending but have not previously said so.

Active projects

1. BMI and cognitive decline (Steve Makkar, CHeBA)
   - Rejected by *Neurology*.
   - Submitted to *Gerontology*.
2. How age and sex interactions influence the effects of *APOE*4* on cognitive decline (Steve Makkar, CHeBA)
   - Rejected by *JAMA Neurology*, *Neurology*.
   - Will be submitted to *Eur J Neurology*.
3. Relationship between education, APOE*4 and risk of cognitive impairment (Steve Makkar, CHeBA)
   - Rejected by *American Journal of Epidemiology.*
   - Submitted to *Archives of Gerontology and Geriatrics*.
4. MINDSED: The effects of sedentary behavior on cognitive function and cognitive decline in older persons without dementia (Rene Melis, Radboud University, The Netherlands).
   - Rejected by *JAMA, PLOS Med*, *BMC Med*.
   - Revision submitted to *Sports Medicine*.
5. Common and unique factors associated with odour identification in Indonesians and white Australians (Yuda Turana, Atma Jaya Catholic University, Indonesia).
   - Rejected by *JAGS, Journal of Gerontology: Medical Sciences*, *Chemical Senses*, *PLOS One*.
   - Submitted to *Aging Clinical and Experimental Research*.
6. The prevalence of subjective cognitive decline in and across different geographical and ethno-cultural regions (Susanne Roehr, University of Leipzig, Germany).
   - Draft in preparation.
7. Reproductive history follow-up on nullipara and number of children and dementia (Jong Bin Bae, Seoul National University, South Korea)
   - Analyses being finalised and draft in preparation.
8. Risk factor clustering (Ruth Peters, NeuRA)
   - Planning the main analyses, including risk factor counts, and preparing AAIC poster.
9. Depression in the pre-clinical phase of AD: trajectories and determinants (Karen Ritchie, INSERM, France; Simone Reppermund, CHeBA)
   - Analysing the data.
10. Interactive effects of diabetes and apolipoprotein E ε4 on cognitive decline in elderly adults (Steve Makkar, CHeBA)
    - Have data from 7 studies.
    - Data not received from PATH, EPIDEMCA, SALSA, Bambui, CFAS, EAS.
    - Physical activity and cognitive decline to be a sub-analysis.
11. Decline in verbal and visual memory in mild cognitive impairment: predictors of AD and associations with biomarkers (Javier Oltra Cucarella, University of Alicante, Spain).
    - Analyses underway.
12. The relationship between alcohol use trajectories and health, mortality and cognition in older adults (Louise Mewton, CHeBA)

- Have data from 12 studies.
- Gothenburg H70 will also contribute.

13. Sleep, Mild Cognitive Impairment, and Dementia in Elderly Cohorts with Ethnoracial Diversity (Seung Wan Suh; KLOSCAD).
    - Data request sent May 3 with a July 3 deadline.
14. Risk of MCI and dementia after cancer, and vice versa (Darren Lipnicki, CHeBA).
    - Data request will be sent later in the year.
15. JPND project on social health and reserve in dementia
    - COSMIC will contribute data to Work Package 4 investigating associations between cognitive and social health.

Project proposals

1. Nutrition and cognitive health in the older population: emphasis on food groups consumption and dietary patterns (Costas Anastasiou, HELIAD)
    - Ready to send for review.
2. Development and validation of risk models for the prediction of dementia in Low- and Middle-Income Countries: A consortium of population-based cohort studies (Eduwin Pakpahan, Newcastle University Institute of Aging)
    - Ready to send for review.
3. The associations among education, occupational complexity, and late-life cognition (Jinshil Hyun, via Mindy Katz, EAS).
    - Ready to send for review.
4. Metabolic syndrome and cognitive decline (Steve Makkar, CHeBA)
    - Being revised.
5. The relationship between blood pressure and risk of cognitive decline (Matthew Lennon, CHeBA).
    - Being finalised.

Potential projects

1. Using computational models to explore the relationship between immunologic and cardiovascular parameters and AD risk (Jaime Ramos-Cejudo, NYU)
    - Determining whether studies have sufficient numbers and full blood count data.
2. Sensory impairment, cognitive, and psychological health (depression, quality of life) (Yvonne Leung, CHeBA)
3. Shared/unique risk factors for neurodegenerative diseases (AD, PD, PDD, LBD) (Darren Lipnicki, CHeBA)
    - In preparation.
4. Biomarkers for left atrial cardiopathy (Steven Levine, SUNY Downstate)
5. Ageing factor (John Crawford and Louise Mewton, CHeBA).
6. Sex differences in risk factors for dementia generally, AD and VaD or mixed in particular in population studies (Jessica Gong, George Institute)

AAIC Satellite Symposium Sydney September 25-27, 2019

1. Possible presentation on COSMIC.

COSMIC network on the Maelstrom Research website

1. Deadline for inclusion has passed.
2. As many studies as possible have been included on the COSMIC network:
    - https://www.maelstrom-research.org/mica/network/cosmic#/
3. COSMIC studies have also been linked to the IALSA network.

Data

1. We will apply for UK Biobank data for potential use as a validation set.
2. SPAH will send recently obtained APOE data.
3. MYNAH need to complete government documents for data sharing.
4. Data manager
    - CHeBA will soon appoint a data manager who will work part time on COSMIC data.

Website

1. Need to add the Shanghai Aging Study.
2. Working on creating a COSMIC internet community with file sharing and editing, comments etc.

ABSTRACT

Background: With no effective treatments for cognitive decline or dementia, improving the evidence base for modifiable risk factors is a research priority. This study investigated associations between risk factors and late-life cognitive decline on a global scale, including comparisons between ethno-regional groups.

Methods and findings: We harmonized longitudinal data for 20 population-based cohorts from 15 countries over 5 continents, including 48,522 individuals (58.4% women) aged 54–105 (mean = 72.7) years and without dementia at baseline. Studies had 2–15 years of follow-up. The risk factors investigated were age, sex, education, alcohol consumption, anxiety, apolipoprotein E ε4 allele (APOE*4) status, atrial fibrillation, blood pressure and pulse pressure, body mass index, cardiovascular disease, depression, diabetes, health, high cholesterol, hypertension, peripheral vascular disease, physical activity, smoking, and stroke history. Associations with risk factors were determined for global cognitive composite (of memory, language, processing speed, and executive functioning tests) and Mini-Mental State Examination scores. Individual participant data meta-analyses of multivariable linear mixed model results pooled across cohorts revealed that for at least one cognitive outcome, age (B = -0.1, SE = 0.01), APOE*4 carriage (B = -0.31, SE = 0.11), depression (B = -0.11, SE = 0.06), diabetes (B = -0.23, SE = 0.10), current smoking (B = -0.20, SE = 0.08), and stroke history (B = -0.22, SE = 0.09) were independently associated with poorer cognitive performance ($p < 0.05$ for all), and higher levels of education (B = 0.12, SE = 0.02) and more physical activity (B = 0.17, SE = 0.06) were associated with better performance ($p < 0.01$ for both). Age (B = -0.07, SE = 0.01), APOE*4 carriage (B = -0.41, SE = 0.18) and diabetes (B = -0.18, SE = 0.10) were independently associated with faster cognitive decline ($p < 0.05$ for all). Different effects between Asian people and white people included stronger associations for Asian people between ever smoking and poorer cognition (group by risk factor interaction: B = -0.24, SE = 0.12), and between diabetes and cognitive decline (B = -0.66, SE = 0.27; $p < 0.05$ for both). Limitations of our study include a loss or distortion of risk factor data with harmonization, and not investigating factors at mid-life.

Conclusions: These results suggest that education, smoking, physical activity, diabetes and stroke are all modifiable factors associated with cognitive decline. If determined to be causal, controlling these factors could minimise world-wide levels of cognitive decline. However, any global prevention strategy may need to consider ethno-regional differences.

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