

The Australian Research Council Longevity Intervention (ARCLI) trial

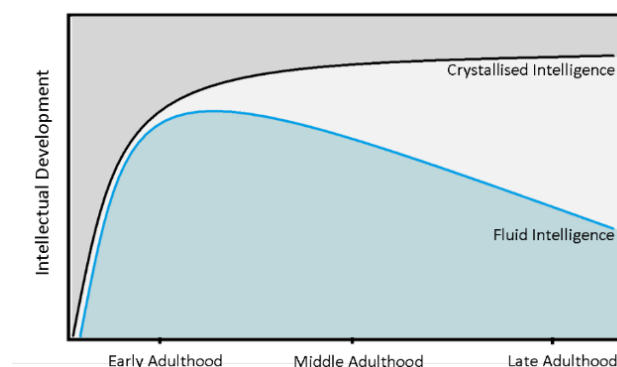
An example of a large trial that was funded after smaller scale trials that revealed a cognitive enhancing effect of two herbal extracts.

Company

Horphag (Switzerland); Soho Flordis International (Australia); Australian Research Council; Philanthropic contributions.

Problem/opportunity

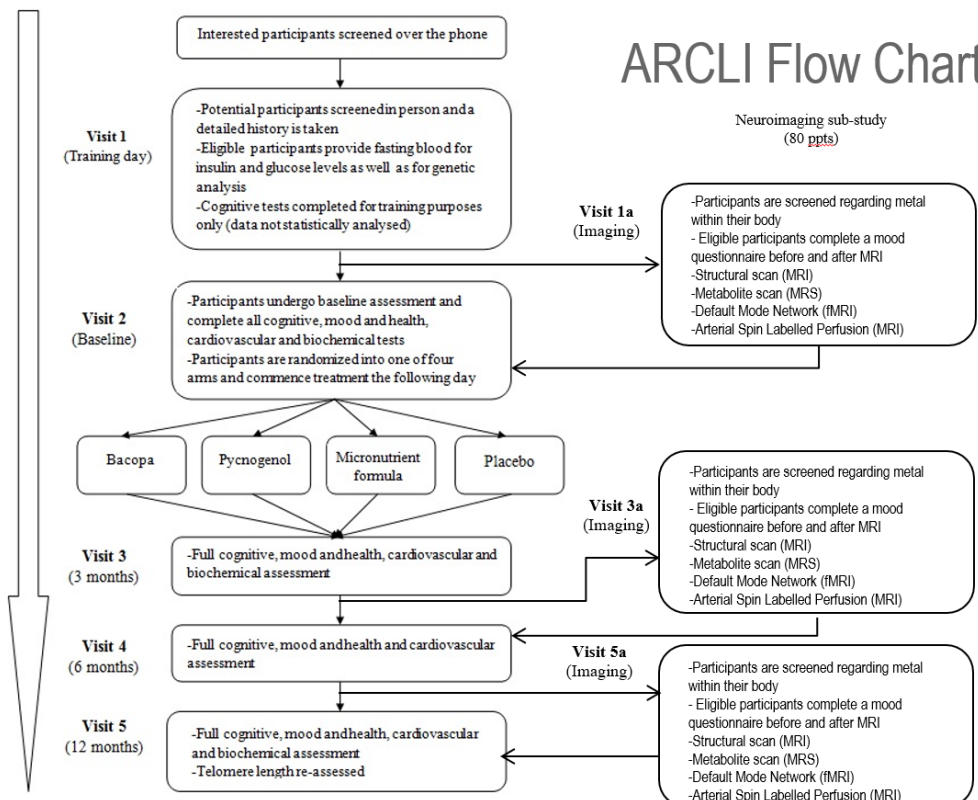
This ambitious large-scale trial extended our first smaller trials on bacopa (KeenMind® - CDRI 08) and Pycnogenol® on cognition in the elderly (see case studies on bacopa (KeenMind® - CDRI 08) and Pycnogenol®). The initial trials indicated that both bacopa (KeenMind® - CDRI 08) and Pycnogenol® improved processing speed and memory (domains that are sensitive to age). Although these smaller trials were published in good scientific journals in psychopharmacology, there were questions about the effect with longer treatment duration. We were also interested in the biological mechanisms associated with improved memory and processing speed and whether these herbal extracts improved other psychological (mood, anxiety, depression and well-being) and health related outcomes (e.g., inflammation, oxidative stress, sleep quality, biochemistry, telomeres, microbiome, cardiovascular function and brain imaging measures). We also wanted to replicate the findings that both herbal extracts improved cognition, particularly in the elderly.



Solution

To confirm these findings and to study the mechanisms by which cognitive enhancement is achieved by these two herbal extracts we designed a large-scale study involving hundreds of participants and an extended duration of treatment (12 months) with three arms (Bacopa (KeenMind® - CDRI 08), Pycnogenol® and Placebo). We tested participants at baseline, 3, 6 and 12 months on a range of outcome measures including:

- Several cognitive batteries.
- Mood, wellbeing, anxiety, depression and sleep quality.
- Cardiovascular function, BP, arterial stiffness, blood flow.
- Genetic markers including telomeres.
- Biochemistry including inflammatory markers and oxidative stress, liver and other safety enzymes.
- Neuroimaging.
- Diet, exercise and other lifestyle markers.
- Microbiome.



Our role

We coordinated one of the largest RCTs on cognitive enhancing herbal extracts for a healthy elderly population. We integrated Government, industry, and philanthropic funding to study the biomarkers of cognitive ageing in the healthy (baseline data), and to study the effect of the interventions (3, 6 and 12 month data). This helped to understand emerging relationships between the microbiome, neuroimaging markers and cognition/well-being in the healthy elderly. The study was conducted to GCP standards and two protocol papers were published.

Outcomes

More than a dozen papers have already been published or accepted for publication on the baseline data and more than 40 publications are expected to be published on the intervention data. The study has also trained more than 50 students, research fellows, Honours and PhD students, international students and has already resulted in more than 20 presentations to national and international conferences. Unblinding of the intervention data is planned for May 6th 2021 (watch this space!). A sample of baseline papers are provided in the references below. The research will add to our knowledge of the efficacy, safety and mechanisms of two high quality herbal products (KeenMind® - CDRI 08 and Pycnogenol®). The study has the potential to help millions of people reduce the effects of cognitive ageing as they grow older.

References

Protocol Papers

- Simpson, T., Deleuil, S., Echeverria, N., Komanduri, M., Macpherson, H., Suo, C., Gondalia, S., Fard, M.T., Pipingas, A., Scholey, A., & Stough, C. (2019). The Australian Research Council Longevity Intervention (ARCLI) study protocol (ANZCTR12611000487910) Addendum: Neuroimaging and Gut Microbiota Protocol. *BMC Nutrition*, 18 (1), 1.
- Stough, C., Pase, M., Cropley, V., Myers, S., Nolidin, K., King, R., Camfield, D., Wesnes, K., Pipingas, A., Croft, K., Chang, D. & Scholey, A. (2012). A randomized controlled trial investigating the effect of Pycnogenol and Bacopa CDRI08 herbal medicines on cognitive, cardiovascular, and biochemical functioning in cognitively healthy elderly people: the Australian Research Council Longevity Intervention (ARCLI) study protocol (ANZCTR12611000487910). *Nutrition Journal*, 11, 1-9

Sample of Baseline Data Papers

- Savage, K., Kingshott, D., Gubko, A., Three, A.W., Burjawi, T., Croft, K., Sarris, J., & Stough, C. (In Press) The relationship between oxidative stress and anxiety in a healthy Older population. *Experimental Aging Research*
- Petrov, K., Hayley, A., Catchlove, S., Savage, K., & Stough, C. (2020). Is poor sleep quality associated with elevated systematic inflammation in healthy elderly participants? *Mechanisms of Ageing and Development*, 192,111388

- Fard, M.T., Cribb, L.T., Nolidin, K., Savage, K., Wesnes, K. & Stough, C. (2020). Is there a relationship between low-grade systemic inflammation and cognition in healthy people aged 60-75 years? *Behavioural Brain Research*, 383, 112502
- Stough, C., Pipingas, A., Camfield, D., Nolidin, K., Savage, K., Deleuil, S., & Scholey, A. (2019). Increases in total cholesterol, and low-density lipoprotein associated with decreased cognitive performance in health elderly adults. *Metabolic Brain Disease*, 34, 477-484.
- Weeks, P., Hayley, A., & Stough, C. (2019). Do individual differences in state and trait anxiety predict sleep difficulties in healthy older adults? *Personality and Individual Differences*, 144, 141-146.
- Camfield, D.A., Nolidin, K., Savage, K., Timmer, J., Croft, K., Simpson, T., Downey, L., Scholey, A., Pipingas, A., Deleuil, S., & Stough, C. (2019). Higher plasma levels of F2-Isoprostanes are associated with slower psychomotor speed in healthy older adults. *Free Radical Research*, 53, 3-38.
- Downey, L.A., Simpson, T., Timmer, J., Nolidin, K., Croft, K., Wesnes, K.A., Scholey, A Deleuil, S., Stough, C. (2018). Impaired verbal episodic memory in healthy older adults is marked by increased F2-Isoprostanes. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, 129, 32-37.

Tags

Bacopa, CDRI 08, KeenMind®, Soho Flordis International, Pycnogenol®, Horphag, ARC, memory, processing speed, biomarkers, oxidative stress, clinical trial