SWINBURNE UNIVERSITY OF TECHNOLOGY

PARTICIPANT INFORMATION AND CONSENT FORM

A RANDOMISED CONTROLLED TRIAL IN 'AT RISK' HUMANS INVESTIGATING THE COGNITIVE BENEFITS OF COMBINED FLAVONOID/FATTY ACID AND UNDERLYING MECHANISMS OF ACTION: THE COGNITIVE AGING NUTRITION AND NEUROGENESIS (CANN) TRIAL.

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Associate Investigators: Dr David White[1], Dr Helen Macpherson[1], Dr Shakuntla Gondalia[1], Ms Rebecca King, Ms Antoinette Goh[1], Ms Renee Rowsell,
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[1] Centre for Human Psychopharmacology, Swinburne University of Technology, Hawthorn.

Introduction

You are invited to take part in this research project which is a collaboration between Swinburne University (AU), the University of East Anglia (UK) and the University of Illinois (US).

This study will test if a food combination, containing a fatty acid blend (fish oil capsule) and plant bioactives (chocolate 'drops') improves brain function (cognition) in individuals experiencing memory difficulties. This study will be conducted in both Norwich (UK) and Melbourne.

This Participant Information and Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not you would like to take part, you may wish to talk about it with a relative, friend or your local doctor.

Participation in this research is entirely voluntary. If you do not wish to take part, there is no obligation. You will receive the best possible care whether you take part or not.

If you decide you want to take part in the research project, you will be asked to sign the consent section. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. By signing it you are telling us that you:

- understand what you have read;
- consent to take part in the research project;
- consent to have the tests and treatments that are described;
- consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

The University of Illinois is providing the funding for this research project and Abbott Nutrition will provide the supplements for this study.

What is the purpose of the research project?

This study aims to assess if 12 month supplementation of a combined fatty acid/flavonoid treatment is effective in improving cognition in older individuals (aged 55 or older) experiencing memory difficulties. In an aging population the incidence of dementia (of which Alzheimer's disease is the most common form) is rapidly increasing. Although there are some drugs available to treat the symptoms, currently there is little that can reverse it or slow its progression. Nutrition is known to be important for brain function right throughout life. In particular, recent research has indicated that particular fatty acids found in fish, namely EPA and DHA, and flavonoids can improve the function of the brain and overall cognition.

Flavonoids are naturally occurring compounds found in plant based foods such as berries, cocoa and tea. The current study will use cocoa flavonoids which are called flavanols. Flavonoids have been shown to possess wide ranging benefits for cardiovascular health and more recently brain function. They are thought to be largely responsible for the benefits associated with increased fruit and vegetable intake. A number of benefits associated with cognitive function and general wellbeing have been previously documented in relation to fatty acids and flavonoids separately; however, no studies have investigated the combined effect of these compounds.

The study will also investigate the effect of the study food on gut bacteria and a number of biomarkers of oxidative stress and inflammation associated with cognitive as well as cardiovascular health. In addition we will profile your genetic make-up to see if individuals with different versions of genes (genotypes) respond differently to the study treatment.

Am I eligible to participate in the study?

To participate in the study you will need to fulfil the following inclusion criteria:

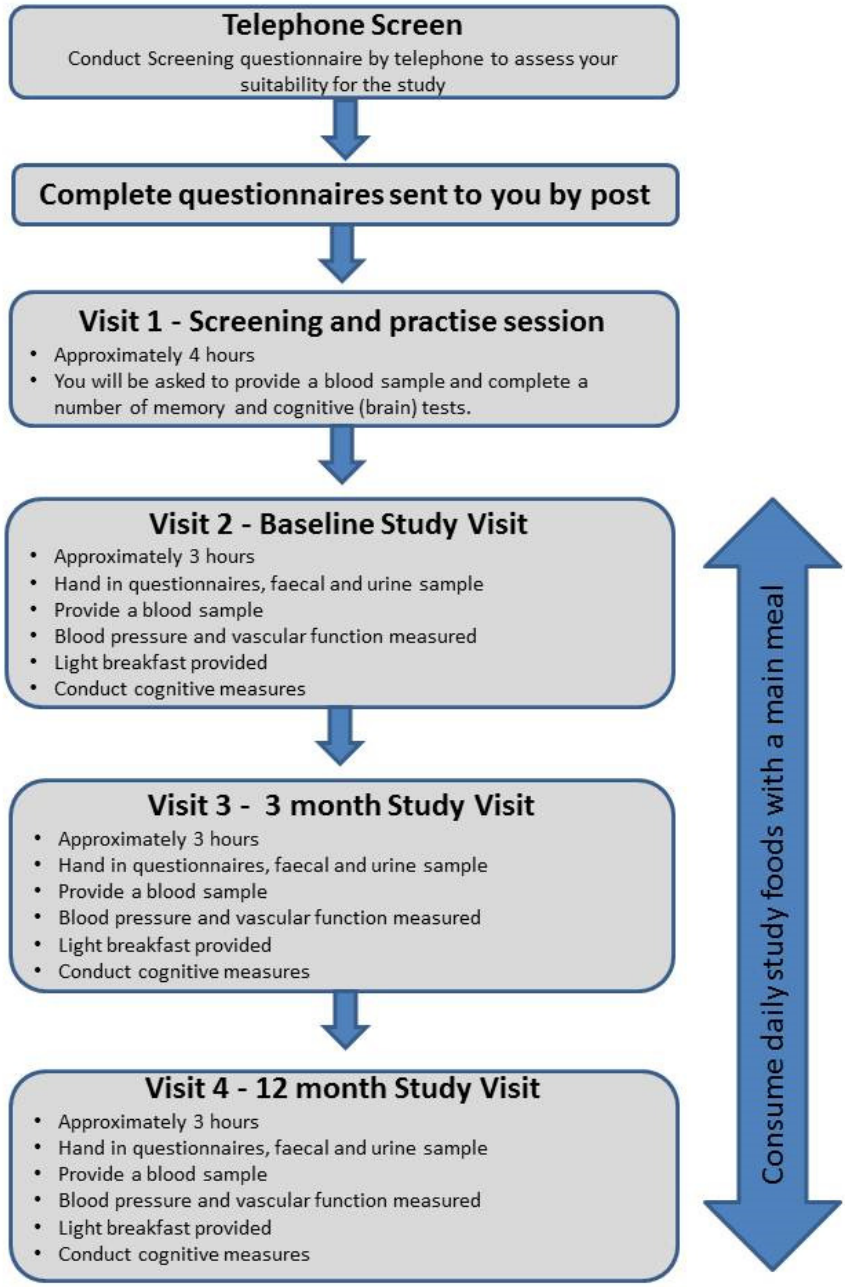
- Aged 55 or older.
- Worried about your memory
- Not diagnosed with Dementia (e.g. Alzheimer's Disease) and do not have a parent or sibling diagnosed with premature dementia <60years
- Do not consume more than one portion of oily fish a week or take fish oil supplements
- Do not have a high flavonoid intake (determined by using a short food frequency questionnaire) or take flavonoid containing supplements
- No history of significant brain trauma, stroke, loss of consciousness greater than 1 hour, epilepsy.
- No history of alcohol or drug dependency within the last 2 years
- not suffering from moderate to severe depression
- No history of / do not currently suffer from heart disease or uncontrolled high blood pressure
- Are on certain medications (to be determined by the researchers) that may affect the study outcome.
- No health conditions that would affect food metabolism including the following: food allergies, kidney disease, liver disease and/or gastrointestinal diseases (e.g. irritable bowel syndrome, coeliac disease, peptic ulcers).
- Are willing and able to participate in all scheduled visits, treatment plan, dietary restrictions, tests and other trial procedures according to the protocol. You are comfortable with using computers.
- Are willing to provide blood and faecal samples throughout the testing phases.

What will I need to do?

Participation in the study will involve attending the Centre for Human Psychopharmacology at Swinburne University in Hawthorn on four separate occasions over a 12-month period. The first of these sessions will take approximately 4 hours, while the following three visits will take no more than 3 hours (these visits will include breakfast). Across this period you will be asked to consume the study foods daily. There is also an optional neuroimaging component to this

study, which will include an MRI scan and an MEG scan.

The Centre for Human Psychopharmacology is located at:
Swinburne University of Technology
Level 3, Advanced Technology Centre (ATC)
427-451 Burwood Rd, Hawthorn



Visit 1 (total time 4 hours):
The first visit is a screening and training day. You may schedule a time to attend the centre that is convenient for you. At this visit the study will be explained to you in detail and you may ask the researchers any questions or raise any concerns that you may have about the study. You may then provide written informed consent if you would like to proceed with your involvement in the study, after which you will be assessed on several paper and pencil memory tests in order to confirm that you are eligible for the study according to the criteria for Mild

Cognitive Impairment or Subject Memory Impairment. A blood sample will be taken to confirm omega-3 fatty acid status and APOE status. The APOE test will determine which version of the gene you possess. There are three different variants (alleles) of the APOE gene; E2, E3 and E4. Those with the E4 allele are at greater risk of cognitive decline in later life. More information regarding this test is available on page 6 of this document. During the training session you will be familiarised with the paper and pencil tests and computerised tasks that will be used throughout the study. You will also have a chance to practice these tasks and ask the experimenter any questions you may have.

Visit 2 (total time approx 3 hours):

The second visit will be scheduled after the results of the APOE and omega-3 fatty acid has been determined. In preparation for visit 2 you will be required to collect and store a faecal sample (as per the procedure provided in the faecal sample collection kit) a day before the actual visit and complete a food questionnaire during the week before. The morning of your testing session you will need to collect a urine sample in the container provided to you. You will need to bring these samples with you when you come to the centre. Additionally you are asked not to consume any food after 10pm on the evening before the visit. You will be required to attend the centre at 9am for a fasting blood sample. The blood sample will be taken by a research nurse or qualified venepuncture technician. They will extract up to 40ml of blood from a vein in your arm using a syringe. The blood samples will be sent to pathology labs for analysis as described below. Following the blood sample you will be provided with a light breakfast and then be given a 15 minute break prior to commencing the testing session. The testing session will then consist of completing a number of questionnaires and computerised tests relating to cognition and your general wellbeing, as well as assessing cardiovascular function. The total time to complete these tasks will be no more than 3 hours.

If you are completing the imaging component of this study you will undergo MRI assessment which will take an additional 1.5hrs.

At the conclusion of visit 2, you will then be provided with the treatment (or placebo) for the next 3 months (90 days). A placebo is a substance not containing the active ingredients under study. The placebo will be administered to half of the study participants to compare the effects of the active treatment. You therefore have a 50% chance of being in the placebo arm of the study. You will be required to take the study treatments daily for the duration of the study. You will be provided with a log to record the time at which you take the treatments each day throughout the study. If for some reason you do not take the treatment one day then you will be required to make a note of this in the log.

Visit 3 and Visit 4 (total time 2 hours each):

The third and fourth visits will be scheduled for 3-months and 12-months following visit 2 respectively. In preparation for these visits you will be required to collect and store a faecal sample (as per the procedure provided in the faecal sample collection kit) a day before the actual visit and complete a food questionnaire during the week before. The morning of your testing session you will need to collect a urine sample in the container provided to you. You will need to bring these samples with you when you come to the centre. Additionally you are

asked to not consume any food after 10pm on the evening before each visit (as per visit 2). The schedule for testing will be the same as for visit 2, starting with a fasting blood sample at 9am. Please remember to bring in your log detailing your daily supplement usage for the experimenter to check. After the blood sample, you will again be provided with a light breakfast followed by a 15 minute break. Testing will then follow the same sequence of mood, cardiovascular and cognitive assessments. At the conclusion of visit 3, you will be provided with the treatment (or placebo) for the next 9 months.

Optional brain imaging component

For a limited number of participants there will also be the option to take part in the brain imaging part of the study. This will involve 2 scans; one in the Magnetic Resonance Imager (MRI) and one in the Magnetoencephalograph (MEG). The brain imaging component is being conducted in order to gain important information as to the potential benefits of the treatment in parts of the brain which are important to memory. Participation in this is entirely voluntary. The MRI scan will be completed immediately following the cognitive testing at 0-months, 3-months and 12-months and will take an additional 1.5 hours. The MEG scan will be completed on a different day to the MRI scan and will also take 1.5 hours to complete. Both of these scanners are located at the Advanced Technologies Centre (ATC) at Swinburne University and further details of these scanning sessions are included in Appendix A.

Methods

Cognitive Measures

A range of measures will be used to assess working memory, secondary memory, processing speed and global cognitive functioning. The majority of these assessments are computerised tasks, presented to you via a colour monitor. At your first visit, these measures will be fully explained and you will be given an opportunity to practice each task to ensure you feel comfortable.

One of the measures, known as the Montreal Cognitive Assessment (MoCA) is a common screening measure for detecting cognitive impairment which may be due to dementia. If you are found to score very low on this measure then you may be ineligible to participate in the study. A very low score on the MoCA indicates that you may be experiencing some form of mild-to-moderate cognitive impairment. It is important to note that the test result itself does not provide enough information in order for us to be able to accurately diagnose the reason for the impairment. For this reason, in the case that you score very low on this test, you will be referred to your local GP so that you may discuss the meaning of the test result in greater detail and follow-up diagnostic testing may be conducted.

Mood and well-being

You will be asked to complete several short questionnaires which will require you to answer some questions regarding your mood, general health and well-being.

Dietary records

In order to assess your normal 'habitual' diet and how well you are adhering to taking the dietary supplements, we will ask you to fill out a three day diet diary in the week before visit 2, and to complete a food frequency questionnaire (FFQ) in the week before visits 2, 3 and 4. The FFQ will ask you how often you consume particular foods and will take approximately 15-20 minutes to complete.

Gut bacteria

You will be required to collect a faecal (poo) samples prior to each testing session. At the first visit (practise session) you will be provided with an easy faecal sampling kit with all necessary

information. The sample is to be collected the day before each testing session and brought with you to the centre. The sample will be used to study the indigenous gut bacterial population. The gut bacteria influence gut and whole body function and are likely to also influence brain function and even behaviour. The composition and function of this bacterial community can be modified by dietary supplementation. Therefore, we will examine associations between your gut bacteria and cognition throughout the study.

Urine analysis

You will be required to collect a urine sample prior to each testing session. At the first visit (practise session) you will be provided with a sample collection jar and instructions. This sample should be collected the morning of each testing session. We will ask that you collect the first void of the morning, and fill at last half of the jar. The sample will be used to assess your general health, and will also be used to assess your treatment compliance.

Blood Measures

A blood sample will be taken at each of the four testing sessions by a registered Division 1 nurse, or qualified venepuncture technician. At each of these visits, up to 40ml of venous blood will be taken from a vein in your arm using a syringe. This is equivalent to approximately two tablespoons of blood. For the first visit, the blood sample will be analysed for some variations in DNA including APOE status(see below), as well as omega status (a high status may result in you being ineligible for this study). This information will be used to determine whether these genetic variations modulate any cognitive effects of the study treatments. On each of the other visits, the blood samples will be used to assess a range of biochemical markers for oxidative stress, inflammation, neuronal activity, microvascular changes and cholesterol metabolism. If any of your blood samples are found to reveal abnormal results, then your results will be forwarded to your GP so that they may discuss the implications of the results in detail and redo the tests if necessary.

APOE Genotype Testing

As part of this study you will undergo a genetic test to determine your apolipoprotein E (APOE) status. The test for APOE status is a blood test that will be conducted at the first testing session.

The APOE gene found on chromosome 19 is related to an increased risk of developing late-onset Alzheimer's disease (AD). The APOE gene comes in several different forms (or alleles) and having one or two copies of the APOE e4 allele increases a person's risk of getting AD. That is, having the e4 allele is a risk factor for AD, but it does not mean that AD is certain. Some people with two copies of the e4 allele do not develop clinical signs of AD, while others with no APOE e4 alleles do. The APOE e4 allele is usually used to determine the risk of developing AD in a large group of people, however, the exact degree of risk of AD for an individual cannot be determined based on APOE status.

You will be provided with an Alzheimer's Disease Genetics fact sheet to read prior to signing the consent form. The results of this test will remain confidential. You can decide whether or not you would like to view the results of this test. If you decide you would like the results, they will not be given directly to you. They will be given to your nominated GP or health care professional who will be able to communicate the results to you.

Cardiovascular Measures

After a short rest period, blood pressure will be measured from your arm while you are lying down. Three measurements will be recorded and averaged to ensure the accuracy of assessment. One further blood pressure measurement will then be taken and used to estimate aortic blood pressure, a cardiovascular disease risk factor.

Next your aortic stiffness, an indicator of arterial health will be non-invasively measured using the same device that was used to take your blood pressure. While you remain lying down, a large blood pressure cuff will be placed around your thigh. The cuff can be placed over the top of clothing. The researcher will use a pencil-like sensor to record a signal from the pulse in your neck. When the researcher obtains a good signal of your pulse, the cuff around your thigh will automatically inflate. The device will automatically estimate the stiffness of your aorta, giving an indication of arterial health.

You should not feel anything unpleasant as all cardiovascular assessment is pain-free. Furthermore, the cardiovascular equipment used adheres to the necessary Australian safety standards.

Brain imaging measures (optional) – See Appendix A

Half of the participants in the study will have the opportunity to participate in the brain imaging component of the study. Details of the requirements are provided in Appendix A of this document. If you are interested in taking part in this aspect of the study, please let one of the researchers know.

STUDY DAY RESTRICTIONS

In preparation for testing days 2, 3 and 4 we ask that you adhere to the following restrictions:

- Avoid alcohol and organised exercise in the 24hours before the study visit.
- Fast from 10pm on the evening before the study visit (please drink plenty of water to stay hydrated)
- no caffeine-containing products on the testing day

How are the faecal samples collected, stored and analysed?

You will be required to collect a faecal sample prior to each testing session. We will give you an easy collection kit along with instructions on how to collect these samples. Upon arrival at Swinburne, the samples will be stored at -80C and later sent to the University of Illinois (USA) for further testing. All samples sent to the University of Illinois will be non-identifiable. That is, the samples will be labelled with unique identification numbers, not names.

In contrast, faecal samples used for genetic analysis will remain securely stored at Swinburne after the genetic tests have been analysed for possible analysis in future research projects subject to ethical approval. Genetic material will be stored without any identifying information but will be potentially re-identifiable. The storage of your genetic material is subject to your consent. If you do not consent to the storage of your genetic material, it will be destroyed upon completion of the trial. You will be asked to provide additional consent for the collection of your sample during the research project in the consent form below. The biological samples collected during the intervention will be kept at Swinburne for up to 10 years.

How are the blood samples being taken, stored and analysed?

A blood sample will be taken at each of the four testing sessions. A fasting blood sample will be taken first thing in the morning when you attend the centre for your study visits. The blood will be taken by a qualified venepuncture technician or research nurse at the Centre for Human Psychopharmacology and securely stored in a freezer. The samples taken at the screening visit will be sent to a pathology lab in Melbourne. All samples sent to pathology labs will be non-identifiable. That is, only participant numbers will be used with respect to blood samples, not names. After the samples have been analysed, they will be destroyed appropriately and therefore not used for any other research other than the current study. Samples taken from

visits 2, 3 and 4, will be securely stored in a freezer, and later sent for analysis at the University of Sterling (UK) and University of East Anglia (UK).

In contrast, blood samples used for genetic analysis will remain securely stored at Swinburne after the genetic tests have been analysed for possible analysis in future research projects subject to ethical approval. Genetic material will be stored without any identifying information but will be potentially re-identifiable. The storage of your genetic material is subject to your consent. If you do not consent to the storage of your genetic material, it will be destroyed upon completion of the trial. You will be asked to provide additional consent for the collection of your blood during the research project in the consent form below. The biological samples collected during the intervention will be kept at Swinburne for up to 10 years.

Will I be rewarded for participating in the study?

You will be compensated a total of $160 for completing this study ($40 for each testing session you complete).

If you are also involved in the additional brain imaging component of the study you will be compensated a total of $240 for completing this study (an additional $80 for the two brain imaging sessions).

What are the possible risks?

Having blood taken may cause some discomfort or bruising. Sometimes, the blood vessel may swell, or blood may clot in the blood vessel. Rarely, there could be a minor infection or bleeding. If this happens, please inform the research nurse or your local health care professional. You will be free to withdraw from the study at any time if you feel unwell. There is also a research nurse located on-site and staff members trained in first-aid in the event you do experience any side effects.

What if new information arises during this research project?

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information and decide if it affects you.

Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part you don't have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

Will my details remain confidential?

Your records relating to this study and any other information received will be kept strictly confidential. However staff participating in your care, the sponsor and other agencies authorised by law, may inspect the records related to the study. In the event you are admitted to hospital as a result of an adverse event resulting from this study, your treating doctor may require access to your study records. Furthermore, this information will be stored for 15 years in a locked cabinet at the Centre for Human Psychopharmacology and can only be accessed by the Principle Investigator/s.

Your identity will not be revealed and your confidentiality will be protected in any reviews and reports of this study which may be published. However, results may be suppressed for commercial reasons as the sponsor of the project retains the rights to the data.

I understand my treating Doctor/s will be notified of my participation in this study and of any clinically relevant information noted by the trial doctor in the conduct of the trial. Please refer to Confidentiality/Privacy Policy PI025 available at www.bellberry.com.au for further information.

What will happen to the results of this study?

It is expected that the results of this study will be published in a peer-reviewed journal and will be presented at Universities and conferences. The identity of participants will not be disclosed and all data will be presented as group data.

How can I access my information?

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about you. You also have the right to request that any information, with which you disagree, be corrected. Please contact one of the researchers named at the end of this document if you would like to access your information.

What happens if I am injured as a result of participating in this research project?

If you are injured as a result of your participation in this trial you may be entitled to compensation.

Sponsors of clinical trials in Australia have agreed that the guidelines developed by their industry body, Medicines Australia, will govern the way in which compensation claims from injured participants are managed by sponsors.

However, as guidelines, they do NOT in any way dictate the pathway you should follow to seek compensation. The sponsor is obliged to follow these guidelines. These guidelines are available for your inspection on the Medicines Australia Website (www.medicinesaustralia.com.au) under Issues/Information – Clinical Trials – Indemnity & Compensation Guidelines. Alternatively, your study doctor can provide you with a hard-copy of the guidelines.

It is the recommendation of the independent ethics committee responsible for the review of this trial that you seek independent legal advice before taking any steps towards compensation for injury.

Is this research project approved?

The Bellberry Human Research Ethics Committee has reviewed and approved this study in accordance with the National Statement on Ethical Conduct in Human Research (2007) incorporating all updates.
This Statement has been developed to protect the interests of people who agree to participate in human research studies.
Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the Committee chair,
Bellberry Human Research Ethics Committee on 08 8361 3222 or email bellberry@bellberry.com.au.

Who do I contact for further information?

If you are interested in participating in this research or you would like more information please contact:

Renee Rowsell
Senior Research Assistant
Email: rrowsell@swin.edu.au
Phone: 03 9214 5656

Antionette Goh
Clinical Trials Co-ordinator
Email: agoh@swin.edu.auPh: 03 9214 5094

Any additional questions regarding this project can be directed to the Principal Investigator, Prof Andrew Scholey, co-director at the Centre for Human Psychopharmacology, on 9214 8932 or on his email ascholey@swin.edu.au

Complaints

The Bellberry Human Research Ethics Committee has reviewed and approved this study in accordance with the National Statement on Ethical Conduct in Human Research (2007) incorporating all updates.
This Statement has been developed to protect the interests of people who agree to participate in human research studies.
Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the Committee chair,
Bellberry Human Research Ethics Committee on 08 8361 3222 or email bellberry@bellberry.com.au.

CONSENT FORM

A RANDOMISED CONTROLLED TRIAL IN 'AT RISK' HUMANS INVESTIGATING THE COGNITIVE BENEFITS OF COMBINED FLAVONOID/FATTY ACID AND UNDERLYING MECHANISMS OF ACTION: THE COGNITIVE AGING NUTRITION AND NEUROGENESIS (CANN) TRIAL.

Principal Investigator: Prof Andrew Scholey

I, _____ (name of participant)
consent to participate in the research project entitled: A Randomised Controlled Trial in 'At Risk' Humans Investigating the Cognitive Benefits of Combined Flavonoid/Fatty Acid and Underlying Mechanisms of Action: The Cognitive Aging Nutrition and Neurogenesis (CANN) trial .
I acknowledge that the nature, purpose and risks of the research projects and alternatives to participation have been fully explained to my satisfaction.

My agreement is based on the understanding that:

- I agree to participate in this activity, realizing that my identity will remain confidential, and that I may withdraw at any time.
- I freely agree to participate in this research project according to the conditions in the Participant Information Sheet which I confirm has been provided to me.
- I understand that my involvement in this study may not be of any direct benefit to me.
- I have been given the opportunity to have a member of my family or another person present while the study is explained to me.
- I will be given a copy of the Participant information and Consent form to keep.
- The possible side effects have been explained to me, to my satisfaction.
- I have been told that no information regarding my medical history will be divulged to unauthorised third parties and the results of any tests involving me will not be published so as to reveal my identity
- I understand that access may be required to my medical records for the purpose of this study as well as for quality assurance, auditing and in the event of a serious adverse event
- I understand the time involved in each of the recording and testing sessions.
- I am aged over 55
- I agree to be interviewed by the researcher
- I agree to complete questionnaires asking me about my medical history
- I agree to refrain from eating and drinking from 10pm the night before study visits (it is ok to drink water)
- I agree to attend Swinburne University in hawthorn for 4 testing sessions
- At Swinburne, this project is for the purpose of research and not for profit.
- I need to complete all four testing sessions to receive the entire study payment
- I am willing to provide faecal, urine and blood samples as outlined in the Participant Information Sheet
- If I am participating in the brain scanning section then I have also read and understood the additional MRI and MEG screening and consent forms attached to this document.
- I consent to my treating Doctor/s being notified of my participation in this study and of any clinically relevant information noted by the trial doctor in the conduct of the trial.

- I declare that all my questions have been answered to my satisfaction
- I have read, or have had read to me, and I understand the participant Information Sheet Version 1.2 dated 2nd Feb 2016.

By signing this document I agree to participate in this project.

Name of Participant..... .....

Signature..... **Date**.....

Declaration by Principle Investigator, Co-Investigator (CI) or Research Assistant (RA)
A verbal explanation of the research project, its procedures and risks has been given to the participant and I believe that the participant has understood that explanation.

Name of Investigator..... .....

Signature..... **Date**.....

Additional Consent for APOE results

As part of this research study, we will be analysing your APOE status as mentioned in pages 5 and 6 of this document. As this information may be of personal significance to you, we are giving you the opportunity to view your results for this test only. If you choose to receive the results back, we will not be able to send them directly to you. We will send them to your GP who will be able to go through the results with you and explain what they mean.

Please tick **one** of the following:

☐ **YES** I would like my APOE test results sent to my GP.

GP Details:

Doctor:	
Clinic	
Address	
Phone No	

☐ **NO** I would not like to view the results of my APOE test (please note you can change your mind and choose to access your results at any time)

☐ **I AM NOT SURE** at this stage and would like to discuss this further with a family member, friend or GP.
Please note: By ticking this box, you will have the opportunity to still view the results throughout the duration of the trial.

Name of Participant..... .....

Signature..... **Date**.....

Name of Investigator..... .....

Signature..... **Date**.....

Additional Consent for the storage of genetic material and faecal samples beyond completion of this trial

Your genetic material and faecal samples used in this study will be stored after the tests have been analysed for possible analysis in future research projects subject to ethical approval. Genetic material and faecal samples will be stored without any identifying information but could potentially be re-identifiable. However, if you do not want your genetic material and faecal sample stored indefinitely please tick 'NO' in the appropriate box below. By ticking 'NO' your samples will be destroyed at the completion of the trial.

Please tick **one** of the following:

☐ **YES** I consent to the storage of my genetic material and faecal samples for possible use in ethically approved future research projects.

☐ **NO** I do not consent to the indefinite storage of my genetic material and faecal samples

Name of Participant..... .....

Signature..... **Date**.....

Name of Investigator..... .....

Signature..... **Date**.....

Appendix A – Optional Brain Imaging Component

The MEG session:

Magnetoencephalography (MEG) is a non-invasive brain imaging technique that is safe. Tiny sensors in a helmet pick up electrical activity of the brain. Before the MEG session begins, the MEG technician will take you through a Swinburne MEG safety questionnaire, which mostly asks questions about metal in your body or on your clothing. A copy of the safety questionnaire is attached to this document. You will be asked to sit in a quiet room and sit in a chair where your head will be raised into the MEG helmet. The researchers will be on the outside of this specially designed room to reduce interference. However, you will be able to speak to the researchers via an intercom at all times. Prior to entering the room you will be asked to remove any metal from your clothes, or to get changed into non-metallic clothes provided by the researchers. Although MEG presents no dangers to anyone metal on clothes and on your person can destroy the sensors of the MEG, so no metallic objects can be taken into the special MEG room. There are two components to the MEG session; the first is a resting-state MEG recording, where you will be asked to sit in the MEG with your eyes closed. The second part will require you to complete a virtual water maze task test, using a joystick to navigate to either a visible or hidden platform within the water. This session will last approximately 1.5 hours.

The MRI session:

Before the MRI session begins, you will be asked to complete a Swinburne MRI safety questionnaire administered by our staff radiographer that largely entails questions regarding any metal you have on or in your body, such as that from any surgery involving metal plates and pace makers, though other questions are asked. A copy of the safety questionnaire is attached to this document. Due to the nature of MRI, that involves strong magnetic fields, no metal can be taken into the room. It is very important that you fill in this questionnaire correctly, as some conditions, i.e. having a pacemaker, can be dangerous. The scanner is also quite noisy so you will be provided with some headphones to reduce this noise. During the MRI scan you will be required to lie at rest while measurements are taken in a relaxed resting state and also complete a short memory task.

Risks specific to the neuroimaging section of the study:

There are no known risks associated with MEG. Although please be aware that whilst the MEG recording is underway the door to the room will be closed and you will be alone in the room. However, you will be in communication with the technician conducting the scan at all times via a two-way intercom. MRI is a little different: it is shaped like a tunnel and is a bit tight for space, so if you suffer from claustrophobia, we recommend that you do not participate in this component of the study. It also makes a loud hammering sound. You will wear earlpugs to lessen the scanner noise. You may also occasionally feel warmth. Foam cushioning and velcro straps are used to keep your head relatively still during scanning. While the cushions and straps are restraining, they should not be uncomfortable. We will be able to see and communicate with you during the scanning. If you are becoming uncomfortable or having difficulty concentrating during the session, we can stop the scanning and if desired, continue at another time. You can also request that the scanning be stopped at any time by pushing on a button.

After your scan session, a radiologist will examine your brain scans (this will not be done on the day of your study). Minor changes are sometimes found in completely healthy people. You should be aware that because the scans are taken for a specific research purpose, not all abnormalities that might be detected by other Magnetic Resonance scans are necessarily seen.

On extremely rare occasions, an abnormality may be found that is significant and which should be investigated further. If such an abnormality is detected in your brain, you will be contacted by Swinburne's radiologist or your nominated health practitioner (GP, psychiatrist or neurologist, which ever you have nominated on your demographic form). It is their responsibility to follow up these findings with you.

Although a significant abnormality is extremely unlikely, you should be aware that if one is detected and you are informed, then this knowledge may have consequences for you. Please take the time to consider carefully what it would mean to you if you were informed of an abnormality in your brain which might, or might not, affect you later in life. If you do not want to know, then it is better not to participate in this part of the study.
Participants must take time to answer all the questions in the attached Swinburne University MEG and MRI consent forms to ensure that there are no MRI or MEG contraindications that may cause risks in or around the scanner.

Additional Consent for participation in the brain imaging component

If you would like to be considered for your participation in the brain imaging component of the study then please be sure to read through both the MEG and the MRI pre-scan information sheets (attached) and complete the checklists to ensure that you are eligible. If you have read through the information and would like to be involved then please indicate below.

Please tick **one** of the following:

☐ **YES** I consent to participating in the brain imaging section of the study and have completed both the MEG and MRI pre-scan checklists

☐ **NO** I do not consent to being involved in the brain imaging component of this study.

Name of Participant..... .....

Signature..... **Date**.....

Name of Investigator..... .....

Signature..... **Date**.....

MRI Pre Scan Information

WHAT IS AN MRI?
Magnetic Resonance Imaging (MRI) is a medical imaging technique that uses a powerful magnetic field and radio-frequencies to obtain very detailed cross-sectional images inside the body.

IS THERE ANY PREPARATION?
To help us provide an efficient service, you could assist us by: wearing clothing that does not have metal fastenings; not wearing any jewellery and removing all eye make-up (as this can interfere with scans of the head). You will also be required to complete an MRI safety questionnaire before your scan.

CAN ANYONE HAVE AN MRI SCAN?
No. There are some preconditions which can make MRI scanning hazardous. Due to the powerful MRI magnetic field any person with a pacemaker, metal clips on arteries or certain implanted devices cannot have an MRI scan. Women who are pregnant or breast feeding cannot have an MRI scan. It is also advisable for some people with specific medical conditions not to have a scan. These conditions will be rigorously screened for during your pre-assessment for MRI scanning.

IS AN MRI SCAN SAFE?
MRI scanning has been in use as a medical imaging tool for many years and with proper safety controls is commonly regarded by clinicians as a safe procedure. It does not employ ionising radiation (such as x-rays) and hence does not induce an additional cancer risk. It does however entail exposure to electromagnetic fields (EMF) which are much higher than levels recommended by international safety guidelines for general exposure (though still within limits of special guidelines for MRI scanning). Very occasionally, these EMFs may cause some tingling or heating sensations. These effects do not persist after scanning and have no known long term impact on health. Your MRI exposure will be carefully controlled to avoid such effects, and you will be constantly monitored for any signs of these effects and may direct us to stop the scan at any time if you experience uncomfortable sensations. The staff on duty will answer any queries you might have on the day, or if in doubt, call our department before your appointment.

WHAT WILL HAPPEN WHEN I ARRIVE?
The MRI Radiographer or another senior MRI staff member will greet you at the MRI unit waiting room and reception, explain the procedure and ask you questions about previous surgery you may have had regarding implanted metal in your body. You will be asked to leave your valuables (coins, keys, watch, jewellery, credit cards, mobile phones, pagers etc) in a locker. The staff member will guide you on to our MRI scan table. Some equipment may be placed around the body part we will be scanning.

THE SCANNING PROCESS
When we are taking the pictures, you will hear a very loud sound, rather like a vibration, and hearing protection will be provided. When you hear this noise it is important that you keep your body very still as movement will degrade the quality of the image. Usually there are about 4 or 5 different scans, lasting for 2-8 minutes each; and for most studies you will be in the scanner for about 60 minutes. You are welcome to bring along your favourite CD or cassette to listen to, during your scan.

WHAT WILL HAPPEN AFTER THE SCAN?

You can leave immediately after your scan. The images that have been taken will be used to address the research question for the study you have agreed to take part in. In addition they will be examined by a Radiologist. On extremely rare occasions, the radiologist might find an abnormality that is significant and which should be investigated further. If the Radiologist finds such a significant abnormality in your brain, he/she will contact the researcher directly involved in the study. It is then their responsibility to follow up with you; they will speak with your GP who can recommend the most appropriate action.

MRI Pre Scan Safety Questionnaire

This questionnaire is designed to screen for various conditions in a potential MRI participant which could lead to moderate or serious injury during MRI scanning. It is VERY important that you complete it as honestly and comprehensively as possible – please ask if you have any questions. This form will be checked by MRI staff on your arrival.

NAME: _____ DATE:_____ ID No. _____

DATE OF BIRTH: _____ HEIGHT: _____ WEIGHT: _____

STUDY/PROJECT NAME: _____

Please circle if any of the following are relevant to you: *Please circle*

Do you have or have you ever had a cardiac pacemaker?	YES/NO
Do you have an implanted cardiac defibrillator?	YES/NO
Do you have an aneurysm clip or been treated for an aneurysm in the head?	YES/NO
Do you have a cochlear or stapes Implant?	YES/NO
Do you have a neurostimulator or spinal cord stimulator?	YES/NO
Do you have any implanted electronic or magnetically activated devices?	YES/NO
Have you ever had any metal enter your eyes? (Cutting metal, grinding or welding)	YES/NO
If yes, was it removed by a doctor?	YES/NO

If you answered "Yes" to any of the questions *above*, please contact MRI on 9214 5514

Please indicate if you have any of the following:

Hip replacement or artificial joint?	YES/NO
Pin, plate or screw?	YES/NO
Prosthesis -eye, limb, penile implant?	YES/NO
Implanted coil, filter, shunt or stent?	YES/NO
Eyeliner or other facial make up?	YES/NO
Piercings or any jewellery?	YES/NO
Hearing aid?	YES/NO
Eyelid spring or wire?	YES/NO
Do you have any tattoos?	YES/NO
Artificial heart valve?	YES/NO
Contraceptive IUD?	YES/NO
Inflatable breast implant?	YES/NO
Are you/could you be pregnant?	YES/NO
Medication patches applied?	YES/NO
Wire mesh Implanted?	YES/NO
Spine or head shunt?	YES/NO
Vascular port or catheter?	YES/NO
Any other implanted metal?	YES/NO
Any metal foreign bodies?	YES/NO
Other concerns?	YES/NO
Are you breast-feeding?	YES/NO
Do you suffer from claustrophobia?	YES/NO
Do you suffer from epilepsy or ever had a seizure?	YES/NO
Do you wear braces, a dental plate or false teeth?	YES/NO
Do you suffer from any heart condition that would make you susceptible to an increased risk of cardiac arrest?	YES/NO
Have you ever had a surgical operation?	YES/NO

If yes, please provide details of body area (head, arm) and medical condition

.....

Have you had a MRI scan before? YES/NO
If yes, where? ..... Clinical purposes or research?.....
Did you experience any problems while having an MRI scan? YES/NO
Do you have any allergies? YES/NO
If yes, details:

.....

GP details (NAME/ADDRESS/TEL NO) .....

MRI Pre Scan Consent

I have read the above information and am aware of the risks and benefits of undergoing an MRI examination.
I have been provided with the opportunity to have any questions answered and I therefore give my consent to an MRI scan. I confirm that the questions have been answered to the best of my knowledge.

PARTICIPANTS NAME.....

SIGNATURE..... DATE.....

MRI STAFF MEMBER NAME: .....

SIGNATURE..... DATE.....

Please empty your pockets of all magnetic items including wallet, bank cards and coins.
You will also need to remove shoes, metal belt buckles and any jewellery you have on.
You will also need to remove your eye glasses the radiographer will provide you with alternatives.

MEG PRE-SCAN INFORMATION

WHAT IS MEG?

Magnetoencephalography (MEG) is a safe, non-invasive and entirely passive human brain imaging technique. The MEG scanner measures the very small magnetic fields outside the head - these arise naturally from electrical activity within the brain.

IS THERE ANY PREPARATION?

The MEG instrument is extremely sensitive to metallic objects entering the shielded room. Hence, you could assist us by:

- wearing clothing that does not have metal fastenings;
- not wearing any jewellery, and
- removing all eye make-up (as this can interfere with scans of the head).

You will also be required to complete a MEG safety questionnaire before your scan.

CAN ANYONE HAVE A MEG SCAN?

No. There are some pre-conditions which can damage the MEG scanner. The MEG scanner is extremely sensitive to the presence of metallic objects, either permanently or temporarily carried in or near to your body. These conditions will be rigorously screened for during your pre-assessment for MEG scanning. Having metallic objects on your person, although not a danger to you, may cause damage to our equipment.

IS AN MEG SCAN SAFE?

MEG scanning has been in use as a medical imaging and research tool for many years and is commonly regarded by clinicians and scientists as a safe procedure. It does not employ ionising radiation (such as x-rays) and hence does not pose an additional cancer risk. The researchers on duty will answer any queries you might have on the day, or if in doubt, please call the chief investigator.

WHAT WILL HAPPEN WHEN I ARRIVE?

The researcher will greet you at the MEG unit waiting room and reception, explain the procedure and ask you questions about previous surgery you may have had regarding implanted metal in your body. You will be asked to leave your valuables (coins, keys, watch, jewellery, credit cards, mobile phones, pagers etc.) in a locker. The researcher will guide you to the magnetically shielded room housing the MEG scanner. Some equipment may be placed around you whilst scanning; this may include headphones and/or a stimulus screen.

THE SCANNING PROCESS

When we are taking the pictures, we will ask you to keep as still as possible. Usually there will be about 4 or 5 different scans, lasting for 2-8 minutes each; and for most studies you will be in the scanner for about 60 minutes. For some studies you are welcome to bring along your favourite CD or cassette to listen to, during your scan, please ask your researcher.

WHAT WILL HAPPEN AFTER THE SCAN?

You can leave immediately after your scan. The images that have been taken will be used to address the research question for the study you have agreed to take part in.

This questionnaire is designed to screen for various conditions in a potential MEG participant. It is VERY important that you complete it as honestly and comprehensively as possible – please ask if you have any questions. This form is to be completed under the supervision of a staff member **PRIOR** to entering the MEG room. Note that answering YES to any of the questions does not automatically disqualify a person from having an MEG scan.

Please answer YES or NO to the following:
Please circle

Have you ever done or been near welding? .....YES / NO
Have you ever been injured by a piece of metal that has not been removed (bullet/shrapnel)? .....YES / NO
Do you know of any metal that has been implanted into your eye, skin or body at anytime? .....YES / NO
Do you have any of the following:

- Aneurysm clip (on a blood vessel) .....YES / NO
- Ocular / eye implant .....YES / NO
- Cochlear / ear implant .....YES / NO
- Hearing aid (removable) .....YES / NO
- Cardiac pacemaker/pacing wires or implanted cardioverter defibrillator .....YES / NO
- Artificial heart valves .....YES / NO
- Other implanted electronics devises (bone growth, neurostimulator) .....YES / NO
- Implanted infusion or drug pump .....YES / NO
- Hip replacement or artificial joint or artificial limb .....YES / NO
- Pin, plate or screw attached to a bone .....YES / NO
- Implanted coil, filter, shunt or stent .....YES / NO
- IUD, diaphragm, or pessary .....YES / NO
- Non-removable piercings or jewellery .....YES / NO
- Permanent make up .....YES / NO
- Medication patches (Nicotine, Nitroglycerine) .....YES / NO
- Dental bridge; partial plates; permanent retainer; temporary spacers .....YES / NO
- Crowns on teeth; posts in teeth .....YES / NO
- Dental implants .....YES / NO

Have you ever had a surgical operation? ..... YES / NO
If yes, please provide details of body area (head, arm) and medical condition

.....

.....

Approximately how many fillings do you have? .....
Do you have any allergies? .....

YES/NO
If yes, details:

.....

GP details (NAME/ADDRESS/TEL NO)

.....

.....

Consent

I have read the above information and am aware of the processes involved in an MEG examination. I have been provided with the opportunity to have any questions answered and I therefore give my consent to an MEG scan. I confirm that the questions have been answered to the best of my knowledge.

STUDY/PROJECT NAME:

.....

PARTICIPANTS
NAME.....

SIGNATURE: .....DATE: ...../...../.....

MEG RESEARCHER NAME:

.....

SIGNATURE: .....DATE: ...../...../.....

Preparing for your MEG Scan

On the day of your MEG scan, we request that you take the following steps:

1) Please empty your pockets of all magnetic items including wallet, bank cards and coins. You will also need to remove any jewellery you have on.
2) Do not wear make up.
3) (If applicable) Do not wear an underwire bra (sports bras that have no underwire are fine).
4) If you wear eye glasses you will not be able to wear them in the MEG scanner. Immediately prior to entering the MEG we can provide you with MEG compatible glasses. If you bring your prescription or know your prescription this will help us to give you the best temporary glasses for your scan. Contact lenses are fine for MEG scans.