MONASH University

EXPLANATORY STATEMENT

Group 1: RCT Participants

(Adult providing own consent)

Project ID: 25221
Project title: BetterBrains: A Person-Centred, Multi-Domain Prevention Randomized Trial to Delay Memory Decline

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The BetterBrains study is designed to help us understand whether a personalised, lifestyle intervention will help protect memory and thinking abilities from declining over a 24-month period. If you are successfully selected to participate, you will be randomly allocated to one of two groups. A group that receives the lifestyle intervention or a control group that receives general education.

You are invited to take part in the BetterBrains study. Please read this information in full before deciding whether or not to you would like to take part. If you would like further information regarding any aspect of this study, you are encouraged to contact the researchers via the phone numbers or email addresses listed above.

You can download an electronic copy of this information to keep. Once you have created a BetterBrains profile and agreed to take part in the study, there is also a copy this information on your profile page on our website www.betterbrains.org.au.

Taking part in the BetterBrains study is voluntary

Taking part in this study is completely voluntary and there will be no cost to you. If you do not want to take part in this study you do not have to and there is no obligation for you to do so. Choosing not to take part in this study will not impact on your current and future medical care in any way. If you do consent to participate, you are under no obligation to continue with the research study and may withdraw at any time.

Withdrawing from the project

If you do consent to participate, you are under no obligation to continue with the research study and may withdraw at any time. If you decide to withdraw from the project, please notify a member of the research team by selecting the 'reconsider my participation' button on the home page of your BetterBrains account (accessible via web and smartphone applications). A member of the research team will then contact you and inform you if there are any special requirements linked to withdrawing. If you do withdraw, you will be asked to complete a 'Withdrawal of Consent' form. This form will be provided to you by the research team.

If you decide to leave the research project, the researchers will not collect additional personal information from you. You will be able to choose whether the study will destroy or retain the information it has collected about you. You should only choose one of these options as indicated on the Withdrawal of Consent form. Where both boxes are ticked in error or neither box is ticked, the study will destroy all information it has collected about you. If you do not

return this form after opting to withdraw from BetterBrains, the study will retain all information it has collected about you. However, to allow for outcome analyses and to enable program evaluation of the trial, any safety data collected such as: medical events, age, medication and medical history will need to be retained to ensure correct safety reporting for the trial. Your safety data will only be excluded from these analyses if you specifically request for it to be destroyed. Data obtained relating to your Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) (if you consented to this optional component of the study) will only be stored for the duration of the project as required (see section: 'storage, retention and destruction of participant information' below).

Why were you invited to take part in this research?

We are inviting you to take part in the BetterBrains study because you are a healthy adult aged between 40-70 years and have a first or second degree relative with dementia or Alzheimer's disease.

What does the research involve?

Consent and Screening

Firstly, you will be asked to read this information (explanatory statement) to see whether the BetterBrains study is something you would like to take part in.

Screening part 1: After you read this explanatory statement, we will ask you to read a number of statements to see if you meet the criteria to take part in the study. If you do not meet the criteria for this study, unfortunately you will not be able to take part.

Screening part 2: If you meet all of the criteria for part 1, we will ask your permission to ask you a number of questions related to your medical history and health to work out if participation in the BetterBrains study is safe and suitable for you. If you do not meet all of these requirements, you will not be able to take part in the study.

Consent: If you have met the criteria for part 1 and part 2 you will be presented with statements outlining aspects of the study that require you to select either 'yes' or 'no' on the BetterBrains website. If you select yes to all of these statements you will then be asked to indicate your consent to be part of the study by typing your name into the bottom of the webpage as an electronic signature.

Online Profile Creation

After completing the screening and consent processes, you will be asked to create an online profile on the study website. We will ask for your full name, date of birth, and email address so that we can contact you about the study, for example, to send appointment confirmations, or reminders if you have forgotten to complete all of the surveys. We will also ask for your residential address so that we can send you a saliva sampling kit via post, and whether you have access to a smartphone and how you would prefer to be contacted by the study team (email/SMS/both).

Lastly, to help us know that you are a real person, we will ask you to upload a copy of your Medicare card, driver's license or another identifying document to your account on the BetterBrains website.

Risk Factor Assessment

After you have created your online profile, you will be asked to complete your risk factor assessment. This assessment includes 11 questionnaires which ask about your: medical history, current physical activity, years of education, mood, stress and sleep quality. These questionnaires will determine whether you have a lifestyle risk factor for dementia or not. Completing the risk factor assessment should take approximately 40 minutes. You will have **4 weeks** to complete your risk factor assessment. If you do not complete your assessment within 4 weeks, you

will be asked to re-take these assessments if you are still interested in participating in the trial. This is to ensure we have the most up-to-date and accurate information about your current health. If you do not complete your risk factor assessment within 4 weeks of your second attempt, it will be assumed that you are not interested in participating and you will be withdrawn from the trial.

You will be able to view the results of your risk factor assessment on the BetterBrains website. If the results show that you do not have any lifestyle risk factors for dementia, then your participation in the study will end at this point. If you have one or more risk factors for dementia, then you will be enrolled in the study and asked to complete your baseline assessment.

Enrolment and Baseline Assessment

The baseline assessment consists of a memory and thinking tasks, and questionnaires which ask about your lifestyle, general health, stress, resilience, and thinking style. The baseline assessment has been organised into 7 blocks. You can work through the assessment blocks as quickly as you like. You can also split them up and complete them over several days. Each block will consist of approximately 20 minutes of memory and thinking tasks and 10 minutes of questionnaires. Before you commence each of the memory and thinking tests, more detail will be provided and you will also be given the opportunity to practise before you start.

Once you've started your baseline assessment, you will have **4 weeks** to complete it. We will send you reminders to log back in and complete your remaining assessment blocks. If you do not complete the baseline assessment within 4 weeks, we will assume that you are no longer interested in being a part of this trial, and you will be withdrawn from the study. Please ensure that you are in a quiet environment, with minimal distractions when completing your baseline assessment blocks.

As you will be participating in this study for 24 months, you will be sent reminder emails to complete the risk and baseline assessments again at 12 and 24 months after your initial assessment.

Saliva Sample

We will send you a DNA kit to provide a sample of your saliva. In the kit, you will be sent instructions on how to deposit saliva in the receptacle, package it properly and send it back (via reply-paid registered postage) to our institute. After returning the kit with your saliva in it, you will not have to do this again in the study.

Using your saliva sample, we will test for a few genes that are known to be important for memory and thinking. Firstly, the *apolipoprotein* E (*APOE*) gene is important because holding a particular variant of this gene (*APOE* ε4) is known to increase risk for Alzheimer's disease at a population level. That is, *APOE* ε4 is present in about 10% to 15% of the population and in about 40% of all people who develop Alzheimer's disease dementia. We will also look at four other genes: the *brain derived neurotropic factor* (BDNF), the *microtubule-associated protein tau* (MAPT), the *kidney and brain expressed protein* (KIBRA), and the catechol-o-methyl transferase (COMT) genes. These genes are all involved to some degree in 'brain plasticity', or how well the brain copes with injury, and so understanding their effects will be important in determining resilience against brain diseases.

Study Group Allocation

As this study is a Randomised Controlled Trial (RCT), once you are enrolled in the study and have completed your baseline assessment, you will then be allocated at random (like tossing a coin) to one of two study groups. One group will receive the personalised behaviour intervention program based on your lifestyle risk factor(s) for dementia. This program will include telephone coaching provided by qualified clinicians (your 'BetterBrains Coach'), and access to educational material about Alzheimer's disease, dementia, and tips for living a healthy lifestyle. The

other group ('Education Group') will receive access to the educational material only. You will be notified of your group allocation via the BetterBrains website.

Education Group

For participants allocated to the education group, you will be provided with access to view educational material regarding Alzheimer's disease, dementia, and tips for living a healthy lifestyle. This information will be available via the 'Brain Blog' on the BetterBrains website and smartphone app. We will send you a notification (via your preferred contact method) when new information is available.

Personalised Behaviour Intervention Group

For participants allocated to the intervention group, you will receive a call from one of the BetterBrains coaches who will discuss with you your lifestyle risk factor(s) for dementia, as identified by the risk factor assessment. Your coach will then assist you to set behaviour change goals related to your risk factor(s), and work with you to identify helpful strategies and local supports and services you can access to achieve your goal. You will receive a follow-up call from your coach at 2 and 6 weeks after this initial call to check in on your progress, answer any questions and address any difficulties you may have. At 6 months after your initial enrolment you will receive a further three calls from your BetterBrains coach to check in on your progress. You will set the dates and times of these calls with your coach. You may also call your coach at any time throughout the trial if you need additional support or have questions.

Participants allocated to the intervention group will also have access to educational material via the 'Brain Blog' (as described above) on the BetterBrains website and smartphone application.

If as part of the trial, your goal requires you to seek assistance from your GP (for example, obtaining a referral to a psychologist, developing of a smoking cessation plan, or completing a review of your heart health), the clinical research team will send a letter to your GP notifying them of your enrolment in the project, and providing further recommendations regarding your selected goal and suggested intervention strategies. Your GP will also be sent a letter notifying them once you have completed the project, or if you withdraw from the project prior to finishing. We will ask for your permission on the study consent form to contact your GP via letter for these purposes.

Participant Experience Survey

If you have been receiving the BetterBrains program, you will be asked to complete an experience survey at the end the BetterBrains program. This survey will ask for your thoughts and experiences of the BetterBrains program. We will also ask you if you are interested in taking part in a group discussion (focus group) either online or face-to-face with other people who have taken part in the BetterBrains program. The focus group is an optional study component and is described below.

Optional Study Components

The BetterBrains Smartphone App

An optional component of this study is downloading the BetterBrains application to your smartphone. If you have been allocated to the personalised behaviour intervention group, this app will be used to supplement contact with your BetterBrains coach. You will be sent weekly alerts via the app to encourage you to continue to work towards your goal. All participants will also be able to access the dementia risk reduction educational material via the app. If you don't have a smartphone (iPhone or Android device), or do not consent to downloading the app, you will still receive all relevant communications from the BetterBrains research team via email and have access to all aspects of the trial via the BetterBrains website.

Medicare Benefits Schedule and Pharmaceutical Benefits Scheme

An optional component of the study is providing your consent to authorise the BetterBrains study to access your Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data. Medicare collects information on your doctor and allied health visits and their associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The purpose of collecting this data in BetterBrains is to learn about the types of health services you are attending and medications you are taking as part of your personalised BetterBrains intervention plan. As this is an optional component of the study you do not need to provide your consent for the study team to access your MBS and PBS if you do not wish to do so. Not consenting to this optional trial component will not affect your participation in the study or your relationship/s with existing health care providers. If you do consent to authorising the study team to access your personal Medicare and PBS claims information, a separate consent form which includes more details about this process will be sent to you via post.

Participant Experience Focus Group

If you have taken part in the BetterBrains program you will be invited to participate in a focus group (face-to-face or online) to talk more about your experiences. You can let us know that you are interested in taking part in the focus group when completing the experience survey and one of our research team will contact you. The researcher will tell you about the focus group and you will have the chance to ask questions. You will be sent a second Explanatory Statement and Consent Form prior to participating in the focus group. You will also be provided with the date, time and location (either face-to-face or online depending on your preference.). The focus group is expected to take 90-120 minutes.

Source of funding

This research project is being funded by the National Health and Medical Research Council (NHMRC). No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

Possible benefits and risks to participants

Possible benefits

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include: being provided with information regarding your modifiable risk factors for dementia risk reduction, receiving health education material related to dementia risk reduction, improved physical and/or mental health from engagement in relevant behavioural change strategies, and/or being part of a community that is committed to promoting and maintaining healthy brains.

Possible Risks

Genetic testing

There are no known risks involved with the collection of a saliva sample. Although this saliva test can identify which versions of *APOE* a person has, it cannot predict who will or will not develop Alzheimer's disease dementia at an individual level, as we currently only understand the risk of this gene at a population level. As such, this is not a diagnostically meaningful measure of risk as recommended by the National Health and Medical Research Council (https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/ps0001_clinical_utility_personalised_medicine_feb_2011.pdf) who state: “APOE testing has been used at population level to detect population level risk. The test is not accurate enough to predict individual risk” (p.5). We therefore will not indicate to you your *APOE* allele carrier

status. If you have any questions or concerns regarding this process, you can speak to the chief investigators for further information, or email us at betterbrains@monash.edu.

Psychological distress
You may feel that some of the questions we ask are stressful or upsetting. If you do not wish to answer a question, you may stop immediately. If you become upset or distressed as a result of your participation in the research project, please email betterbrains@monash.edu or call us on and the research team will be able to direct you to appropriate support. Any support services that we recommend will be provided in the State with which you reside, and will not be provided by members of the research team. In addition, the National Crisis Support and Suicide Prevention service, Lifeline, can be reached at 24 hours a day, 7 days a week at 13 11 14.

Research involving possible incidental findings

Your participation in this research project may result in the emergence of incidental findings. For example, it may be identified that you are experiencing symptoms of depression. If any incidental findings emerge as part of your participation in this research study that are relevant to your ongoing wellbeing and/or health care, then this information will be provided to you and your General Practitioner (GP) via letter.

Confidentiality

Any information obtained in connection with this research project, whether demographic, medical, cognitive, or genetic, will remain confidential and de-identified. The term de-identified means that any data that you provide to us will be given a unique study code, and that identifiable information (such as your name and email address) will be removed from that data. We will not disclose any identifying information about you, or provided by you during the research, without your written permission or as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your express permission. Specifically, any data will be presented at a group level, and at no time will your data be identifiable.

Storage, retention and destruction of participant information

Physical data will be stored in locked cabinets in a secure (locked) office by the project lead. All electronic data will remain confidential and will be de-identified (in re-identifiable format using your BetterBrains participant ID number). All electronic data will be kept on servers located at Monash University and Melbourne University. Data transmission is encrypted, and these servers are password-protected, and physically located within Australian borders. These servers also have restricted access, whereby only members of the research team as listed on the ethics approval for this project and approved by the principal investigator, will be authorised to access this data. Any identifiable information will be linked to your study ID number in a separate electronic file stored on a Monash University server that is appropriate for the storage of very sensitive data, password-protected, and that only the study team has access to.

De-identified saliva samples will be temporarily stored in a secure location at the Turner Institute for Brain and Mental Health (Monash University, Clayton, Victoria). At the end of the trial, a commercial vendor will be identified to conduct genotyping. Genetic information will be kept separate from the identifiable information for each participant.

All data will be kept for a minimum of 7 years following the completion of the project. When data is disposed of, the chief investigators will ensure that electronic data is deleted so that the data cannot be recovered.

Use of data for other purposes

By signing the consent form, you consent to the research team collecting and using personal information about you for the research project and other related future research projects that the chief investigators will use to extend this research.

With the advent of genome-wide research, and as candidate genes become available, we will keep your saliva sample for further genetic testing within the study. If you do not wish for us to store your sample for future studies, please let us know in writing at betterbrains@monash.edu.

MBS and PBS data will not be used in any future or unspecified research outside of this research study.

Results

As scientific papers are published from this study in scientific journals, we will post information about these papers on the website for participants to read. As research can take a long time to analyse, finalise and publish, some of these findings will be published after the study ends. In this case, we will provide information about the study findings via email in addition to posting it up on the website. Any findings or data published from this study will be de-identified.

Complaints

Should you have any concerns or complaints about the conduct of the project, you are welcome to contact the Executive Officer, Monash University Human Research Ethics Committee (MUHREC):

Executive Officer
Monash University Human Research Ethics Committee (MUHREC)
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Thank you,
A/Prof Yen Ying Lim