

Well-being and health Assessment Research Unit (WARU),
Carwyn James Building,
Aberystwyth University,
Penglais,
Aberystwyth,
Ceredigion.
SY23 3FD

Date: 11 May 2023

A supplement on cognitive function and brain activity in middle age and older healthy adults

PARTICIPANT INFORMATION SHEET

Dear _____

You are being invited to participate in one of our research studies being conducted by the Well-being and Health Assessment Research Unit (WARU) at Aberystwyth University, funded by Welsh Government through a Covid Recovery Challenge Fund led by Future Foods. Before you decide to participate, please read the information below about the project, and what will be involved. Take the time to read this information carefully and if you wish, discuss it with friends, relatives or your GP. Please ask us if you are unclear on any information and take time to decide whether you want to take part. It is your decision.

Will I be safe taking part in a research project whilst there are COVID-19 restrictions in place?

At WARU, Aberystwyth University we are following the guidance set out by the Government on May 11th, 2020 and updated on the 22nd June 2021, 'Working safely during coronavirus (COVID-19)'. We have adapted bespoke working practices for COVID-19, that all researchers would be obliged to follow.

We will provide you with as much coaching as you need, so that you feel confident when taking part in the study.

Why have I been offered entry into this study?

You have been offered entry into this study as you have expressed interest in the activities at WARU and may be interested in participating in one of our studies. Additionally, we believe you may fit the eligibility criteria we are looking for.

Why is this study being performed?

Nowadays, the oral use of probiotics is widespread, in foods (i.e., yogurt), drinks (i.e., kombucha) and supplements. Heat-treated probiotics (essentially pasteurised or killed), cell-free supernatants, and purified key components can confer beneficial effects, mainly immune effects, protection against bacterial infections, and maintenance of gut health, which can positively impact on mental health and cognitive ability. Postbiotics, as they are called, have an advantage for food industry applications as they can easily be supplemented in several food lines/products and are shelf stable. *PoZibio*TM capsules contains the probiotics *Lactobacillus paracasei* which is a species of lactic acid bacteria

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often used in the fermentation of dairy products. It's found in the human intestinal tract and mouth, but also in foods such as yogurt and naturally fermented vegetables and milk. This has been heat-killed in *PoZibio*TM.

We would like to explore if *PoZibio*TM in healthy middle aged and older subjects (>50 years) is beneficial in terms of cognitive function. We will use Electroencephalography (EEG) to measure electrical activity of the brain while performing 3 cognitive function tasks in a computer program called E-Prime. These tasks include the Stroop task, the Go/No-go task, and the Flanker task. These are all standardised psychological tasks that have been used extensively within academia to measure higher areas of cognition including processing speed, attention, accuracy, and response inhibition. Prior to the cognitive testing, we will also require you to take part in an eyes open/closed task (lasting app).

We will measure generic quality of life with the EQ-5D (5L) questionnaire which will be accessed in a computer program called JISC, and global cognitive function will be measured using the Mini-Mental State Exam (MMSE) questionnaire. We will collect venous blood samples for the investigation into the chemical composition using metabolomics at AberInnovation and Aberystwyth University, the quantification of short chain fatty acids as well as clinical biochemistry (Chem21 to include glucose and lipid panel tests) at Bronglais hospital.

What exactly would I have to do as a participant?

After pre-induction over the phone, if you are still interested, we will run through an in-person eligibility session. We will ask you to digitally complete a Mini-Mental State Exam (MMSE) and Geriatric Depression Scale questionnaire to obtain a cognitive baseline score and to assess for depressive symptomatology. Please note that these questionnaires are not diagnostic and are not intended for clinical assessment purposes. Our purpose in using these questionnaires is to ensure that we have a consistent sample of participants, who share similar characteristics, with inclusion and exclusion scores deriving from previous literature. These questionnaires should take no longer than 15 minutes combined to complete. If you obtain a geriatric depression score equal to or greater than 6, or a MMSE score <25, then unfortunately you will not be eligible to participate, and you shall be provided, and talked through, a participant exclusion feedback form. If you are at all concerned about your scores, then we would advise you to contact your local GP. For further information regarding the questionnaires, you may also contact Dr Victoria Wright in the psychology department (viw8@aber.ac.uk), and for any additional support, you might consider contacting Mind, Samaritans, or MentalHealth.org (the details for which shall be provided via email and within the participant exclusion feedback form). If you're deemed suitable and you are still keen to pursue, then the study will be split into four additional experimental sessions between WARU and the Psychology (P4 and P5) buildings, which can be combined if needed into two sessions (see testing sequence below). You will be randomised to one of two supplements, 2 x *PoZibio*TM capsules daily or 2 x placebo capsules daily for 6 weeks, to be consumed in the morning. Please note that these capsules are not suitable for vegetarians or vegans. Randomisation will be blinded, and neither you nor the researcher will know what group you're in, until after the end of the study.

The WARU visits (see flowchart)

Whilst undergoing the study, if necessary, we will be easily contacted by email, Teams and phone.

In-person eligibility session.

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Upon obtaining your written consent, we will ask you to digitally complete a Mini-Mental State Exam (MMSE) and Geriatric Depression Scale, in person.

Testing Sequence

Testing day 1 (start)

On your pre-organised day and time, come to WARU (refer to campus map below) after a 12 hour fast for a venous blood draw (3 tubes), followed by tea and toast (please bring your own breakfast if you'd prefer). You will be asked to digitally complete an EQ-5D (5L) questionnaire on a computer program called JISC, which should take approximately 5 minutes to complete. We will measure your height and weight, waist, and hip circumference. Then you are free to leave, unless you choose to combine testing day 1 and 2 together, in which case a researcher shall guide you to the P5 building.

Testing day 2 (can be combined with day 1 if needed)

If you choose not to combine testing days 1 and 2 together, then a researcher will meet you at the main reception (first building on your left upon main entry to Penglais campus) and guide you to the P5 building, where you will be encouraged to go to the toilet prior to testing. You will then be taken to P4, where the EEG laboratory is located. Please note that the laboratory is unfortunately only accessible via stairs (approximately 15 steps in total).

This will be your first Electroencephalography (EEG) and cognitive assessment. You will first be asked to participate in an eyes open/closed task so that we can obtain an EEG for your resting state. Following this, cognitive testing will begin. The cognitive tasks shall be completed on a computer in a program called E-Prime, and there will be 3 tasks in total: the Stroop task, the Go/No-go task, and the Flanker task. You shall be given a chance to practice each task with the researcher present, and to ask any questions, before each experiment begins. After each task, the EEG program will be stopped, and a new data file will be created, before recording for the following task takes place. This will provide the opportunity in between tasks for a sip of water, or a toilet break, if necessary, although the EEG cap will have to remain in place, and the nearest accessible toilets are located in P5. Altogether these tasks shall take approximately 60-70 minutes to complete, but we must allow an additional 45 minutes for the application of the EEG cap. We encourage you to bring your own bottled drinks, and snacks will be available. You will also have access to the 'break out' room on the second floor of P5, where there are chairs and tea/coffee machines available should you wish to use them prior to or following your EEG participation. Following your participation, you will be directed to the collection of the capsules back at WARU. Please note that upon completion of the experiments, you will not receive any scores indicating how you have performed. However, once you have finished your full participation in this study, if you are interested in the overall general findings of the study, then please email WARU@aber.ac.uk.

Testing day 3 (after 6 weeks of consuming capsules)

After the 6-week supplementation period we would like you to complete the activities that you undertook during testing day 2. A staff member will meet you in the P5 lobby. This will be your final assessment of EEG and cognitive testing. If you decide to combine testing days 3 and 4 together, then a staff member can escort you down to WARU.

Note: We urge all participants to try to combine testing days 3 and 4 together (if possible), to ensure that cognitive testing and the venous blood draw occur within the same 48-hour window to when the last capsules of the 6-week trial are taken.

Testing day 4 (can be combined with day 3 if needed)

Within 48 hours after testing day 3, still following the supplementation regime, we would like you to come to WARU after a 12 hour fast for your venous blood draw (3 tubes), followed by tea and toast (please bring your own breakfast if you'd prefer). Then you will be asked to digitally complete the EQ-5D (5L) and MMSE questionnaire. We will measure your height and weight, waist, and hip circumference.

There will be an optional feedback questionnaire at the end.

What will I gain?

There is no financial gain for you if you decide to join this study. You will allow us to gain important insight into the *PoZibio*TM supplement to improve cognitive performance in healthy volunteers, which may be applied to other cohorts such as those suffering from vascular dementia and Alzheimer's disease.

Are there potential side effects?

The supplements have already been tested for any adverse effects in a human cohort, however if any negative effects occur, please refrain from continuing in the study. The supplements are not suitable for vegetarians or vegans.

EEG is non-invasive, however placing the EEG electrodes along the scalp can be time consuming (approximately 45 minutes), and you will be required to sit relatively still during the application and testing process (the application and testing process combined will take approximately 2 hours). The application of the EEG cap will require EEG gel (saline solution) to be applied to your scalp, which will make your hair messy upon removal of the cap. Towels will be placed along your shoulders to avoid the solution meeting your clothes, and these towels (in addition to paper towels) will be provided to remove any excess gel from your hair. Hair washing facilities will also be available in P5 for you to use, but this will require a short walk from P4 back to P5, so bring a hat to cover your head if this would make you more comfortable. Venous blood draws can also cause localised soreness, stress and dizziness.

What if I no longer want to be a part of the study?

Whilst we would be sorry to see you leave the study, participation is entirely voluntary, and you are free to withdraw at any stage without explanation. All data collected over the investigation can be withdrawn, however only up to the point of data analysis. If you chose to leave the study, this will not affect your involvement in future research studies managed by the WARU.

What if I feel unwell during the study, or if I or a member of my family/household develop COVID-19 related symptoms? What if something else goes wrong during the study?

If you, or a member of your family/household become unwell during the study, please alert a member of the research team immediately using the contact information at the end of this document.

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Participation in the study should be suspended immediately until further discussion with the research team has taken place. If you become unwell at any point and need medical assistance, please contact 111 and seek advice from the NHS health sector or your doctor's surgery. We have a duty of care towards you and can help monitor your health remotely over 14 days and will help in any way we can.

Please alert a member of the research team immediately using the contact information at the end of this document.

Will the information and data be confidential?

Yes. Only those researchers involved will be able to look at the information you provide. Specific details, which identify you, will only be available to the researchers. After the end of the study, any information relating to you will be made pseudonymous (coded without your name associated). You will not be identifiable in any publication that may arise from this research. If you meet the exclusion criteria for the study, then your personal details shall be removed from the study.

Please note that in exceptional circumstances confidentiality may have to be breached in cases where persons are considered to be at risk or if required by law.

Will my GP be informed?

No.

What will happen to the samples collected?

The urine samples that are collected will be examined at analytical laboratories in Aberystwyth University, Bronglais hospital and AberInnovation. All samples will be stored securely and pseudonymously (coded). We will perform tests in blood to investigate the metabolism and excretion kinetics of the supplements and clinical biochemistry at Bronglais hospital. After the study has finished, the samples will be stored in our laboratory freezers in accordance with government regulations. Your name and details will no longer be associated with the samples. We will keep some samples securely for up to 5 years so that if new techniques or biomarkers are discovered, in line with this study, we can do further testing without having to collect new samples from other volunteers.

Who has reviewed the project?

This project has been reviewed and approved by the Research Ethics Panel, Aberystwyth University (ethics@aber.ac.uk). As the research team, we are required to conduct the research in accordance guidelines set out.

Does the project conform to GDPR guidelines?

This research is being conducted in accordance with the GDPR guidelines. The AU Data Protection Manager provides oversight of AU activities involving the processing of UK GDPR and special category data, and can be contacted at infocompliance@aber.ac.uk. Your personal data will be stored securely and processed for metabolomic analysis. The legal basis that would be used to process your personal data will be 'a task in the public interest'. If you are concerned about how your personal data is being processed, please contact AU in the first instance at infocompliance@aber.ac.uk. If you

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remain dissatisfied, you may wish to contact the Information Commissioner's Office (ICO). Contact details, and details of data subject rights, are available on the ICO website at: <https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights/>.

What do I do next?

Either contact the WARU team (waru@aber.ac.uk) or phone 01970622299 to confirm you wish to proceed, and we will contact you shortly. If you have any further questions after reading this document, please do not hesitate to contact us. We hope you agree to participate and look forward to hearing from you very soon.

Many thanks,
WARU Team

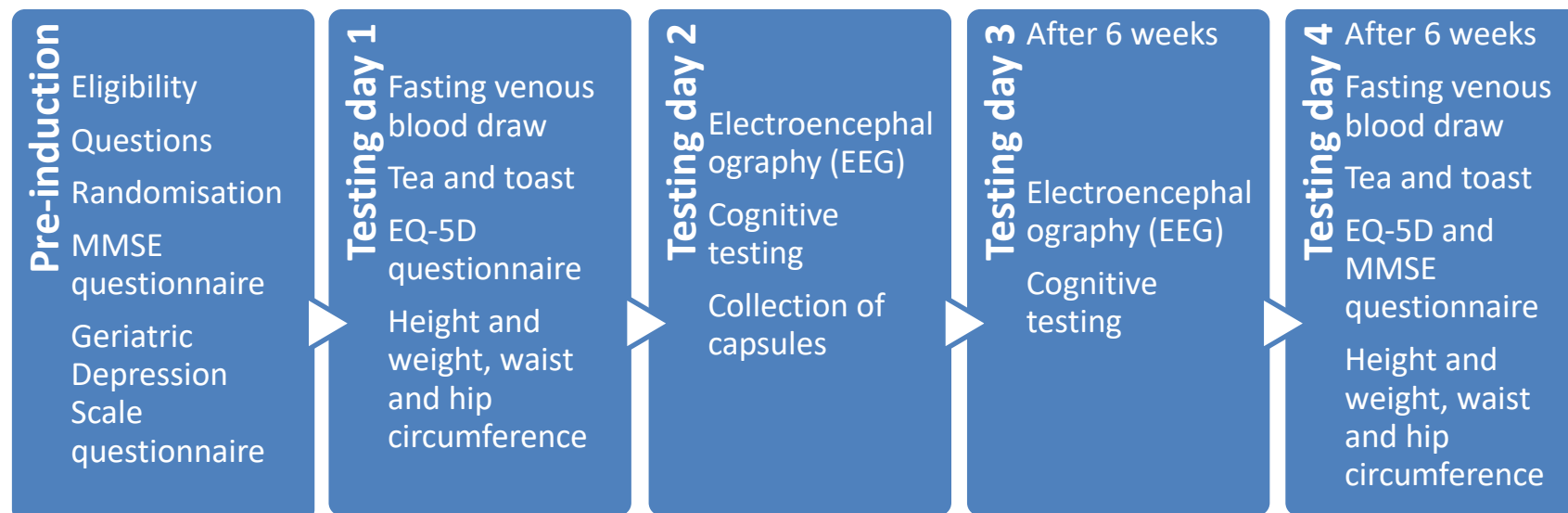
Contact for support:

Samaritans: 01970 116 123
jo@samaritans.org
<https://www.samaritans.org/branches/samaritans-aberystwyth-and-mid-wales>

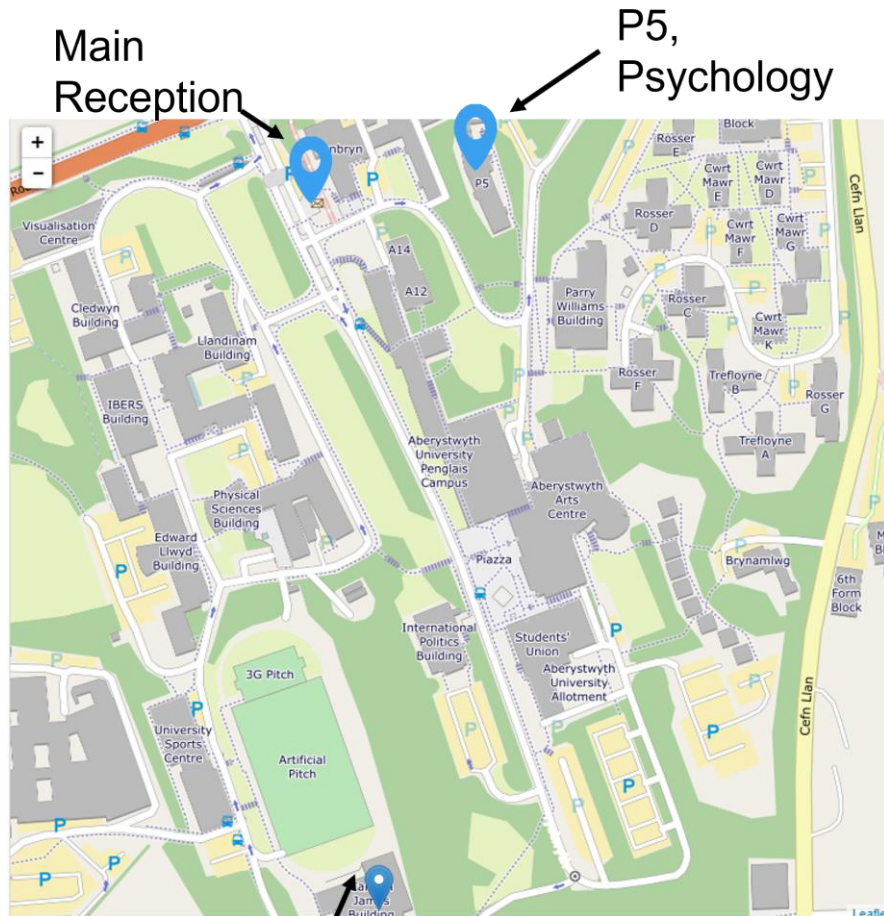
Mind: 01970 626 225
info@mindaberystwyth.org
<http://mindaberystwyth.org/>

Mentalhealth.org.uk: <https://www.mentalhealth.org.uk/your-mental-health/getting-help>

Flowchart of the experimental sequence



Campus Map



WARU, Carwyn James
building

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