

# Effects of a supplement on cognitive function and brain activity in middle age and older healthy adults

<b>Submission date</b> 10/05/2023	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 15/05/2023	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 15/05/2023	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

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. Post-biotics, 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™ capsules contains the probiotics *Lactobacillus paracasei* which is a species of lactic acid bacteria 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™.

Understanding whether cognition, in middle aged and older healthy adults, may be positively affected by the oral consumption of postbiotics, is important for helping us better understand the neuroprotective and enhancing properties of postbiotics and their future implementation into food and supplements. Electroencephalography (EEG) is a low cost, non-invasive method to record an electrogram of the spontaneous electrical activity of the brain. The bio signals detected by EEG have been shown to represent the postsynaptic potentials of pyramidal neurons in the neocortex and allocortex. It shall be combined with 3 psychological tasks (Stroop, Go/No-Go, and Flanker), to measure a variety of cognitive domains including attention, processing speed, accuracy, and response inhibition (Davidson et al., 2003; Feil et al., 2003; Redick et al., 2011). An eyes open/closed task will obtain baseline measurements for resting state. The Mini Mental State Exam (MMSE) questionnaire and geriatric depression scale (GDS) shall be used as screening tools to assess global cognitive function and depressive symptomology in participants prior to taking part. The EQ-5D questionnaire shall be used to obtain an overall profile of the health state and quality of life of participants.

We will collect venous blood samples (3 x 4.5mL) 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 (C-reactive protein in plasma as a marker of inflammation, Kidney function tests including sodium/potassium /creatinine/urea, cholesterol and Triglycerides, and Liver function tests (LFTs) Aspartate

aminotransferase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), Gamma-glutamyltransferase (GGT), Prothrombin time (PT), Albumin) at Bronglais hospital.

Who can participate?

Anyone that is aged over 50 years and meets the eligibility criteria

What does the study involve?

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. 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'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 buildings, which can be combined if needed into two sessions. You will be randomised to one of two supplements, 2 x PoZibio™ capsules daily or 2 x placebo capsules daily for 6 weeks, to be consumed in the morning. Randomisation will be blinded, and neither you nor the researcher will know what group you're in, until after the end of the study.

Testing Sequence

Testing day 1 (start)

On your pre-organised day and time, come to WARU after a 12 hour fast for a venous blood draw (3 tubes), followed by tea and toast. 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.

Testing day 2

A researcher will meet you and guide you to the psychology building, where you will be encouraged to go to the toilet prior to testing.

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. Following your participation, you will be directed to the collection of the capsules back at WARU.

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. This will be your final assessment of EEG and cognitive testing.

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. 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 are the possible benefits and risks of participating?

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™ 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.

Where is the study run from?

Well-being and Health Assessment Research Unit (WARU) at Aberystwyth University (UK)

When is the study starting and how long is it expected to run for?

May 2022 to December 2023

Who is funding the study?

Welsh Government through a Covid Recovery Challenge Fund led by SMART recovery Future Foods (UK)

Who is the main contact?

Amanda Lloyd PI [abl@aber.ac.uk](mailto:abl@aber.ac.uk)

Victoria Wright [viw8@aber.ac.uk](mailto:viw8@aber.ac.uk)

## Contact information

### Type(s)

Principal Investigator

### Contact name

Dr Amanda Lloyd

### ORCID ID

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### Contact details

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## Additional identifiers

### EudraCT/CTIS number

Nil known

**IRAS number****ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

23766

## **Study information**

**Scientific Title**

Effects of a post-biotic supplement (Pozibio) on cognitive function and brain activity in middle age and older healthy adults

**Acronym**

PZAC

**Study objectives**

Primary objectives:

1. Test our hypothesis that exposure to PoZibio™ will alter brain activity and cognitive function in middle aged and older adults.
2. Determine the feasibility of using PoZibio™ in middle aged and older adults.

Secondary objectives

1. Determine if the administration of PoZibio™ alters specific cognitive domains including attention, processing speed, executive function, or depressive symptoms in study subjects.
2. Establish the variability in the effects of PoZibio™ for conducting power analysis for future studies with the investigational product.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 26/04/2023, Research Ethics Committee at Aberystwyth University (Aberystwyth University, Reception, Penglais, Aberystwyth, Ceredigion, SY23 3FL, UK; +44 (0) 1970 621694; lif1@aber.ac.uk), ref: 23766

**Study design**

Randomised placebo controlled parallel trial

**Primary study design**

Interventional

**Secondary study design**

Randomised parallel trial

**Study setting(s)**

Home, University/medical school/dental school

**Study type(s)**

Prevention, Quality of life

## **Participant information sheet**

See study outputs

## **Health condition(s) or problem(s) studied**

Clinically relevant benefits in terms of cognitive function

## **Interventions**

A randomised, placebo-controlled parallel human clinical trial of heat-treated *Lactobacillus paracasei* (post-biotics) in healthy middle-aged and older subjects is proposed, to assess the potential for clinically relevant benefits in terms of cognitive function. We are aiming to recruit a cohort (n = 30) of middle-aged and older adults (>50 years) who will be randomised using SPSS software into PoZibio™ (2 x capsules daily) or placebo (2 x capsules daily) supplementation for 6 weeks. Subjects will be asked to take both capsules in the morning with their breakfast. The placebo will be matched to the active product by taste and texture.

We shall combine Electroencephalography (EEG) with 3 psychological tasks (Stroop, Go/No-Go, and Flanker), to measure a variety of cognitive domains including attention, processing speed, accuracy, and response inhibition. An eyes open/closed task will obtain baseline measurements for resting state. The Mini Mental State Exam (MMSE) questionnaire and geriatric depression scale (GDS) shall be used as screening tools to assess global cognitive function and depressive symptomology in participants prior to taking part. The EQ-5D questionnaire shall be used to obtain an overall profile of the health state and quality of life of participants.

We will collect venous blood samples (3 x 4.5mL) 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 (CRP, Kidney function tests: Sodium/potassium/creatinine/urea, Cholesterol/Triglyceride, Liver function tests (LFTs) Aspartate aminotransferase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), Gamma-glutamyltransferase (GGT), Prothrombin time (PT), Albumin) at Bronglais hospital.

## **Intervention Type**

Supplement

## **Primary outcome measure**

Measured at baseline and 6 weeks:

1. Cognitive Control (Selective attention, processing speed, mental flexibility) measured using the Stroop task in E-Prime
2. Response inhibition (core construct in cognitive control and self-regulation) measured using the Go/No-go task in E-Prime (commission errors score)
3. Selective attention and response inhibition (core constructs in cognitive control and self-regulation) measured using the Flanker task in E-Prime (response time and accuracy)
4. Electroencephalogram (EEG) during the Stroop task assessing event related potentials (ERP's) in the P3 component and the N2 component across the frontal and parietal regions
5. Electroencephalogram (EEG) during the Flanker task assessing event related potentials (ERP's) in the P3 component and the N2 component across the frontal and parietal regions
6. Electroencephalogram (EEG) during the go/no-go task assessing event related potentials (ERP's) in the P3 component and the N2 component across the frontal and parietal regions
7. Electroencephalogram (EEG) during the stroop, Flanker and go/no-go tasks assessing alpha and delta activity

8. EuroQol 5 Dimension 5L questionnaire: Generic quality of life. Mobility- Level 1-5 Self-Care- Level 1-5, Usual Activities- Level 1-5, Pain/Discomfort- Level 1-5, Anxiety/Depression- Level 1-5, EQ-VAS: Numerical value between 0-100 representing how the patient perceives their overall health to be.

### **Secondary outcome measures**

Measured at baseline and 6 weeks:

1. C-reactive protein in plasma as a marker of inflammation
2. Kidney function tests including sodium/potassium/creatinine/urea
3. Total Cholesterol using blood test
4. Total Triglyceride using blood test
5. Liver function tests (LFTs). Aspartate aminotransferase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), Gamma-glutamyltransferase (GGT), Prothrombin time (PT), Albumin, using blood test
6. Changes in short chain fatty acids concentrations in plasma measured using Gas Chromatography-Flame Ionization Detection

### **Overall study start date**

16/05/2022

### **Completion date**

31/12/2023

## **Eligibility**

### **Key inclusion criteria**

1. Subjects over 50 years of age
2. Subjects with Mini-Mental State Exam (MMSE) of 25-30 inclusive (global cognitive function)
3. Subjects who are able to undergo EEG and to commit to visits to WARU/P5.
4. Subjects who are able to provide venous blood samples.
5. Subjects able to provide written informed consent PRIOR to performing any study procedures.

### **Participant type(s)**

Healthy volunteer, All

### **Age group**

Adult

### **Lower age limit**

50 Years

### **Upper age limit**

100 Years

### **Sex**

Both

### **Target number of participants**

40

## Key exclusion criteria

1. Subjects with diagnosis of Alzheimer's disease or other dementia
2. Subjects taking medication for the treatment of dementia (such as acetylcholinesterase inhibitors (Aricept, Exelon), memantine (Namenda) or other medications with similar mechanisms of action) or medical foods (such as Cerefolin, Souvenaid, Axona) for the treatment of dementia.
3. Subjects who are already regularly taking probiotics, post-biotics, nutraceutical and/or vitamin supplements related to PoZibio™ within 30 days of screening.
4. Subjects with Geriatric Depression Scale > 6
5. Subjects with a Mini Mental State Exam score below 25
6. Subjects who are pregnant or lactating
7. Subjects with medical condition or disease that is life threatening
8. Subjects who smoke cigarettes or use other products containing nicotine.
9. Subjects diagnosed with diabetes.
10. Subjects taking warfarin.
11. Subjects who identify as being vegetarian or vegan
12. Subjects who have a diagnosed or suspected mental health condition, or who have any concerns surrounding their mental health
13. Subjects who have immediate family members with diagnosed mental health condition or suspected mental health concerns

## Date of first enrolment

15/05/2023

## Date of final enrolment

31/07/2023

## Locations

### Countries of recruitment

United Kingdom

Wales

### Study participating centre

#### Aberystwyth University

Well-being and Health Assessment Research Unit (WARU)

Cledwyn Building

Penglais Campus

Aberystwyth

United Kingdom

SY23 3DD

## Sponsor information

### Organisation

Welsh Government

**Sponsor details**

Food Business Manager

Food Division

Llandudno Junction

Llandudno Junction

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LL31 9RZ

+44 (0)300 062 5139

wendy.jones@gov.wales

**Sponsor type**

Government

**Website**

<http://gov.wales/?skip=1&lang=en>

**ROR**

<https://ror.org/000wh6t45>

**Funder(s)**

**Funder type**

Government

**Funder Name**

Llywodraeth Cymru

**Alternative Name(s)**

Welsh Government, The Welsh Government

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Local government

**Location**

United Kingdom

**Results and Publications**

Publication and dissemination plan



Planned publication in a high-impact peer-reviewed journal

### Intention to publish date

31/12/2023

### Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date

### IPD sharing plan summary

Data sharing statement to be made available at a later date

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>		11/05/2023	11/05/2023	No	Yes
<a href="#">Protocol file</a>			12/05/2023	No	No