ISRCTN10175490 https://doi.org/10.1186/ISRCTN10175490

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

Submission date
10/05/2023

Recruitment status
No longer recruiting

Registration date
15/05/2023

Overall study status
Completed

Last Edited
15/05/2023

Condition category
Other

[X] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] 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 PoZibioTM 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 suffers 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 Decmeber 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
Victoria Wright viw8@aber.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Dr Amanda Lloyd

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Prevention, Quality of life

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(s)
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.

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Upper age limit
100 years

Sex
All

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, Excelon), 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

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

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?
Participant information sheet		11/05/2023	11/05/2023	No	Yes
Protocol file			12/05/2023	No	No
Protocol file	version 3	12/03/2025	27/10/2025	No	No