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The impact of Pozibio and/or Cerbella supplement on the function of the gut, brain, and gut-brain axis, when compared with a placebo control in healthy middle-aged and older adults

Submission date
08/09/2024

Recruitment status
No longer recruiting

Registration date
23/09/2024

Overall study status
Completed

Last Edited
03/11/2025

Condition category
Other

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Omega 3 (Ω-3) polyunsaturated fatty acids, such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), have been shown to improve learning and memory age-related cognitive decline in adults. Additionally, ginseng extracts have been shown to improve cognitive performance in healthy volunteers, as well as subjects suffering from vascular dementia and Alzheimer's disease. Numerous studies suggest green tea may confer health benefits due to its pharmacological and biochemical properties. Cerbella™ soft gels contain a liquid combination of fish oil (standardised to EPA and DHA), panax ginseng extract (standardised to ginsenosides), green tea extract (standardised to green tea catechins) in a flavoured base of lecithin phospholipids. In addition, heat-treated (pasteurised or killed) probiotics (widely available in foods and drinks, such as yoghurt or kombucha) known as postbiotics (in the form of supplements, cell-free supernatants, and purified key components), can confer beneficial immune effects, protection against bacterial infections, and maintenance of gut health which can positively impact on mental health and cognitive ability. Postbiotics are advantageous for food industry applications as they can easily be supplemented in several food lines/products and are shelf stable. PoZibio™ capsules contain the probiotics Lactobacillus paracasei D3.5, which is a species of lactic acid bacteria (often used in the fermentation of dairy products) which has been heat-killed in PoZibio™. It's found in the human intestinal tract and mouth, but also in foods such as yoghurt and naturally fermented vegetables and milk. This study of heat-treated Lactobacillus paracasei D3.5 (post-biotics) and/or Cerbella supplementation in healthy middle-aged and older subjects is proposed, to assess the potential for improved physiological, gut and cognitive health. The study will also explore if consumption of Cerbella™ soft gels or PoZibio™ capsules, in healthy middle-aged and older subjects (>55 years), is beneficial in terms of cognitive function and overall health and well-being compared to a placebo control.

Who can participate?
Healthy middle-aged and older adults (>55 years) volunteers

What does the Study involve?
After being provided with study information, participants complete an online eligibility screening through REDCap or over the phone. Eligible participants are invited to an in-person or remote induction session where they receive home sampling kits for urine and stool tests and complete consent forms. Appointments are scheduled for day 0 and day 60, during which participants undergo EEG testing and behavioral tasks, and provide biological samples. Before day 0, participants complete self-report questionnaires online or in paper form. At the first visit, they provide urine, stool, and blood samples, followed by EEG and cognitive tasks at the second visit. On day 60, these activities are repeated. After the trial, participants may complete a feedback survey and are informed of their assigned group, receiving vouchers for their participation.

What are the possible benefits and risks of participating?
Participants will receive a £20 Amazon voucher for each batch of testing sessions (day 0 and day 60), equating to a total of £40 for completion of the trial. Participants will also allow researchers to gain important insight into the Cerbella™ and Pozibio™ supplements, and the extent to which they support or improve overall physical and mental health in older, healthy populations, which may be applied to other cohorts such as those suffering from vascular dementia and Alzheimer's disease.

The supplements have already been tested for any adverse effects in a human cohort, however, if any negative effects occur, participants should 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 30 minutes), and the participant will be required to sit relatively still during the application and testing process (the application and testing process combined will take approximately 1-1.5 hours). The application of the EEG cap will require EEG gel (saline) to be applied to the participant's scalp, which will make their hair messy upon removal of the cap. Towels will be placed along participants' shoulders to avoid the solution meeting their clothes, and these towels (in addition to paper towels) will be provided to remove any excess gel from their hair. Hair-washing facilities will also be available for participants to use. In addition, capillary blood draws can cause localised soreness to their fingers.

Where is the study run from?
WARU, Aberystwyth and Trimsaran Community Centre, South Wales and the University of South Florida

When is the study starting and how long is it expected to run for?
September 2023 to August 2025

Who is funding the study?
1. Innovate UK
2. Better Brain for All

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
The impact of Pozibio and/or Cerbella supplement on the function of the gut, brain, and gut-brain axis, from a physiological and cognitive perspective, when compared with a placebo control in healthy middle-aged and older adults

Acronym
Better Brain

Study objectives
A randomised, double-blinded, placebo-controlled, parallel human clinical trial of heat-treated Lactobacillus paracasei D3.5 (post-biotics) and/or Cerbella supplementation in healthy middle-aged and older subjects is proposed, to assess the potential for improved physiological and cognitive health. The study will explore if consumption of Cerbella™ soft gels or PoZibio™ capsules, in healthy middle-aged and older subjects (>55 years), is beneficial in terms of cognitive function and overall health and well-being when compared to a placebo control.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 23/07/2024, Aberystwyth University Research Ethics Panel (Research, Business & Innovation, Visualisation Centre, Penglais, Aberystwyth, SY23 3BF, United Kingdom; +44 (0) 1970622385; ethics@aber.ac.uk), ref: 25719

Study design
Randomized double-blinded placebo-controlled multicentre parallel human intervention trial

Primary study design
Interventional

Study type(s)
Prevention, Quality of life

Health condition(s) or problem(s) studied
Healthy middle-aged and older subjects to assess the potential for improved physiological, gut and cognitive health

Interventions
A randomised, double-blinded, placebo-controlled, multi-centre, parallel human intervention trial of heat-treated Lactobacillus paracasei D3.5 (post-biotics) and/or Cerbella supplementation in healthy middle-aged and older subjects is proposed, to assess the potential for improved physiological, gut and cognitive health.
Participants will be randomised using an online tool by site and gender into 1 of 4 groups:
1. PoZibio™ (1 x 167mg capsule daily) and matching Cerbella placebo (1 x soft gel daily)
2. Cerbella (1 x soft gel daily) and PoZibio placebo (1 x 167mg capsule daily)
3. PoZibio™ (1 x 167mg capsule daily) and Cerbella (1 x soft gel daily)
4. Placebo (1 x capsule daily) and placebo (1 x soft gel daily).

In detail:
Upon the first point of contact, participants shall be provided with an information sheet detailing the study, followed by a REDCap link for completion of eligibility screening.

Online Eligibility Session
- Provide basic details (name, DOB, gender, preferred contact method), and answer a few medical health questions, within REDCap (compliant with GDPR standards), to assess eligibility. For participants without access to a valid email address or home PC, these details will be obtained over the phone with a member of the Well-being and Health Research Assessment Unit (WARU) team.
- Receive an invitation for an in-person induction session (via email or over the phone).

Online/remote Induction Session
- Participants shall be posted their consent form to complete, along with written instructions for how to use the urine and stool home sampling kits. For participants without access to an email address, they will also be posted a paper copy of the participant information sheet.
- Participants shall be posted their urine and stool home sampling kits.
- The researcher will schedule the participant's day 0 and day 60 appointments via phone or email and provide the opportunity for participants to ask questions.
- Measure height, weight, waist, and hip circumference.

Two Days before Day 0 Assessments
- Participants with access to a PC and a valid email address will be sent a REDCap link for completion of the self-report questions.
- Participants without access to a PC or valid email address shall be posted paper copies of the questionnaires at the same time as their consent form and urine/stool home sampling kits, which participants can complete at home the day before their assessments and bring with them, OR they can complete them with the researcher whilst their EEG cap is fitted.

Experimental visit 1 and 2- week 0 EEG and Behavioural Tasks
Visit 1 week 0:
- Stool samples will have been collected within the 12 hours before this appointment, and urine samples will have been collected that morning.
- Collection of capillary blood samples.

Visit 2 week 0 - within 48 hours of visit 1
- Participants are to arrive with clean, dry hair.
- EEG cap preparation (participants without access to a PC at home can complete paper versions of the questionnaires in this time (duration = 25-30 minutes)
- Completion of the behavioural tasks for cognitive assessments within E-Prime (an 'eyes open /closed task', the Stroop task, and the Go/No-go task) (Updated 27/10/2025: Resting State task followed by the Stroop Task and an Nback Task)
- Thorough instructions and practice rounds will be provided, and the opportunity to ask questions.
- Collection of supplements from the WARU team.
- Visits 1 and 2 may be combined

Day 60 EEG and Behavioural Tasks
- Repeat the activities explained above

After the trial:
- Optional completion of a feedback questionnaire (this can be completed digitally or provided during their day 60 appointment).
- Participants will be informed of which group they were randomly assigned to.
- Participants will be provided with vouchers (via email or post) to compensate for their participation.

Intervention Type
Supplement

Primary outcome(s)
Current primary outcome measures as of 27/10/2025:
1. Cognitive Control (Selective attention, response inhibition and processing speed) measured using the Stroop Task in EPrime (faster response time and improved accuracy; reduced Stroop interference) from baseline score at 60 days after intervention
2. Working memory and mental flexibility, measured using the NBack Task in EPrime (faster response time and improved accuracy for correctly identifying targets) from baseline score at 60 days after intervention
3. Assessing event-related potentials (ERPs) using an electroencephalogram (EEG) in the N2, P3 and LPC components across the frontal and parietal regions, during a Stroop and NBack task. After 60 days of intervention, reduced N2 amplitude and/or shorter N2 latency; larger P3 amplitude and shorter latency; increased LPC amplitude and shorter latency. Indicative of

improved conflict detection, stimulus categorisation, and cognitive control.
4. Assessing Delta, Theta and Alpha activity using an EEG during the Stroop and NBack tasks. After 60 days of intervention, reduced theta activity (frontal midline) during incongruent trials (improved conflict monitoring); increased alpha power (parieto-occipital) during tasks (improved attentional control); reduced delta activity (frontal) indicating reduced cognitive load during tasks.

Previous primary outcome measures:
1. Cognitive Control (Selective attention, processing speed, mental flexibility) measured using the Stroop task in E-Prime (faster response time and improved accuracy) from baseline score at 60 days after intervention
2. Response inhibition (core construct in cognitive control and self-regulation) measured using the Go/No-go task in E-Prime (fewer commission errors) score from baseline score at 60 days after intervention
3. Assessing event-related potentials (ERPs) in the P3 component and the N2 component across the frontal and parietal regions measured using an electroencephalogram (EEG) during the Stroop task after 60 days of intervention, no delay of the P3 component and more N2 components when compared with baseline
4. Assessing event-related potentials (ERPs) in the P3 component and the N2 component across the frontal and parietal regions measured using an EEG during the go/no-go task after 60 days of intervention, no delay of the P3 component and more N2 components when compared with baseline and the placebo group (at day 60)
5. Assessing alpha and delta activity measured using an EEG during the Stroop and go/no-go tasks after 60 days of intervention, increased alpha and delta activity when compared with baseline

Key secondary outcome(s))
The following secondary outcome measures will be assessed at baseline and 60 days after intervention:
1. Cognition measured using the Mini-Mental State Exam (MMSE) (removed 27/10/2025)
2. Health measured using the 36-item Short Form Health Survey (SF-36)
3. Sleep quality measured using the Pittsburgh Sleep Quality Index (PSQI)
4. Gastrointestinal health measured using the Gastrointestinal Symptom Rating Scale (GSRS)
5. Mental wellbeing measured using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWS)
6. Inflammation measured using fecal mucin levels with an ELISA kit
7. Inflammation measured using fecal calprotectin levels with an ELISA kit
8. Leaky gut markers (LBP, sCD14, Zonulin) measured in plasma with an ELISA kit
9. Inflammatory cytokines (TNF-alpha, IL-6) measured in plasma
10. Total short-chain fatty acids concentrations in plasma measured using Gas Chromatography-Flame Ionization Detection
11. Metabolomic Fingerprint in Plasma: Polar and non-polar chemistry in plasma measured using Flow Infusion Electrospray Ionisation Mass Spectrometry (FIE-MS)
12. Metabolomic Fingerprint in Urine: Polar and non-polar chemistry in urine measured using Flow Infusion Electrospray Ionisation Mass Spectrometry (FIE-MS)
13. Microbiome in Stools: Microbiome diversity and phylogenetic abundances in stools measured using whole genome sequencing

Completion date
31/08/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 27/10/2025:
1. Subjects over 55 years of age
2. Subjects able to provide written informed consent PRIOR to performing any study procedures
3. Subjects who can commit to visits to one of the centres
4. Subjects who are willing to complete a series of questionnaires including the: Pittsburgh Sleep Quality Index (PSQI), 36-Item Short Form Health Survey (SF-36), Warwick-Edinburgh Mental Wellbeing Scale (WEMWS), and the Gastrointestinal Symptom Rating Scale (GSRS)
5. Subjects who are willing to provide capillary blood, stool, and urine samples, and commit to EEG appointments

Previous inclusion criteria:
1. Subjects over 60 years of age
2. Subjects able to provide written informed consent PRIOR to performing any study procedures
3. Subjects who can commit to visits to one of the centres
4. Subjects who are willing to complete a series of questionnaires including the: Pittsburgh Sleep Quality Index (PSQI), Mini Mental State Exam (MMSE), 36-Item Short Form Health Survey (SF-36), Warwick-Edinburgh Mental Wellbeing Scale (WEMWS), and the Gastrointestinal Symptom Rating Scale (GSRS)
5. Subjects who are willing to provide capillary blood, stool, and urine samples, and commit to EEG appointments

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
55 years

Upper age limit
111 years

Sex
All

Total final enrolment
117

Key exclusion criteria
Current participant exclusion criteria as of 24/09/2024:
1. Subjects with a diagnosis of Alzheimer’s disease, Parkinson's 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 who are pregnant or lactating
7. Subjects with a medical condition or disease that is life-threatening
8. Subjects who smoke cigarettes or use other products containing nicotine
9. Subjects who have been taking antibiotics, and/or having diarrhea and vomiting in the past 30 days
10. Any subjects to whom PI feels not to be eligible based on critical conditions
11. Subjects who have a diagnosed or suspected mental health condition, or who have any concerns surrounding their mental health
12. Subjects who are vegetarian/vegan

Added 27/10/2025:
Note: During screening, participants were asked about any dietary restrictions. Those who were vegetarian/vegan were informed that they could still take part in the trial, but that they would only be randomly allocated to one of two out of the four arms (active PoZibio ™/Cerbella™ placebo or double placebo). This change was made to make the trial more inclusive.

Previous participant exclusion criteria:
1. Subjects with a 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 who are pregnant or lactating
7. Subjects with a medical condition or disease that is life-threatening
8. Subjects who smoke cigarettes or use other products containing nicotine
9. Subjects who have been taking antibiotics, and/or having diarrhea and vomiting in the past 30 days
10. Any subjects to whom PI feels not to be eligible based on critical conditions
11. Subjects who have a diagnosed or suspected mental health condition, or who have any concerns surrounding their mental health
12. Subjects who are vegetarian/vegan

Date of first enrolment
08/09/2024

Date of final enrolment
31/05/2025

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

United States of America

Study participating centre
Wellbeing and Health Assessment Research Unit (WARU)
Department of Life Sciences - Wellbeing and Health Assessment Research Unit (WARU)
Carwyn James Building, Aberystwyth University, Penglais Campus
Aberystwyth
United Kingdom
SY23 3FD

Sponsor information

Organisation
Aberystwyth University

ROR
https://ror.org/015m2p889

Funder(s)

Funder type
Government

Funder Name
Innovate UK

Alternative Name(s)
Technology Strategy Board

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Better Brain for All

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plan 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			09/09/2024	No	Yes
Protocol file	version 2	10/09/2024	10/09/2024	No	No
Protocol file	version 3	12/03/2025	27/10/2025	No	No