Gut-brain health effects of PREbiotics in older adults with suspected COgnitive DEcline: the PRECODE study

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mental impairment disorders
Study type	Interventional

Summary

ID

NL-OMON56688

Source
ToetsingOnline

Brief title
PRECODE

Condition

- Mental impairment disorders

Synonym
personal experience of decreased cognitive ability with age, Subjective Cognitive Decline

Research involving
Human

Sponsors and support

Primary sponsor: Wageningen Universiteit
Source(s) of monetary or material Support: Cosun Nutrition Centre,Oceanium Ltd,Public private partnership (TKI): Cosun Nutrition Centre;Roquette (France);Sensus

(Netherlands);Oceanium (Scotland),Roquette,Sensus B.V

Intervention

Keyword: ageing, cognitive decline, dietary fibre, gut-brain axis

Outcome measures

Primary outcome

The primary study parameters are baseline (before week 1) and follow-up (after week 26) measures of

(1) BOLD signal activity and task accuracy during n-back task fMRI.

Secondary outcome

The secondary study parameters include

(1) Neuropsychological test battery (NTB)

(2) Brain health parameters (in plasma): Tryptophan metabolites (indoles); Aβ1-42/Aβ1-40 ratio; cortisol levels; brain-derived neurotrophic factor (BDNF); T1/T2 weighted anatomical scans of brain regions of interest- hippocampus, temporal- and prefrontal cortices.

(3) Gastrointestinal health parameters (plasma and faeces): intestinal barrier function, faecal microbiota composition (qualitative and quantitative), intestinal inflammation, intestinal transit time (ITT), short- (SCFA) and branched chain fatty acid (BCFA) concentrations, faecal water content & pH; gastrointestinal symptoms questionnaire and Bristol Stool Scale (BSS).

(4) Immune and metabolic markers: inflammatory marker panel, fasting glucose and insulin, HbA1c, lipogram (LDL, HDL, total cholesterol, triglycerides).

Study description

Background summary

Due to the greying of society, a triplication of the number of people with dementia worldwide, with Alzheimer*s disease (AD) as the commonest form, is expected by 2050. Compelling evidence points towards a crucial role of intestinal health as one potential etiological modifier of dementia, with the (microbiota) gut-brain axis (MGBA) receiving increasing attention. A number of preclinical studies have demonstrated benefit of various sources of dietary fibre for their capacity to improve gut health, cognitive functioning, general mood, glycaemia, immunogenicity, and, to inhibit tau phosphorylation, the latter which is a hallmark in AD brain. The proposed mechanism of dietary fibres is by changing gut microbiota and its metabolites, thereby having effects on the gut-brain axis and other health parameters.

Subjective cognitive decline (SCD) lies on the continuum of AD, and subjects with this condition are at increased risk of further conversion to mild cognitive impairment (MCI) or AD. Currently, no cure is available for AD. Various symptomatic and a few disease-modifying treatments are available, but these treatments only have very limited or mild clinical effects and are often accompanied by severe side effects.

Clinical follow-up studies to evaluate the effect of dietary fibre in older adults with suspected cognitive decline are required, but are still lacking to date.

Study objective

The primary objective of this study is to investigate the effect of 26 weeks of supplementation with three different dietary fibres (chicory inulin, resistant dextrin, and seaweed polysaccharide) compared to a placebo (maltodextrin) on microbiota gut-brain health effects in older adults (aged 60-79) with Subjective Cognitive Decline Plus (SCD+) by assessing changes in brain function and working memory by blood oxygen level dependant (BOLD) signal activity and task accuracy during n-back task functional magnetic resonance imaging (fMRI) assessment.

The secondary objectives are to investigate the effects of 26 weeks of supplementation with dietary fibre (chicory inulin, resistant dextrin, and, seaweed polysaccharide) compared to placebo (maltodextrin) in older adults on the following parameters related to potential gut-brain pathways: (1) neuropsychological test battery scoring, (2) other relevant brain health parameters, (3) other relevant intestinal health parameters, and (4) immune and metabolic parameters.

Study design

Randomised, double-blinded, placebo-controlled intervention study with parallel design and four arms.

Intervention

To investigate the effects of the 26 weeks of supplementation of the dietary fibres on the primary and secondary outcomes, four study arms - three interventions and one placebo- are applied, with different dosages modified to each individual fibre's tolerance level and expected mechanism(s) of action:

1. Placebo (Maltodextrin) (7g per day, divided over two dosages)
2. Chicory inulin - (12g per day, divided over two dosages)
3. Resistant dextrin - (14g per day, divided over two dosages)
4. Seaweed polysaccharide - (1g per day, divided over two dosages). Will additionally contain 7g/day of placebo as a volumetric and isocaloric filler.

Study burden and risks

Participants in the three intervention arms will receive dietary fibre twice a day. Dosages have been evaluated and have no expected side effects, except possible mild gastrointestinal symptoms/discomfort that should improve with time. To prevent potential gastrointestinal discomfort, dosage will be tapered up over a one-week period. The use of dietary fibre is considered safe. For two periods of seven days at baseline and at follow-up, participants will be asked to wear a Samsung 2.0 Smartwatch to measure heart rate, physical activity, and mood. The wearable sensor can be worn while participants lead a regular lifestyle, and although the watch can cause slight discomfort after prolonged wearing (like a regular watch), it can be taken off (for a limited time) when uncomfortable.

An additional burden is the five study visits with multiple outcome assessments that will take place at Wageningen University and Gelderse Vallei Hospital (Ziekenhuis Gelderse Vallei) at baseline (before week 1) and follow-up (after week 26) including neuropsychological testing, MRI-scanning, blood drawing and faeces and urine sample collection, and clinical measurements. At mid-study (week 13) participants will visit Wageningen University only for neuropsychological testing, blood collection and clinical measurements. MRI scanning might cause mild discomfort (due to loud noises and lying down for 30 minutes), but precautions will be taken to make participants as comfortable as possible (including earplugs and cushions). Drawing blood samples might cause mild pain and sometimes bruising, which will usually fade on its own.

Subjective cognitive decline plus is a predecessor stage of AD, but at which stage the cognitive decline can still be reversed. Thereby a substantial health

benefit can still be gained. In fact, SCD+ represents a sensitive at-risk population, especially with the inclusion of extra lifestyle for brain health (LIBRA) factors, which makes it an ideal fit for our study. To the best of our knowledge, not a single trial assessing the effects of prebiotic supplementation in older adults with suspected cognitive decline has been performed yet nor has one been registered (clinicaltrials.gov).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Written informed consent
2. Fluency in Dutch (speaking, reading, writing)
3. Age between 60-79 years (at screening)
4. Subjective cognitive decline plus (SCD+), (criteria of Jessen et al. 99):

4.1 Self-reported worsening of memory;
4.2 Indication of repetitive concerns (worries) associated with SCD;
4.3 With at least one of the following two features present:
(i) onset of SCD within the last 5 years;
(ii) age at onset >=60 years of age;
5. Presence of self-reported risk factors for cognitive decline based on the weighted LIBRA criteria:
at least 2 modifiable risk factors need to be present:
(i) Diabetes mellitus type II 1 (has your doctor ever told you that you have diabetes yes/no)
(ii) High cholesterol 1 (has your doctor ever told you your cholesterol is too high yes/no)
(iii) Hypertension 1 (has your doctor ever told you that you have high blood pressure yes/no)
(iv) High BMI 1,2
(v) Heart disease 1 (has your doctor ever told you that you have a heart or blood vessel condition)
(vi) Unhealthy diet 1 (lower regular adherence to Mediterranean diet components such as fish, vegetables, olive oil, pasta
and red wine)

1Criteria defined by the short version questions from LIBRA Administration
2 Defined as >=25 kg/m2 for 60-69 years old, and >=28 kg/m2 for >=70 years old, based on self-reported height and weight.

Exclusion criteria

1. Current participation in other intervention trials
2.Technologically illiterate (complete incompetence in working with computers, apps, online questionnaires, smartwatches etc.)
3.No internet access from home
4.Clinical diagnosis of >=1 of the following:
- Neurological pathology (e.g. MCI, dementia, multiple sclerosis, Parkinson*s disease, epilepsy);
- Current malignant disease(s), with or without treatment;
- Current psychiatric disorder(s) (e.g. major depressive disorder, bipolar disorder, schizophrenia, psychosis, anxiety, posttraumatic stress disorder);
- Symptomatic/decompensated cardiovascular disease (e.g. stroke, angina pectoris, heart failure, recent myocardial infarction);
- Severe visual impairment or blindness
- Hearing or communicative impairment.
- Gastrointestinal tract disorder such as irritable bowel syndrome or inflammatory bowel disease (e.g. Chron*s disease or ulcerative colitis).
5. Current or recent (<6 weeks) use of prebiotic, probiotic, or dietary fibre supplement that may modulate the microbiota, or unwilling to stop the use of

supplements during the study
6. Current or recent (<6 weeks) of algae/phytoplankton supplements such as spirulina or chlorella, or unwilling to stop the use of supplements during the study
7. Use of psychotropic medication (anti-depressants, anti-psychotics)
8. Use of antibiotics in the 3 months before starting the study or planned use during the study
9. Being an employee of the Human Nutrition and Health Division of Wageningen University.
10. Significant cognitive impairment assessed using the Modified Telephone Interview for Cognitive Status battery (TICS-m score <23)
11. Request to have Apo-E genotype result disclosed
12. Allergy to fish or shellfish
13. Having a contra-indication to MRI scanning including:
- Ferromagnetic implants:
- Active implantable medical devices such as: insulin pump / medicine pump / neurostimulator; pacemaker / defibrillator;
- Other passive implants such as: punctured port-a-cath; synthetic heart valve
- Intra-orbital or intra-ocular metallic fragments
- Claustrophobia
14. Any other relevant medical or surgical history that is not mentioned in above criteria, which could influence the study outcome measurements, as determined by the researchers.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-07-2024
Enrollment:	164

Type:	Actual

Ethics review

Approved WMO Date:	22-04-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-08-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-11-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85910.091.23