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Changes in brain function among individuals with a mild memory impairment

Submission date
03/12/2015

Recruitment status
No longer recruiting

Registration date
21/12/2015

Overall study status
Completed

Last Edited
28/09/2022

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Mild cognitive impairment (MCI) is a condition which causes problems with memory, thinking and behaviour (cognitive function). People with MCI have difficulties with certain aspects of daily life, but they are not as severe or noticeable to others as someone with dementia. It is possible that carotenoids (naturally occurring pigments produced by plants, algae and some bacteria) may play a role in individuals with MCI, given their presence in the brain and how they protect against cell damage. In the retina (the layer at the back of the eye which is sensitive to light), there is a yellow pigment called macular pigment. This pigment is made up of three carotenoids (lutein, zeaxanthin and meso-zeaxanthin). These carotenoids are obtained solely from the diet and are believed to be important for preserving and improving vision. Recent research has found that two of these carotenoids (lutein and zeaxanthin) are also present in brain tissue, leading researchers to believe that these carotenoids may protect the nerve cells (neurons) in the brain (neuroprotection), as they do the cells in the retina. Studies have also suggested that diets high in omega-3 (an essential fatty acid found in oily fish) and vitamin E (a powerful antioxidant) could also produce these neuroprotective effects. The aim of this study is to find out whether taking supplements containing the carotenoids (lutein, zeaxanthin and meso-zeaxanthin) and fish oil (rich in omega-3) and vitamin E could help to improve cognitive function in people with MCI.

Who can participate?
Adults aged 65 years or over who are suffering from MCI and those with no cognitive impairment.

What does the study involve?
Both the participants with MCI and those without MCI are randomly allocated to one of two groups. Those in the first group are given tablets containing carotinoids (10mg lutein, 10mg meso-zeaxanthin and 2mg zeaxanthin), vitamin E (15mg) and fish oil (1g) to take every day for 24 months. Those in the second group are given a placebo (dummy tablet) to take every day for 24 months. At the start of the study and then again after 12 and 24 months, participants in both groups attend study visits, where they are asked to complete a number of questionnaires designed to test their cognitive function. Blood samples are also taken in order to analyse the composition of their blood, such as the concentration of carotenoids and fats. Carotenoid levels in at the skin surface are also measured using the Pharmanex® BioPhotonic Scanner (Nu Skin).

At these study visits, participants also undergo a number of medical tests to test their vision and likelihood of developing Alzheimer's disease.

What are the possible benefits and risks of participating?
Participants who are taking the supplements may benefit from improvements to their cognitive function and vision, however this is not guaranteed. There are no major risks of taking part in the study, although blood tests could cause pain and bruising as well as carrying a small risk of infection.

Where is the study run from?
Waterford Institute of Technology (Ireland)

When is the study starting and how long is it expected to run for?
January 2016 to December 2019

Who is funding the study?
Howard Foundation Holdings Limited (UK)

Who is the main contact?
1. Ms Rebecca Power (public)
rpower@wit.ie
2. Prof. John Nolan (scientific)
jmnolan@wit.ie

Contact information

Type(s)
Public

Contact name
Ms Rebecca Power

Contact details
Waterford Institute of Technology
Carriganore House
WIT West Campus
Carriganore
Waterford
Ireland
X91 K236
+353 (0)51 845505
rpower@wit.ie

Type(s)
Scientific

Contact name
Prof John Nolan

ORCID ID
https://orcid.org/0000-0002-5503-7084

Contact details
Waterford Institute of Technology
Carriganore House
WIT West Campus
Carriganore
Waterford
Ireland
X91 K236
+353 (0)51 834074
jmnolan@wit.ie

Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Cognitive impAiRmEnt Study: Supplementation with the macular carotenoids, vitamin E and fish oil

Acronym
CARES

Study objectives
Supplementation with the macular carotenoids, vitamin E and fish oil will improve the cognitive function of subjects with a mild cognitive impairment

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Waterford Institute of Technology Research Ethics Committee, 02/11/2015, ref: 15/CLS/01
2. University Hospital Waterford South East Region Ethics Committee (Ireland), 07/11/2015

Study design
Single-centre double-blind placebo-controlled randomised clinical trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Mild Cognitive Impairment (MCI)

Interventions

MCI subjects (n=60) will be randomised in a 50:50 masked fashion to either active supplement or placebo. Control subjects with no cognitive impairment (n=60) will be randomised in a 50:50 masked fashion to either active supplement or placebo.

Active supplement group: Participants are given MacuShield (containing 10mg lutein, 10mg meso-zeaxanthin and 2mg zeaxanthin), vitamin E (15mg) and fish oil (1g) to take daily for a total period of 24 months.

Placebo group: Participants are given a placebo to take daily for a total period of 24 months.

Participants in both groups are asked to attend study visits at baseline, 12 and 24 months. Follow-up visits will consist of measurements on cognition, visual function and macular pigment (see section titled "outcome measures" for details). In addition, demographic, lifestyle, and health information will be recorded. A blood sample will be taken to measure the levels of carotenoids and vitamin E in serum, the lipid profile and red cell DHA and EPA, and for additional blood tests (full blood count, urea and electrolytes, thyroid function tests, B12, Folate, glycosylated haemoglobin (HbA1C), homocysteine and cholesterol).

As of 18/02/2016, the additional blood tests participants undergo have been updated to include: Full blood count, sodium, potassium, chloride, urea, creatinine, thyroid function assessment (Thyroid Stimulation Hormone (TSH) and Free T4), vitamin B12, Folate, homocysteine, cholesterol (lipid profile), high sensitivity C-reactive protein, and complement factor assessment (Membrane Attack Complex (MAC) and Complement component 3 (C3).

Intervention Type
Supplement

Primary outcome(s)
Cognitive function will be measured at baseline, 12 and 24 months using the following methods:
1. Montreal Cognitive Assessment (MoCA)
2. Alzheimer's Questionnaire (AQ)
3. Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)
4. Bristol Activities of Daily Living Scale (BADLS)
5. An electroencephalogram or EEG system (BP LiveAmp System, Brain Vision UK)
6. Tests of attention, memory, executive function and decision making from the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition, UK)

As of 18/02/2016, the following outcome measure will no longer be measured:
Phonemic fluency (the FAS test) which involves naming as many words as possible within a 1 minute time limit, starting with each letter of the alphabet

Key secondary outcome(s))
1. Macular pigment will be measured by dual-wavelength autoflourescence using the Spectralis HRA + OCT Multicolour at baseline, 12 and 24 months
2. Visual function will be assessed using both best-corrected visual acuity and letter contrast sensitivity at 5 spatial frequencies at baseline, 12 and 24 months
3. Serum carotenoid (lutein, zeaxanthin, meso-zeaxanthin) and vitamin E concentrations will be measured from a blood sample using a reverse-phase High Performance Liquid Chromatography (HPLC) method at baseline, 12 and 24 months
4. Serum lipid concentrations will be measured from a blood sample using mass spectrometry at baseline, 12 and 24 months

5. Red cell DHA and EPA will be measured from a blood sample using gas chromatography at baseline, 12 and 24 months
6. Development of Alzheimer's disease will be determined based on consensus panel assessment at baseline, 12 and 24 months, and using the 4 Mountains test at baseline

Original secondary outcome measure point 1:
1. Macular pigment will be measured by dual-wavelength autoflourescence using the Spectralis HRA + OCT Multicolour and using customised heterochromatic flicker photometry (cHFP) at baseline, 12 and 24 months

Completion date
30/12/2019

Eligibility

Key inclusion criteria
MCI participants:
1. Males and females aged 65 years and over
2. Self or family member reported memory loss
3. Functionally independent in activities of daily living (as per BADLS)
4. Fulfils criteria for minimal cognitive impairment (as per RBANS)
5. Consensus panel agreement on the diagnosis of MCI (where applicable)

Non-MCI participants:
1. Males and females aged 65 years and over
2. Functionally independent in activities of daily living (as per BADLS)
3. Confirms absence of any cognitive impairment (as per RBANS)

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Total final enrolment
120

Key exclusion criteria
1. Active depression (under active review)
2. Established diagnosis of early dementia (on cognitive enhancement therapy)
3. Current psychiatric illness (under active review of psychotropic medications)
4. Stroke disease (clinical stroke or stroke on CT)
5. Rapidly progressive or fluctuating symptoms of memory loss
6. Already consuming carotenoid supplements (e.g. Macushield) or fish oil supplements (e.g.

Souvenaid)
7. Already on cholinesterase inhibitors or NMDA receptor antagonists
8. Fish allergy
9. Acute angle glaucoma

Date of first enrolment
04/01/2016

Date of final enrolment
23/08/2018

Locations

Countries of recruitment
Ireland

Study participating centre
Waterford Institute of Technology
Macular Pigment Research Group
Carriganore House
West Campus
Carriganore
Waterford
Ireland
00000

Study participating centre
Age-Related Care Unit
University Hospital Waterford, Dunmore Road
Waterford
Ireland
00000

Sponsor information

Organisation
Waterford Institute of Technology Macular Pigment Research Group

Funder(s)

Funder type

Industry

Funder Name
Howard Foundation Holdings Limited

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Participants with MCI	25/05/2020	10/06/2020	Yes	No
Results article	Cognitively healthy participants	07/12/2021	10/01/2022	Yes	No
Protocol file			28/09/2022	No	No