Gut-to-brain Signalling of Post-Ingestion Nutrients in lean and obese subjects

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To study the effects of post-ingestion nutrients on brain activity and brain dopaminergic responses in lean subjects, and in obese subjects before and after diet-induced weight loss.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Appetite and general nutritional disorders
Study type	Interventional

Summary

ID

NL-OMON50660

Source
ToetsingOnline

Brief title
SPIN trial

Condition

- Appetite and general nutritional disorders

Synonym
obesity, Post-ingestion nutrient signals/effects

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Mediq TEFA

Intervention

Keyword: Brainactivity, Dopamine, Obesity, Post-ingestive nutrient signals

Outcome measures

Primary outcome

The effect of intragastric infusion of nutrients on:

- Brain activity assessed as the induced change in BOLD signal and resting state brain connectivity measured with fMRI.

- Striatal dopamine response, measured as the change in D2/D3R binding potential of IBZM assessed by SPECT.

Secondary outcome

The effect of intragastric infusion of nutrients on:

- Glucoregulatory and gut hormone release

- Objective scores of hunger and satiety during a buffet test meal after the infusion of the nutrients.

- Subjective (VAS) scores of hunger and satiety

- Neuropsychological functioning and feeding behaviour characteristics assessed by questionnaires and tasks

Assess the correlations between brain activity and weight loss maintenance one year after the diet intervention

Study description

Background summary

The worldwide obesity epidemic is a major health burden. Obesity is caused by disturbed feeding behaviour, leading to overconsumption of high-calorie and highly palatable food. Feeding behaviour is regulated by a complex interplay of the homeostatic and hedonic systems, and influenced by peripheral inputs. Recent evidence suggests that ingested nutrients trigger gut-to-brain signals that stimulate central (brain) dopamine release. Changes in post-ingestion

nutrient signals may be involved in the development of the pathological (habitual/compulsive) feeding behaviour in obese humans. However, the mechanism of nutrient-triggered dopamine release and its potential role in obesity remain to be elucidated. Gaining more insight in post-ingestion nutrient signalling is necessary to develop new therapeutic options to restore disturbed feeding behaviour in obesity.

Study objective

To study the effects of post-ingestion nutrients on brain activity and brain dopaminergic responses in lean subjects, and in obese subjects before and after diet-induced weight loss.

Study design

Single-blind randomized cross-over study

Intervention

Intragastric infusion of nutrients

Study burden and risks

Lean subjects will visit the AMC on 6 occasions (1 training, 3 fMRI, 2 SPECT sessions). Obese subjects will visit the AMC on 5 occasions at baseline (1 training, 3 fMRI, 1 SPECT sessions), and on 4 occasions after a 3-month dietary weight loss intervention (3 fMRI, 1 SPECT session) and on one occasion 1 year after the diet intervention to assess weight loss maintenance. The diet intervention is designed to result in ~10% body weight loss. The effect of the intragastric infusion of nutrients on BOLD will be assessed by fMRI, which is a non-invasive imaging modality. The effect of intragastric nutrient infusion on striatal D2/3R-BP will be assessed by SPECT using the radioligand [123I]-iodobenzamide (IBZM). IBZM has a European (CPMP) registration, and has been shown to have no serious side effects. The dose equivalent per IBZM-SPECT is 4.9 mSV (144MBq). Therefore, the total dose equivalent for each participant will amount to less than 11.3mSv and 15.3mSv, which is the maximum NCS-recommended dose for female research subjects >50 years and male subjects > 50 years respectively (risk category IIb). For the intragastric nutrient infusions, a nasogastric tube will be inserted prior to brain imaging sessions. To minimalize the risks associated with participation (tube complications, radiation exposure), subjects with risk factors for tracheal tube placement (e.g. swallowing disorder) and bleeding risk (use of anticoagulants) will be excluded, tube tolerability will be assessed during a training session, and the study is designed so that each participant will not be exposed to more than 2 SPECTs. Therefore, we believe that the scientific value of our findings will

outweigh the burden and risks associated with participation.

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

Age: 50-70 years for female subjects and 40-70 years for male subjects, for female subjects: postmenopausal, BMI <25 kg/m2 for lean subjects and >30 kg/m2 for obese subjects, insulin resistance for obese subjects, stable weight for 3 months prior to study inclusion

Exclusion criteria

Use of any medication except for those related to treatment of components of the metabolic syndrome (not including insulin, oral glucose lowering drugs, alpha- and beta-blockers)
Any actual medical condition except for treated hypothyroidism and the metabolic syndrome
History of any psychiatric disorder, neurological disorders, eating disorders (anorexia, binge eating, bulimia), alcohol abuse or upper gastrointestinal tract surgery/abnormalities.
Shift work
Intensive sports (>3/week)
Restrained eaters
Smoking
XTC, cannabis, amphetamine or cocaine abuse
Alcohol abuse (>3 units/day)
Occupational radiation exposure
Contraindication for MRI
Lactose/gluten intolerance
Soya oil, egg or peanut allergy
Childhood onset of obesity (<4 years)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-12-2017
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	06-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 28668
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL61132.018.17
OMON	NL-OMON28668