Vitamin D3: Identification of central nervous system targets using high-technology functional MRI (D-LIGHTFUL)

Published: 05-07-2018
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Primary objective: To examine the effects of calcitriol on the activity of dopaminergic central nervous system regions involved in the visualization and regulation of food intake using functional magnetic resonance imaging (fMRI). Secondary…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48648

Source
ToetsingOnline

Brief title
D-LIGHTFUL

Condition

- Other condition
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Obesity

Health condition

endocriene aandoeningen, obesitas

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Metabole Fonds

Intervention

Keyword: Calcitriol, Dopamine, Obesity, Vitamin D

Outcome measures

Primary outcome

The effect of calcitriol on brain activity in the hypothalamus and reward areas

as well as functional connectivity as measured by fMRI during food stimuli.

Secondary outcome

The effect of calcitriol on:

- Subjective (VAS) scores of hunger and satiety

- Neuropsychological functioning and feeding behavior characteristics as

assessed by questionnaires

- Objective scores of hunger and satiety as measured during an ad-libitum

buffet meal

- The gut microbiota and its association with changes in fMRI responses

- Circulating levels of glucose, insulin, and hormones

Study description

Background summary

Obesity rates are at an all-time high, and low levels of calcitriol are associated with high adiposity. Evidence from animal studies suggests that dopamine circuits are a novel mechanism by which calcitriol treatment may beneficially affect food intake and obesity. While altered dopamine signaling has been implicated in the progression of obesity and addiction (drug abuse,

food addiction), a role for calcitriol in these disease states has not been experimentally explored.

Study objective

Primary objective: To examine the effects of calcitriol on the activity of dopaminergic central nervous system regions involved in the visualization and regulation of food intake using functional magnetic resonance imaging (fMRI).

Secondary objectives: To examine the satiety-inducing effect of calcitriol and its association with changes in fMRI responses. To investigate the effect of calcitriol on the microbiota and its association with changes in fMRI responses.

Study design

Single center, double-blinded, randomized intervention study.

Intervention

All participants will receive in random order (after the baseline mri) a single-dose of calcitriol 4µg (= intervention) and 0.9% NaCl (= placebo). These interventions will be scheduled approximately one week after each other to allow for sufficient washout of carryover effects.

Study burden and risks

Participants will be invited for a baseline screening visit at the Academic Medical Center (brief physical examination, medical history, in- and exclusion criteria, informed consent, resting energy metabolism, anthropometrics (i.e., BOD POD), venipuncture). If eligible for participation, subjects will receive one-single dose of calcitriol 4.0µg (=intervention) and saline (=placebo). These interventions will be scheduled approximately one week after each other to allow for sufficient washout of carryover effects. The total duration of the study is two weeks and consist of: i) two study days (duration: 1 day each), and ii) a total of four safety monitoring blood draws (to check calcium levels in order to minimize the risk of hypercalcemia; duration: 10 min each). During both study visits, fMRI scans are made and food and eating behavior questionnaires are filled out. In addition, blood (75 ml in total) and stool samples are collected.

Risks: (A) Calcitriol: Side-effects of calcitriol are caused by hypercalcemia. In order to minimize the risks of adverse events, participants will be checked frequently during treatment. During clinical use of calcitriol, current practice guidelines recommend check plasma calcium levels every three days. To ensure safety, we will check calcium blood test 4, 24, and 72 hours after

treatment (see table 1. Study procedures). (B) Venous blood draw: The venipunctures in our study can be an unpleasant experience for the subjects. There is a low risk of phlebitis at the needle sites; this is unpleasant, but not harmful, of temporary nature and self-limiting. (C) MRI: MRI is a non-invasive imaging modality. All subjects will receive extensive information about the MRI procedures beforehand. Subjects with contraindication to MR scanning (e.g. pacemakers, claustrophobia, etc.) will be excluded.

Benefits: There is no direct benefit for subjects participating in this study. However, if calcitriol indeed increases cognitive control and inhibits reward-related regions during food visualization, calcitriol could be a prospective agent in the treatment of obesity. Obesity is associated with an increased risk of cardiovascular disease, diabetes and cancer, resulting in a significant economic burden on society. We therefore feel that we do not expose the participants to an unacceptable risk of side effects.

Group relatedness: Obesity is a growing problem in industrialized countries, where approximately a third of the population is obese, and was declared a global epidemic by the World Health Organization in 2003. Obesity has been associated with a number of health problems, including diabetes, heart disease, and different types of cancers, as well as decreased life expectancy. As a universally growing problem, there is a clear need for the development of new treatments for obesity.

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 between 18 - 35 years
- Ability to provide informed consent
- Right-handedness
- Stable weight (<5% change) for 3 months prior to study assessment,
Additionally, for the obese subset:
- BMI between 30 - 40 kg/m2
- Metabolically unhealthy, defined as fasting plasma insulin levels >74 pmol/l at screening

Exclusion criteria

- Any medical or psychiatrical disorder (except stable obesity-related glucose intolerance, hypertension, dyslipidemia and/or controlled hypothyroidism)
- Subjects taking any of the following medications: anticonvulsants, corticosteroids, digitalis, magnesium-containing preparations (e.g. antacids), thiazide-diuretics, phosphodiesterase inhibitors, serotonergic medications (e.g. SSRI, SNRI, MAO inhibitors, buproprion, tricyclic antidepressants, St. John*s Wort), codeine (CYP2D6 inhibition), tamoxifen, timolol, warfarin, exogenous insulin, GLP-1 agonists, DPP4 inhibitors, SGLT2 inhibitors, beta-blockers, homeopathic supplements
- The use of weight loss agents (e.g. orlistat, phentermine, topiramate, fenfluramin, dexfenfluramine, amphetamines, GLP-1 agonists) or use within 3 months prior to study
- Weight loss surgery or gastrectomy
- Childhood-onset obesity
- Breakfast skippers
- Shift workers
- Contraindication to MRI scanning (e.g. claustrophobia, pacemaker, metal IUD)
- Significant sensory or motor impairment
- Subjects who cannot adhere to the experimental protocol for any reason

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-02-2019
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Decostriol
Generic name:	Calcitriol

Ethics review

Approved WMO Date:	05-07-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	23-01-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2019
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-003465-10-NL
CCMO	NL63096.018.17