Het effect van het toevoegen van een subtotale gastrectomie aan een laparoscopische gastric bypass procedure op het striataal D2/D3 receptor beschikbaarheid. Een enkelvoudig geblindeerde, gerandomiseerde, single center studie¡¯

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Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24208

Bron
NTR

Verkorte titel
SUGAR trial

Aandoening

Obesity

Ondersteuning

Primaire sponsor: Academic Medical Center (AMC), Amsterdam
Overige ondersteuning: Academic Medical Center (AMC), Amsterdam

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Striatal D2/D3 receptor availability and dopamine release as well as whole brain (serotonergic) activity, including the response to visual food stimuli.

Toelichting onderzoek

Achtergrond van het onderzoek

Unsuccessful weight loss after bariatric surgery is commonly defined as weight loss <20% of total body weight (TBW) measured over a 10-year period. About 24-26.5% of all the patients undergoing laparoscopic Roux-en-Y gastric bypass surgery (LRYGB) meet this criterium, with the highest failure rate amongst the super-morbidly obese (BMI >45 kg/m2). A common explanation for the factors leading to unsuccessful weight loss is a lack of dietary adherence due to a sensation of hunger.

Ghrelin is an orexigenic hormone produced in the stomach. Under normal physiological conditions, ghrelin initiates food intake but it can also induce craving for food, even in the satiated state. Within the brain, ghrelin signals in brain regions involved in homeostatic control of food intake such as in the arcuate nucleus and in brain circuits contributing to hedonic control of food intake such as the ventral tegmental area (VTA); this occurs mainly through dopamine signalling. We and others have consistently shown that striatal dopamine receptor availability in obese subjects is decreased, suggesting that dopaminergic signalling is involved in pathological feeding behaviour. In line, in obesity visual food cues induce an exaggerated dopamine response linking dopamine to food intake. Since ghrelin and dopaminergic signalling are related, failure to loose substantial weight after bariatric surgery might in part be explained by ongoing ghrelin production from the residual stomach. Indeed, circulating ghrelin concentrations show a biphasic response after bariatric surgery with an early rise followed by a decrease to pre-surgery levels. Studies comparing LRYGB with laparoscopic sleeve gastrectomy (LSG) show lower plasma ghrelin levels in LSG groups. This is attributed to removal of the ghrelin producing cells.

Ghrelin also impacts glucose metabolism with a negative effect on insulin secretion along with higher glucose levels. Besides ghrelin, we and others have shown that the brain dopaminergic and dopaminergic systems are involved in the regulation of peripheral glucose metabolism through both homeostatic and hedonic brain regions.

This study aims to investigate the effects of LRYGB with subtotal gastrectomy (LRYGB+) as compared to standard LRYGB on the striatal dopaminergic and whole brain serotonergic

system, feeding behavior, and on glucose metabolism in the super obese.

Our hypothesis is that adding a subtotal gastrectomy to standard LRYGB induces an increase in striatal D2/D3 receptor availability and an increased dopaminergic surge after a dexamphetamine challenge and a higher serotonergic response correlated to lower plasma ghrelin levels. We further hypothesize that these findings lead to less craving for food and have beneficial effects on body weight loss and glucose metabolism.

Doel van het onderzoek

We hypothesize that adding a subtotal gastrectomy to LRYGB (LRYGB+) will decrease circulating acylated ghrelin more effectively than LRYGB alone and will restore dopamine D2/D3 availability and dopamine release in the striatum and increase cerebral serotonin signalling, both contributing to weight loss, improved feeding behaviour and an amelioration in glucose metabolism.

Onderzoeksopzet

Baseline (pre-operative): fMRI, SPECT imaging, intravenous glucose tolerance test, mixed mealtest, neurophysiological questionnaires and tasks.

3 Months post-operative: intravenous glucose tolerance test and neurophysiological questionnaires.

12 Months post-operative: fMRI, SPECT imaging, intravenous glucose tolerance test, mixed mealtest, neurophysiological questionnaires and tasks.

Onderzoeksproduct en/of interventie

LRYGB vs. LRYGB+subtotal gastrectomy (LRYGB+)

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Age 25-65 years

BMI > 45.0 kg/m2 at the start of the LRYGB trajectory (defined as the first visit to the surgery outpatient clinic of the Slotervaart hospital)

Stable weight defined as not losing or gaining >5% of total body weight 4 weeks prior to inclusion

ASA classification1-2

Written informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Positive serology screening for H.Pylori or positive H.Pylori culture after gastroscopy

Auto-immune atrophic gastritis (positive antibodies against intrinsic factor and/or anti-parietal cells)

Any psychiatric disease (treated or untreated) or eating disorder

Revisional LRYGB surgery

Drug addiction (present or in medical history)

Frequent use of recreational drugs

Childhood-onset obesity

Untreated thyroid dysfunction

American Society of Anaesthetics (ASA) score ¡Ý3

Age >65 years

Work with radiation

Contraindication for MRI (claustrophobia, metal objects etc.)

Shift work

Smoking

Any medical condition except for stable obesity related conditions (except for insulin-treated DM)

History of cardiac diseases

Pregnancy

Genetic causes of obesity

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	05-07-2016
Aantal proefpersonen:	32
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing
Soort: Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 47736
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6865
NTR-old	NTR7043
CCMO	NL52188.048.15
OMON	NL-OMON47736

Resultaten