

# 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;

No registrations found.

|                              |                |
|------------------------------|----------------|
| <b>Ethical review</b>        | Not applicable |
| <b>Status</b>                | Recruiting     |
| <b>Health condition type</b> | -              |
| <b>Study type</b>            | Interventional |

## Summary

### ID

NL-OMON24208

### Source

NTR

### Brief title

SUGAR trial

### Health condition

Obesity

## Sponsors and support

**Primary sponsor:** Academic Medical Center (AMC), Amsterdam

**Source(s) of monetary or material Support:** Academic Medical Center (AMC), Amsterdam

## Intervention

## Outcome measures

### Primary outcome

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

### Secondary outcome

Aspects of motivation and impulse control of feeding behaviour (questionnaires, tasks and phMRI)

Assessment of craving and hunger (questionnaires)

Fasting and postprandial acylated ghrelin (IGTT)

Glucose metabolism (IGTT)

Gut hormones, free fatty acids

Body weight loss

Feelings of craving and hunger (Questionnaires)

Food addiction according to Yale Food Addiction scale

## Study description

### Background summary

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/m<sup>2</sup>). 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 lose 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 serotonergic 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.

## **Study objective**

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.

## **Study design**

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.

## Intervention

LRYGB vs. LRYGB+subtotal gastrectomy (LRYGB+)

## Contacts

### Public

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## Eligibility criteria

### Inclusion criteria

Age 25-65 years

BMI > 45.0 kg/m<sup>2</sup> 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 classification 1-2

Written informed consent

### Exclusion criteria

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 ≥3

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

## Study design

### Design

|                     |                               |
|---------------------|-------------------------------|
| Study type:         | Interventional                |
| Intervention model: | Parallel                      |
| Allocation:         | Randomized controlled trial   |
| Masking:            | Single blinded (masking used) |
| Control:            | Active                        |

## Recruitment

NL  
Recruitment status: Recruiting  
Start date (anticipated): 05-07-2016  
Enrollment: 32  
Type: Anticipated

## Ethics review

Not applicable  
Application type: Not applicable

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 47736  
Bron: ToetsingOnline  
Titel:

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

No registrations found.

## In other registers

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

## Study results