# Visualizing differences in cerebral dopamine- and serotonin transporters between lean subjects and obese subjects with normal- and decreased insulin sensitivity

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We hereby hypothesize that obesity results in an increase in cerebral SERT and DAT, compared to healthy controls. Cerebral SERT and DAT increase will be more prominent in insulin resistant obese subjects compared to obese subjects with normal...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

# Summary

### ID

NL-OMON36484

**Source** ToetsingOnline

**Brief title** Brain Imaging in Obesity

# Condition

• Glucose metabolism disorders (incl diabetes mellitus)

#### Synonym

glucose intolerance, insulin resistance

### Research involving

Human

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### **Sponsors and support**

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

### Intervention

Keyword: dopamine, insulin sensitivity, obesity, serotonin

#### **Outcome measures**

#### **Primary outcome**

Difference in cerebral binding of the radioligand [123I]FP-CIT to serotonin-

and dopamine transporters between obese subjects and healthy volunteers and

between obese subjects with- and without insulin resistance.

#### Secondary outcome

Correlation between binding of the radioligand [123I]FP-CIT to cerebral

serotonin- and dopamine transporters and:

- 1. amount of fat
- 2. glucoregulatory hormones in plasma
- 3. appetite regulating peptides in plasma

# **Study description**

#### **Background summary**

The role between obesity, insulin resistance (IR) and the brain has been of interest for several years. In recent years, research suggests a role for cerebral dopamine and serotonin. From animal- and some humane research it has become clear that there is ground for the hypothesis that cerebral dopamine transporter (DAT) and serotonin transporter (SERT) are related to both BMI and glucose metabolism. SERT- and DAT knockout mice have an obese phenotype. In humans, we found that SSRI treatment (inhibiting serotonin reuptake via SERT) improves insulin resistance. In addition, treatment with a dopamine agonist in hamsters reduced hyperinsulemia and body weight gain. We are able to measure cerebral SERT and DAT in humans with SPECT using the radioligand [123I]FP-CIT.

#### Study objective

We hereby hypothesize that obesity results in an increase in cerebral SERT and DAT, compared to healthy controls. Cerebral SERT and DAT increase will be more prominent in insulin resistant obese subjects compared to obese subjects with normal insulin sensitivity.

#### Study design

Observational study

#### Study burden and risks

[123I]FP-CIT used in the SPECT-scans has a European (CPMP) registration. In the trials preceding the marketing authorization it has been shown that no serious side effects occur after administration of this radioligand. (Booij et al. 24-30). To minimize uptake of the radioligand in the thyroid, kaliumiodide tablets are provided to study participants on the day before- and morning of the scan. Subjects will be exposed to radiation of 2.7 mSv. To assess the risks of exposure to radiation, we asked for a radiation advice by the department of radiology of the AMC. This was sent to the local METC apart from the study protocol and states that radiation exposure as a consequence of this study is mediocre (WHO Class IIb). The MRI-scan requires lying still as possible for 15 minutes on a solid plate, which might cause minor discomfort. There are no expected advantages as a consequence of study participation.

It is well known that treatment and prevention of obesity and T2DM is far from being effective. The obesity epidemic is progressing with all its consequences. We therefore think it is of utmost importance to contribute to better understanding and possibly better treatment and prevention. To show the role of SERT and DAT in obesity and changes in glucose metabolism would mean whole new insights on pathophysiologal mechanisms. Moreover, better pathophysiological insight might lead to new, improved treatment of obesity and type 2 diabetes (T2DM). It could also lead to newer and more preventive strategies. To answer our study questions and contribute to unravelling the pathophysiological pathways of obesity and insulin resistance in a reliable way, the use of SPECT-scan with the named amount of radiation is inevitable. There are no known circulating markers which reflect quantitative measures of the dopaminergic or serotonergic pathways in the brain. Imaging is the only way to study this.

# Contacts

**Public** Academisch Medisch Centrum

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# **Trial sites**

### **Listed location countries**

Netherlands

# **Eligibility criteria**

#### Age

Adults (18-64 years) Elderly (65 years and older)

### **Inclusion criteria**

BMI > 30 kg/m2, age 18-40 years, Caucasian

### **Exclusion criteria**

DM with need of therapy (insulin or oral therapy); use of any medication; renal insufficiency (kreat > 150  $\mu$ mol/L; elevated liver enzymes (>2x above the upper limit of normal); hypothyroidism; intoxications (alcohol- (>3/day), ecstasy-, amphetamine- or cocaine abuse), smoking; shift work

# Study design

## Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

### Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	01-01-2011
Enrollment:	36
Туре:	Actual

# **Ethics review**

Approved WMO	
Application type:	First submission
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.

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# In other registers

### Register

ССМО

**ID** NL34575.018.10