Hepatic insulin resistance and Dopaminergic dysfunction in a Ultra High Risk (UHR) population for Schizophrenia

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1)To determine whether subjects at ultra high risk to develop schizophrenia display hepatic insulin resistance as compared to healthy controls matched for age, sex, BMI, ethnicity, visceral and subcutaneous fat mass.2)To determine whether...

Ethical review	Approved WMO
Status	Pending
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON31345

Source
ToetsingOnline

Brief title
IHR-HIR

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Schizophrenia and other psychotic disorders

Synonym
delusion, psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Dopamine, Insuline, Resistance, UHR

Outcome measures

Primary outcome

Glucose productions (suppression)

Secondary outcome

n.a.

Study description

Background summary

(page 2-4 of the protocol)
The lack of firm knowledge of disease pathology impedes the development of rational and novel therapeutic strategies in schizophrenia. However, there are several data indicating that dopaminergic dysfunction in the central nervous system is involved in the pathogenesis of schizophrenia.
Numerous reports have pointed to a possible relationship between diabetes and schizophrenia. Since psychotropic medication may affect body composition and glucose metabolism, direct metabolic squeal of the disease process per se on whole body glucose and lipid metabolism is difficult to establish in studies were non drug naïve patients are included. Recently, we have shown that drug naïve, first episode schizophrenic patients display hepatic insulin resistance as compared to matched controls. This finding could not be attributed to differences in intra abdominal fat mass or other known factors associated with hepatic insulin resistance, suggesting a direct link between schizophrenia and hepatic insulin resistance.
Intriguing animal studies suggest a key role for pre-autonomic neurons in the hypothalamus in the regulation of hepatic glucose production and hepatic insulin sensitivity through sympathetic as well as parasympathetic outflow via the brain stem nuclei to the liver. This may be an indication of the hypothalamic involvement of hepatic insulin resistance as found in schizophrenic patients.
Based on the above we hypothesize that dopaminergic deregulations in schizophrenia that may be responsible for positive and negative symptoms may also be responsible for the induction of hepatic insulin resistance.

Study objective

1)To determine whether subjects at ultra high risk to develop schizophrenia display hepatic insulin resistance as compared to healthy controls matched for age, sex, BMI, ethnicity, visceral and subcutaneous fat mass.

2)To determine whether dopaminergic dysregulation is associated with the occurrence of hepatic insulin resistance.

Study design

The hepatic insuline resistance will be analyised in a group of UHR subjects and healthy controls, by means of a hyperinsulinemic euglycemic clamp. UHR subjects who develope psychosis and are still antipsychotic naïve will be asked to participate for a second time.

Intervention

n.a.

Study burden and risks

Stabile isotopes are not radioactiev and are therefor harmless.
Patients will be in hospital for about 7 hours.

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 18-35
"Ultra high risk" symptoms for development of psychosis as defined by McGorry et al (2002).
Healthy controls matched for age, sex, BMI, IQ, ethnicity, viceral and subcutanious fat mass.

Exclusion criteria

Previous psychotic episode
Previous use of antipsychotics, or regular use of cocaine or amphetamins
Type I and II diabetes mellitus
Renal insufficiency
Family history for type II diabetes mellitus.
Familial dyslipidemia
Treatment with drugs which are known to interfere with glucose or lipid metabolism
Alcohol consumption in excess of 3 units per day or in the last 3 days before the clamp

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2007
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Actrapid Human Insuline
Generic name:	Insuline
Registration:	Yes - NL intended use

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.

In other registers

Register	ID
EudraCT	EUCTR2007-004637-42-NL
CCMO	NL19328.018.07