Bromocriptine bij type 2 diabetes mellitus

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We hypothesize that in patients with T2DM i. dopamine release is reduced in comparison to a cohort of matched historical healthy and lean controls, ii. restoring the peak in morning dopamine signalling will partially restore dopamine release, and...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22542

Bron
Nationaal Trial Register

Verkorte titel
AWAKENING trial

Aandoening

Type 2 diabetes mellitus

Ondersteuning

Primaire sponsor: Amsterdam UMC, location AMC Meibergdreef 9 1105AZ Amsterdam The Netherlands
Overige ondersteuning: Het Diabetes Fonds

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Dexamphetamine-stimulated dopamine release and insulin sensitivity

Toelichting onderzoek

Achtergrond van het onderzoek

Insulin resistance and b-cell failure are the hallmark of T2DM. While compensating for □-cell failure with insulin treatment is effective in reducing hyperglycemia and haemoglobin A1C (HbA1C), it has serious side effects (i.e. hypoglycaemia, body weight gain) and poses a burden for the patient. Reducing insulin resistance in diabetes patients would be another logical target, but most treatment modalities have either no or modest effect on insulin sensitivity. Moreover, the lack of detailed knowledge on the pathophysiology of insulin resistance in humans is hampering the development of novel therapies. For many years, diabetes research has focussed on peripheral determinants of insulin sensitivity and although these often ground-breaking discoveries in animals led to useful novel insights in insulin signalling, translation to clinical treatment is still scarce. The brain as master regulator of energy metabolism has long been ignored in clinical diabetes research. It has been shown however that dopaminergic signalling is disturbed in obesity and we have recently shown that stimulation of striatal dopaminergic signalling improves insulin sensitivity. We here aim to follow the physiology of daily rhythmic dopamine release in reducing insulin resistance in T2DM. Furthermore we will explore the potential of bromocriptine, a dopamine agonist, as a therapeutic option for T2DM.

Objective: With this proof-of-concept study, we will address i. differences in dopamine release in T2DM patients versus historical lean controls, ii. whether timed restoring of dopamine signalling improves dopamine release and iii. whether this reinstatement of daily dopamine rhythms is associated with an improvement in insulin sensitivity. We hypothesize that in patients with T2DM i. dopamine release is reduced in comparison to a cohort of matched historical healthy and lean controls, ii. restoring the peak in morning dopamine signalling will partially restore dopamine release, and iii. this increase in dopamine release is associated with an increase in insulin sensitivity.

Study design: a single-arm intervention study.

Study population: we intend to include 40 T2DM patients, aged 50-70 years.
Intervention: Bromocriptine (Dopamine D2 receptor agonist) orally, once daily (within 2 hours after awakening) during 12 weeks (in 4 weeks the dose will be up titrated to 5 mg, which is then continued for another 8 weeks).

Main study parameters/endpoints:
The effect of the bromocriptine intervention on i. dexamphetamine-stimulated dopamine release (SPECT imaging; Δ D2/3R BPND), and ii. insulin sensitivity of adipose tissue, liver and skeletal muscle (hyperinsulinemic, euglycemic clamp; percentage of insulin-induced suppression of free fatty acids (FFA) and endogenous glucose production (EGP), and insulin-stimulated rate of disappearance, respectively). Furthermore, we aim to assess the correlation between bromocriptine-induced changes in stimulated dopamine release and changes in insulin sensitivity.

Doel van het onderzoek

We hypothesize that in patients with T2DM i. dopamine release is reduced in comparison to a cohort of matched historical healthy and lean controls, ii. restoring the peak in morning dopamine signalling will partially restore dopamine release, and iii. this increase in dopamine release is associated with an increase in insulin sensitivity.

Onderzoeksopzet

A total of 8 visits:
Visit 1
Visit 2 and 3
Visit 4 after 2 weeks
Visit 5 after 4 weeks
Visit 6 after 8 weeks
Visit 7 after 12 weeks
Visit 8 after 13 weeks

Onderzoeksproduct en/of interventie

Bromocriptine orally, once daily during 12 weeks

Contactpersonen

Publiek

Amsterdam UMC, location AMC
Jamie van Son

+31205666964

Wetenschappelijk

Amsterdam UMC, location AMC
Jamie van Son

+31205666964

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Overweight/obese (BMI>25.0 kg/m2) T2DM patient, treated with oral medication only

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- any current somatic (except for stable obesity- or T2DM-related comorbidities) or psychiatric disorder;
- shift work
- uncontrolled hypertension
- the use of excessive alcohol or recreational drugs
- smoking
- any use of medication (including NSAIDs) except for lipid lowering, blood pressure lowering drugs and occasional use of paracetamol (less frequent than 2 days a week)
- history of psychiatric disorder or drug- or alcohol abuse
- history of cerebro- and/or cardiovascular diseases
- history of the use of dexamphetamine or dopamine agonists
- abnormal ECG at rest or during the exercise stress test
- positive family history of sudden death
- childhood-onset obesity
- history of bariatric surgery
- allergy or hypersensitivity to ergot alkaloids
- allergy or hypersensitivity to sympathomimetic amines

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	22-03-2019
Aantal proefpersonen:	40
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	22-03-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 49251
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7622
CCMO	NL67560.018.18
OMON	NL-OMON49251

Resultaten