Conditioning of insulin responses: a high rist- high gain intervention for diabetes type-2

Published: 15-10-2018
Last updated: 10-01-2025

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Ethical review	Approved WMO
Status	Completed
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON49422

Source
ToetsingOnline

Brief title
Conditioning of insulin responses

Condition

- Diabetic complications

Synonym
diabetes type-2

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: ZonMW en Diabetesfonds

Intervention

Keyword: conditioning, diabetes type-2, insulin, placebo

Outcome measures

Primary outcome

Main study parameters are blood insulin and glucose levels during the evocation day in the experimental patients group versus the control patients group. Insulin and glucose will be measured 8 times: at baseline, after each of the 6 applications of nasal spray and 15 minutes after the last spray administration.

Secondary outcome

Secondly, we investigate the effects of conditioning with insulin on C-peptide, hunger, approach-avoidance tendencies, food intake and cognitive functioning measured with a memory task. Finally, a comparison between patients and healthy participants will be made on the study outcomes.

Study description

Background summary

Recent studies in healthy volunteers demonstrated that insulin and glucose levels can be altered though the mechanism of classical conditioning. This is particularly relevant for patients who suffer from a dysfunction of the insulin system such as diabetes type-2. It however remains unknown whether this mechanism of classical conditioning of endocrine parameters can be applied to patients with diabetes type-2.

Study objective

The primary objective of this study is to investigate the effects of classical conditioning with intranasal insulin on endogenous insulin and glucose levels in diabetes type-2 patients and healthy controls. Additionally, we will examine the effects of conditioning on hunger, food consumption, approach-avoidance

behaviour and cognitive performance.

Study design

Thirty-two patients with diabetes type-2 and thirty-two healthy controls will be randomized based on a 1:1 ratio to an experimental or control group in a double-blind manner. A validated two-phase experimental design will be used involving an acquisition day and an evocation day. During the acquisition day, participants in the experimental groups will receive 6 intranasal applications of 20 International Units (IU) of soluble insulin intranasal spray within a period of 75 minutes. The odour of aroma oil will serve as a conditioned stimulus (CS). During the subsequent evocation day, the participants in the experimental groups will receive 6 administrations of a placebo spray combined with the odour of aroma oil. Participants in the control groups will receive placebo spray with an odour of aroma oil during both the acquisition day and the evocation day. Insulin, glucose and C-peptide levels will be measured 8 times during each experimental day in the blood. After each spray administration, hunger will be measured. After the last blood measurement, participants will be asked to do a simple computer test (approach-avoidance task with food items), a memory task and a food intake task (Bogus test).

Intervention

In the experimental groups, participants will receive 6 intranasal applications of 20 IU insulin during the acquisition day and 6 applications of a placebo nasal spray during the evocation day. In the control groups, participants will receive a placebo spray during both days.

Study burden and risks

Risks associated with the study procedures are minimal. Participants will be invited to two sessions that will take place on two consecutive days and will last 5 hours (2,5 hour per session) in total. The blood samples will be taken during the sessions with an intravenous infusion that will be placed by a professional nurse. The administration of intranasal insulin is safe and easy. Adverse events are uncommon for intranasal application of insulin except for transient local side effects such as irritation of the nose, sneezing or nasal discharge. Since intranasal insulin has direct effects on the brain, it avoids common serious side effects as observed with intravenous insulin injections such as hypoglycaemia and hypertension. Several studies have been conducted in healthy volunteers and patients with diabetes type-2 with dosages up to 160 units of intranasal insulin without reporting adverse events.

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

For patients:
- Diagnosis of diabetes mellitus type 2
- Taking metformin or participating in a life style intervention (e.g., diet)

Exclusion criteria

- Use of insulin or, insulin stimulating medications ;
- Use of medication that influences glucose metabolism, for example, corticosteroid medication, chemotherapy, beta-blockers;
- Diagnosis of an acute not-infectious disease (degenerative diseases, malignant neoplasms such as cancer, diabetes type-1, auto-immune diseases);

- Diagnosis of an acute infectious diseases (such as meningitis, hepatitis B, bacterial pneumonia);
- Current diagnosis of a mental disorder;
- Chronic and/or acute rhinitis, anatomic deviations of the nose;
- Substance abuse (e.g., drugs or alcohol);
- Pregnancy or an intention to get pregnant

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	27-05-2019
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Insulin NovoRapid
Generic name:	Insulin NovoRapid
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	15-10-2018

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	15-02-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	18-05-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	21-10-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2018-003124-37-NL
CCMO	NL67066.058.18

Study results

Date completed:	24-06-2021
Results posted:	06-04-2022
Actual enrolment:	64

First publication
06-04-2022