Conditioning of insulin responses

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23109

Source
Nationaal Trial Register

Brief title
Conditioning of insulin responses

Health condition

Diabetes type-2

Sponsors and support

Primary sponsor: Leiden University, Leiden University Medical Center
Source(s) of monetary or material Support: Diabetes fonds, ZonMW

Intervention

Outcome measures

Primary outcome

Main study parameters are blood insulin and glucose levels during the evocation day in the conditioned patient group versus the control patient group. Separate analyses will be run for each outcome (insulin and glucose). Repeated measures ANCOVA will be used to compare the conditioned and control groups on 7 blood measurements (insulin and glucose separately), controlling for the baseline measurement. In case of a large amount of missing data or large variations in the timing of blood draws, the linear-mixed effects model approach will be applied to the analysis.

February 23, 2022:

The data collection has been finished. The full data for 62 out of 64 participants is available for the main outcome measures. Two blood samples from one participant and one blood sample from another participant are missing due to problems with blood collection. The Repeated Measures ANCOVA, that was reported as a primary analysis, is sensitive to missing values, and it would exclude the participants with missing blood samples. Therefore, we will perform the linear-mixed effects analysis (as reported in the first version of the pre-registration in case of presence of missing values). The linear mixed-effects model will be equivalent to the pre-registered repeated-measures ANCOVA. The analysis will include baseline blood measures, group (patients versus healthy controls), condition (conditioned versus control), time and the interaction between these variables as fixed effects. Random intercept per participant and random slopes per group will be included into the model in case they improve the model fit. Additional models will be performed with sex as a fixed factor to investigate possible sex differences in the effects in insulin and conditioning. Separate models will be performed for day 1 and day 2 and for each of the outcome repeated measures: blood glucose, insulin, c-peptide, and hunger.

Secondary outcome

1. Insulin and glucose levels during the evocation day in the conditioned healthy volunteers versus control healthy volunteers groups.
2. C-peptide levels during the evocation day in the conditioned patient group versus the control patient group; and conditioned healthy volunteers group versus the control healthy volunteers group.
3. Insulin, glucose and C-peptide levels during the acquisition day in the conditioned patient group versus the control patient group; and conditioned healthy volunteers group versus the control healthy volunteers group.
4. Hunger during the acquisition and evocation day in the 4 groups.
5. Memory (immediate and delayed recall) during the acquisition and evocation day in the 4 groups.
6. Approach-avoidance tendencies towards food during the acquisition and evocation day in the 4 groups
7. Food consumption at the end of the acquisition and evocation day in the 4 groups.

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.

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 volunteers. Additionally, we will examine the effects of conditioning on C-Peptide, hunger, food consumption, approach-avoidance tendencies towards food, and cognitive performance.
Thirty-two patients with diabetes type-2 and thirty-two healthy volunteers will be randomized based on a 1:1 ratio to a conditioned or control group in a double-blind manner. A validated two-phase experimental design will be used involving an acquisition and an evocation day. During the acquisition day, participants in the conditioned 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 conditioned 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 and the evocation day. Blood levels of insulin, glucose and C-Peptide will be measured each session on baseline, after each spray administration, and additionally 15 minutes after the last spray administration (in total 8 measurements per day). Moreover, hunger of participants will be measured 8 times during each session. Additionally, at the end of each session, a memory test, an approach avoidance task (with food items) and a bogus test will be administered.

Study objective

We expect to find increased insulin and decreased glucose in the patient conditioned group in comparison to the patient control group after the placebo administration during the evocation day when controlling for baseline insulin and glucose levels, respectively. The same hypothesis pertains the healthy volunteers groups: we expect to find increased insulin and decreased glucose in the conditioned group in comparison to the control group after the placebo administration during evocation, when controlling for baseline insulin and glucose levels, respectively. Moreover, we expect that the conditioned patient group and the conditioned healthy volunteer group will demonstrate increased C-peptide levels, less hunger, better memory, less food approach bias and less food consumption during the Bogus test on both sessions in comparison to the patient control and healthy volunteers control groups.

Study design

The study consists of a telephone screening and 2 test days. Blood samples (for measuring insulin, glucose and c-peptide) will be drawn 8 times during each day. Hunger will be measured 8 times during each day. Memory, approach-avoidance tendencies towards food and food consumption will be measured twice, at the end of the acquisition and evocation days.

Intervention

In the conditioned 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 6 placebo sprays during both days.

Contacts

Public
Leiden University
Andrea Evers

+31 71 527 6891
Scientific
Leiden University
Andrea Evers

+31 71 527 6891

Eligibility criteria

Inclusion criteria

Patients:
- Mentally capable and older than 18 years old;
- Diagnosis of diabetes type-2
- Take metformin as a treatment and/or participate in a lifestyle intervention (e.g., diet) to control their diabetes.
Healthy controls:
- Mentally capable and older than 18 years old;

Exclusion criteria

Patients:
- 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.
Healthy controls:
- Diagnosis of diabetes type-1 or type-2
- 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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-05-2019
Enrollment:	64
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	05-06-2019
Application type:	First submission

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
NTR-new	NL7783
Other	LUMC METC : P18.222; NL67066.058.18

Study results