# The effect of intravenous lactate administration on brain lactate concentrations and pH during euglycemia and hypoglycemia in patients with type 1 diabetes with and without impaired awareness of hypoglycemia

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

# **Summary**

### ID

NL-OMON43132

**Source** ToetsingOnline

### Brief title The effect of intravenous lactate on brain lactate during hypoglycemia

### Condition

• Glucose metabolism disorders (incl diabetes mellitus)

### Synonym

diabetes, Diabetes Mellitus

### **Research involving**

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Human

### **Sponsors and support**

**Primary sponsor:** Radboud Universitair Medisch Centrum **Source(s) of monetary or material Support:** Het Diabetes Fonds en The European Foundation for the study of Diabetes

### Intervention

Keyword: awareness of hypoglycemia, lactate, T1DM

### **Outcome measures**

#### **Primary outcome**

The main study parameter of part 1 is the change in brain lactate concentration

in response to lactate infusion compared to placebo during hypoglycemia in

patients with T1DM and NAH. The main endpoint of part 2 is the difference in

brain lactate handling during hypoglycemia with lactate infusion between

patients with T1DM and NAH compared to patients with IAH.

#### Secondary outcome

Secondary endpoints include the change in brain lactate upon infusion during

euglycemia, changes in brain pH and differences between patients with T1DM-NAH

and IAH.

# **Study description**

#### **Background summary**

Patients with type 1 diabetes (T1DM) who are unable to perceive symptoms of hypoglycemia, referred to as impaired awareness of hypoglycemia (IAH), are at very high risk of severe hypoglycemia. IAH affects approximately 25% of patients with T1DM. Brain lactate may be involved in the development of IAH. We found indications of increased brain lactate utilization during hypoglycemia in T1DM patients with IAH, which did not occur in patients with normal awareness

of hypoglycemia (NAH). Conversely, administration of lactate to patients with NAH has been shown to attenuate counterregulatory hormone responses to and symptomatic awareness of hypoglycemia, thus causing a situation that resembles IAH. It has, however, not been demonstrated whether the excess of lactate is actually taken up or metabolized by the brain, and if so whether this occurs under euglycemic or hypoglycemic conditions or both.

### **Study objective**

This project consists of two related studies. The objective of part 1 is to investigate the effect of elevated plasma lactate levels that are sufficient to impair awareness of hypoglycemia on brain lactate concentrations during euglycemia and hypoglycemia in T1DM patients with NAH. The objective of part 2 is to compare the effect of exogenous lactate on brain lactate concentrations between T1DM patients with NAH and T1DM patients with IAH. In both studies, we will also assess changes in brain pH, because lactate administration is known to alter blood pH levels

### Study design

Explorative, single-blind placebo controlled, randomized cross-over intervention study

#### Intervention

Part 1: On two separate occasions, patients with T1DM and NAH will undergo hyperinsulinemic euglycemic-hypoglycemic glucose clamps with or without the infusion of exogenous lactate. 1H magnetic resonance spectroscopy (MRS) will be applied to measure brain lactate levels and 31P-MRS will be used to determine changes in brain pH levels. Part 2: Patients with T1DM and IAH will undergo a hyperinsulinemic euglycemic-hypoglycemic glucose clamp with infusion of lactate. 1H- and 31P-MRS will be applied to measure brain lactate concentrations and changes in brain pH levels, respectively. Data will be compared with those of lactate administration obtained in patients with NAH during study 1.

### Study burden and risks

The hypoglycemic condition is likely to produce typical symptoms (e.g. sweating, feeling hungry, palpitations) in T1DM-NAH patients, but is usually well-tolerated and less pronounced when lactate is infused. The risk for more severe hypoglycemia is negligible. The use of venous and arterial catheters may lead to hematomas and phlebitis, yet this is self-limiting and has in our hands never lead to permanent damage. 1H- and 31P-MRS are non-invasive methods involving high magnetic fields, which are not associated with adverse events

other than possible claustrophobia due to lying in the small MR-bore.

# Contacts

#### Public

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# **Trial sites**

### **Listed location countries**

Netherlands

# **Eligibility criteria**

#### Age

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

### **Inclusion criteria**

- Diabetes duration \* 1 year
- Age: 18-50 years
- Body-Mass Index: 18-30 kg/m2
- HbA1c: 42-75 mmol/mol (6-9%)
- Outcome Clarke questionnaire: 0-1 or ><=3
- Blood pressure: <160/90 mmHg

### **Exclusion criteria**

- Inability to provide informed consent

- Use of medication other than insulin, oral contraceptives or stable thyroxine supplementation therapy

- Presence of any other medical condition that might interfere with the study protocol, such as brain injuries, epilepsy, a major cardiovascular disease event, known liver disease, anxiety disorders or a history of panic attacks.

- Microvascular complications of T1DM except background retinopathy

- MR(I) contraindications, such as pregnancy, severe claustrophobia, metal parts in body

## **Study design**

### Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

### Recruitment

...

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	25-11-2016
Enrollment:	20
Туре:	Actual

# **Ethics review**

Approved WMO	
Date:	01-11-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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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** CCMO Other ID NL58348.091.16 nog niet bekend