The rate of glucose uptake over the blood-brain barrier in humans in vivo, measured by 13C magnetic resonance spectroscopy

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To investigate the time difference between the blood glucose excursion and the subsequent appearance of cerebral 13C glucose after intravenous glucose loading.

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

Summary

ID

NL-OMON36330

Source
ToetsingOnline

Brief title
Glucose uptake in human brain

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes, Diabetes Mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Diabetes fonds

Intervention

Keyword: 13C MR Spectroscopy, Brain, Glucose

Outcome measures

Primary outcome

• the time difference between the cerebral 13C glucose peak and the blood

glucose peak after intravenous glucose loading

Secondary outcome

• areas under the cerebral 13C glucose and blood glucose response curve

• times until 13C glucose and blood glucose have returned to baseline values

Study description

Background summary

Glucose is the principal source of energy for normal brain function. The brain accounts for more than half the body's glucose use. Since the brain*s capacity to store glucose as glycogen is limited, a continuous supply of glucose from the circulation is mandatory. Glucose is transported across the blood-brain barrier into the brain through glucose transporter-1 (GLUT-1) and directly into neurons at places where the blood-brain barrier is absent through GLUT-3. Both glucose transporters mediate facilitative energy-independent transport, so that glucose is taken up by brain tissue relatively unimpeded.
The rate of glucose transport into the brain depends on the concentration of transporter proteins, the concentration difference between intra- and extracellular glucose levels and the metabolism of glucose. Several models have been devised that describe the flow of glucose from blood to brain and within different brain cells under basal and hyperglycaemic steady-state conditions. However, little is known about the rate of cerebral glucose uptake under in vivo non-steady state-conditions, e.g. after glucose loading. It is similarly unknown whether patients with type 1 diabetes behave differently than non-diabetic subjects. Such knowledge is especially relevant with respect to the recent clinical introduction of real-time glucose sensors in the management of (type 1) diabetes. Real-time glucose sensors measure glucose levels semi-continuously in the interstitial fluid, but do so at an estimated lag time relative to blood of 4-10 minutes (1) or greater (2).
13C Magnetic Resonance Spectroscopy (MRS) of the brain provides a unique tool

to investigate the dynamics of cerebral glucose uptake in humans in vivo. We recently developed a protocol to investigate the effects of steady-state normo- and hypoglycaemia on brain glucose uptake and subsequent metabolism in humans in vivo (3). In this protocol, a 30 ml bolus of 100% 13C labelled ([1-13C]glucose) 20% w/w glucose solution is infused over 10 minutes to rapidly increase plasma 13C enrichment. Peak values of 13C labelled glucose in the brain appeared to lag 5-10 minutes behind peak plasma glucose levels. However, since glucose was measured every 5 minutes, the lag time could not be measured more precisely. The objective of the current research project is to accurately assess the time difference between blood glucose and cerebral glucose using 13C MRS in response to immediate, transient hyperglycaemia.

Study objective

To investigate the time difference between the blood glucose excursion and the subsequent appearance of cerebral 13C glucose after intravenous glucose loading.

Study design

Interventional study to investigate the rate of glucose uptake in the brain by MR spectroscopy and [1-13C]glucose infusion.

Volunteers receive a bolus of [1-13C]glucose intravenously. During an hour blood will be sampled from an arterial line to determine plasma glucose values and in the brain glucose uptake is measured by 13C MR spectroscopy. Diabetic patients who participate receive a standardized dose of insulin.

Intervention

Administration of [1-13C] glucose
Blood sampling through arterial line
Insulin administration in patients

Study burden and risks

Burden:
Time investment
Staying sober
Arterial and venous lines
MR scan

Risks:
Findings on cerebral MR scan
Hematoma due to intraarterial and intravenous cannulations
Phlebitis due to IV glucose infusion

Claustrophobia in MR scanner

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

All volunteers:
age between 18-60 years;Patients with Type 1 Diabetes Mellitus:
Stable glycaemic control with HbA1c 6.5-9.0%
Duration of diabetes >5 years

Exclusion criteria

All volunteers:
History of epilepsia or operations of the brain
Metal implants or pace-maker;Patients:
All complications of Diabetes except background retinopathy
Hypoglycemia unawareness
Medication other then oral anti-conceptiva or thyroxine supplements

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-06-2011
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO

Date:	10-05-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL35311.091.11