Intermittent Fasting and Insulin Sensitivity

In

Lean Healthy Male Subjects.

Gepubliceerd: 15-06-2009 Laatst bijgewerkt: 18-08-2022

We hypothesize that peripheral insulin sensitivity increases after a period of intermittent fasting because of an increased turnover of IMCL and/or subsequent changes in the composition of intramyocellular lipids (glyco(shpingo)lipids and...

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

Samenvatting

ID

NL-OMON28815

Bron
Nationaal Trial Register

Verkorte titel
IFIS

Aandoening

insulin resistance, intermittent fasting

Ondersteuning

Primaire sponsor: M.J.Serlie M.D. PhD
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Overige ondersteuning: fund = initiator = sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Insulin sensitivity of glucose metabolism.

Toelichting onderzoek

Achtergrond van het onderzoek

An important adaptation during fasting is a change in fuel utilization. In skeletal muscle, fatty acids and ketone bodies will be used for ATP production and glucose uptake and subsequent glucose oxidation will be minimized. The supply of fatty acids is derived from lipolysis and partly by oxidation of stored intramyocellular triglycerides and diacylglycerol.

Our early ancestors (50.000 â€“ 10.000 B.C.) had no unlimited access to food as most people in Western countries have these days. Furthermore they had to hunt/gather to obtain food and periods of fasting and exercise were followed by periods of feeding and rest with implications for metabolism (â€œcycles of feast and famineâ€). In the last few hundred years, but most notably very recently, a tremendous change has occurred in feeding and exercise behaviour leading to the troublesome obesity and diabetic epidemic. Some postulate that 10.000 years ago our genome was made, build for the cycles of feast and famine, but not made for the continuous oversupply of food and lack of exercise in our modern era. This hypothesis is outlined underneath.

A recent study found that intermittent fasting (IF) for two weeks, mimicking cycles of feast and famine, improves insulin sensitivity. In this study total IMCL and the expression of glucose transporter GLUT 4 did not change. This could indicate that IMCL composition and lipid turnover may be responsible for the difference found in insulin sensitivity. In the same study, during the hyperinsulinemic euglycemic clamp, IMCL decreased very rapidly, indicating that even under hyperinsulinemic conditions, fatty acid oxidation is the main

energy providing flux and by definition glucose is preferentially stored as glycogen. Lipolysis is almost completely suppressed by high levels of insulin, meaning that the substrates for fatty acid oxidation come from stored intramyocellular lipids instead of from fatty acid uptake from the plasma compartment. Depletion of IMCL can then be followed by replenishment, indicating turnover. This could be physiological during cycles of feast and famine.

We hypothesize that peripheral insulin sensitivity increases after a period of intermittent fasting because of an increased turnover of IMCL and/or subsequent changes in the composition of intramyocellular lipids (glyco(shpingo)lipids and acylcarnitineprofiles) and by that a more favourable intramyocellular milieu with less oxidized lipids, preserved mitochondrial function and insulin signalling.

Doel van het onderzoek

We hypothesize that peripheral insulin sensitivity increases after a period of intermittent fasting because of an increased turnover of IMCL and/or subsequent changes in the composition of intramyocellular lipids (glyco(shpingo)lipids and acylcarnitineprofiles) and by that a more favourable intramyocellular milieu with less oxidized lipids, preserved mitochondrial function and insulin signalling.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

After the first study day, volunteers are randomly assigned to:

1. Two weeks standard diet;

2. Two weeks of intermittent fasting.

After these two weeks, a study day as previously described will follow where after volunteers change diet (standard vs IF, or IF vs standard).

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Lean healthy male volunteers;

2. Age 18 - 35 years;

3. BMI 20-25 kg/m2;

4. Stable weight three months prior to study inclusion;

5. Normal oral glucose tolerance test (OGTT) using the ADA-criteria.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Any medication;

2. DM II in first degree family members;

3. Hypertriglyceridemia or any other lipid metabolism disorder;

4. Intensive sports (> three times weekly);

5. Any medical disorder of significant relevance;

6. 'Breakfast-skipper'.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-01-2007
Aantal proefpersonen:	8
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	15-06-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1731
NTR-old	NTR1841
Ander register	MEC AMC : 06-170
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
1:
Pro OGTT
Soeters MR, Serlie MJ.
Ned Tijdschr Geneeskd. 2009 Apr 18;153(16):742. Dutch.

2:Effects of Insulin on Ketogenesis Following Fasting in Lean and Obese Men.
Soeters MR, Sauerwein HP, Faas L, Smeenge M, Duran M, Wanders RJ, Ruiter AF, Ackermans MT, Fliers E, Houten SM, Serlie MJ.
Obesity (Silver Spring). 2009 Feb 19. [Epub ahead of print]

3:
Type 2 iodothyronine deiodinase in skeletal muscle: effects of hypothyroidism and fasting.
Heemstra KA, Soeters MR, Fliers E, Serlie MJ, Burggraaf J, van Doorn MB, van der Klaauw AA, Romijn JA, Smit JW, Corssmit EP, Visser TJ.
J Clin Endocrinol Metab. 2009 Jun;94(6):2144-50. Epub 2009 Mar 17.

4:
Muscle acylcarnitines during short-term fasting in lean healthy men.
Soeters MR, Sauerwein HP, Duran M, Wanders RJ, Ackermans MT, Fliers E, Houten SM, Serlie MJ.
Clin Sci (Lond). 2009 Apr;116(7):585-92.

5:
Muscle adaptation to short-term fasting in healthy lean humans.
Soeters MR, Sauerwein HP, Dubbelhuis PF, Groener JE, Ackermans MT, Fliers E, Aerts JM, Serlie MJ.
J Clin Endocrinol Metab. 2008 Jul;93(7):2900-3. Epub 2008 Apr 8.

6:
Gender-related differences in the metabolic response to fasting.
Soeters MR, Sauerwein HP, Groener JE, Aerts JM, Ackermans MT, Glatz JF, Fliers E, Serlie MJ.
J Clin Endocrinol Metab. 2007 Sep;92(9):3646-52. Epub 2007 Jun 12.

7:
Recombinant human C1-inhibitor in the treatment of acute angioedema attacks.
Choi G, Soeters MR, Farkas H, Varga L, Obtulowicz K, Bilo B, Porebski G, Hack CE, Verdonk R, Nuijens J, Levi M.
Transfusion. 2007 Jun;47(6):1028-32.