

Einfluss von Fructose-Überernährung und Fischöleinnahme auf die Fettneubildung durch die Leber und die Insulinempfindlichkeit bei gesunden Männern

David Faeh^{1,2}, Kaori Minehira¹, Jean-Marc Schwarz^{3,4}, Raj Periasami⁴,
Park Seongsu³, Luc Tappy¹

¹Department of Physiology, University of Lausanne, 1005 Lausanne, Switzerland

²University Institute of Social and Preventive Medicine, 1005 Lausanne, Switzerland

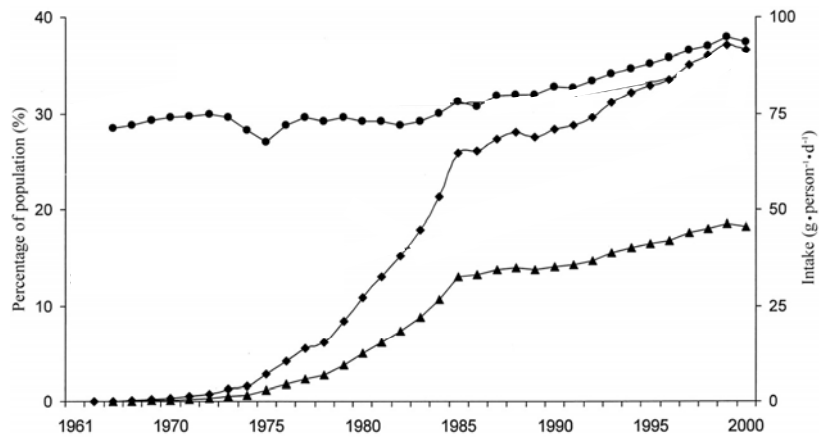
³Department of Medicine, University of California at San Francisco, San Francisco, USA

⁴Basic Science, Touro University, Mare Island, CA, USA

Fructose

- Saccharose (Haushaltzucker) besteht je zur Hälfte aus Fruktose (Fructose) und Glukose (Traubenzucker)
- Fruktose ist Bestandteil vieler Esswaren und Getränke

Fruktosekonsum in den U.S.



Estimated intakes of **total fructose (●)**,
high-fructose corn syrup (HFCS,◆) and
free fructose (▲).

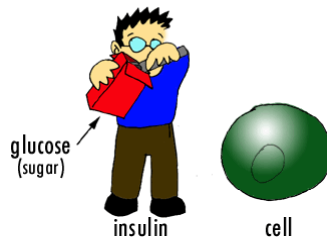
Bray et al, 2004

Hintergrund

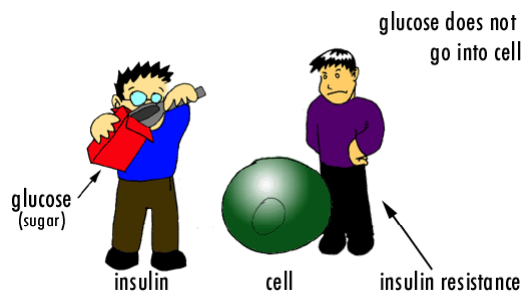
- Fruktose kann...
 - ...in der Leber in Fett umgewandelt werden
 - ...Blutfettwerte erhöhen
 - ...im Tierversuch Insulinresistenz hervorrufen

- Fischöl kann...
 - ...Blutfettwerte senken
 - ...im Tierversuch Insulinresistenz vorbeugen

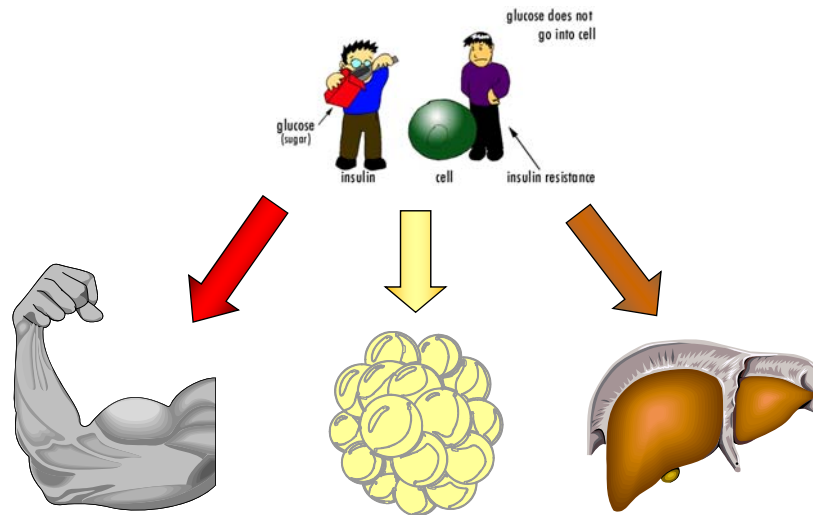
Wirkung von Insulin



Insulinresistenz



Insulinresistenz



Versuchsplan

- 7 junge, gesunde, männliche Probanden
- Fischöl während 28 Tagen
- Fruktose während 6 Tagen
- Fischöl und Fruktose
- Kontrolltest

Resultate: Fruktose

6 Tage fruktosereiche Ernährung hat...

- ...die Blutfettwerte (TG) um 80 % erhöht
- ...die Fettneubildung durch die Leber um das 6-fache erhöht
- ...eine Insulinresistenz im Fettgewebe und in der Leber bewirkt
- ...keinen Einfluss auf die Muskel-Insulinwirkung ausgeübt

Resultate: Fischöl

Fischöleinnahme während 28 Tagen in Kombination mit 6 Tage fruktosereicher Ernährung hat...

- ...die durch Fruktose erhöhten Blutfettwerte (TG) gesenkt (um 37%)
- ...die Fettneubildung durch die Leber tendenziell gesenkt (NS)
- ...keinen Einfluss auf die Insulinresistenz

Schlussfolgerungen

1. Fruktose kann sich negativ auf den Stoffwechsel auswirken, bereits nach 6 Tagen
2. Fischöl kann erhöhte Blutfettwerte senken, hat aber keinen Einfluss auf die Insulinresistenz

MERCI

- Reserve

Background

Metabolic consequences of fructose overfeeding

1. Hypertriglyceridemia (rodents & humans)
2. Increased hepatic de novo lipogenesis (DNL)
(rodents & humans)
3. Hepatic, adipose tissue and whole body insulin resistance (rodents)

Huang, et. al, 1997; Bantle et. al, 2000; Parks et. al, 2000; Pagliassotti et. al, 2004

Background

Metabolic impact of fish oil supplementation. Fish oil...

1. ...decreases triglycerides (rodents & humans)
2. ...may suppress hepatic lipogenic enzymes (FAS, ACC, SREBP-1, etc.) (in vitro and rodents)
3. ...may prevent development of insulin resistance (rodents)

Podolin et. al, 1998; Xu et. al, 1999

Aims

To test the effect of fructose and fish oil on...

- ...blood triglycerides, glucose, lactate
- ...hepatic DNL
- ...insulin resistance (hepatic, adipose tissue and whole body)

Subjects

Seven healthy men

- Mean age: **24.7 ± 1.3** years
- Mean BMI: **22.0 ± 0.75** kg/m²
- Mean body fat: **16.5 ± 0.7** %
- Mean waist circ.: **80 ± 2.9** cm

Study design

- Each subject was examined after every of the four conditions (randomized):
 - **Fish oil** (7.2 g per day for 4 weeks)
 - **Fructose** (3 g per kilo BW per day for 6 days = plus 30% of energy intake)
 - **Fish oil and Fructose**
 - **Control**

Study design

Isocaloric diet for 6 days



DIETARY INTERVENTION

METABOLIC INVESTIGATION

Study design

Isocaloric diet for 6 days



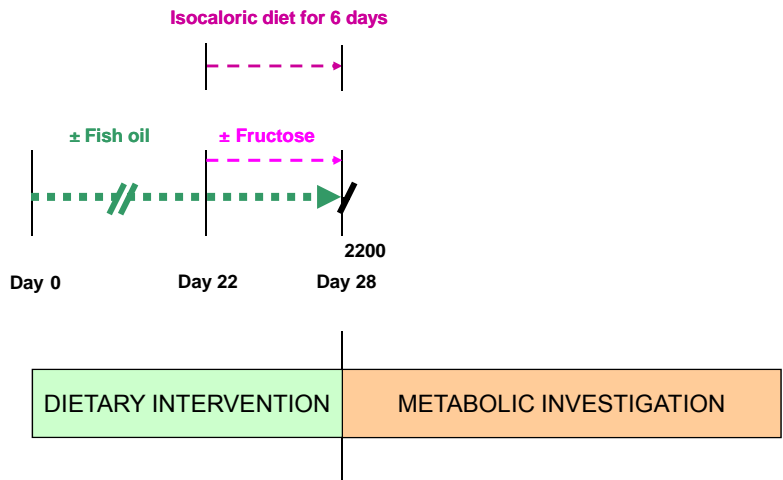
± Fish oil



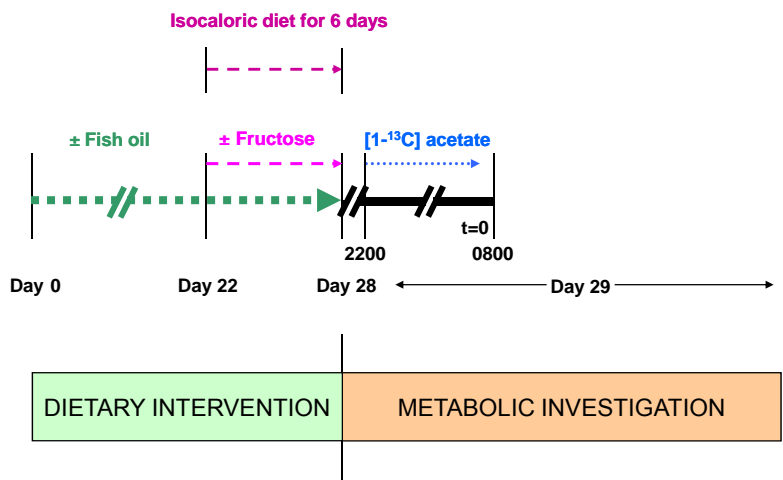
DIETARY INTERVENTION

METABOLIC INVESTIGATION

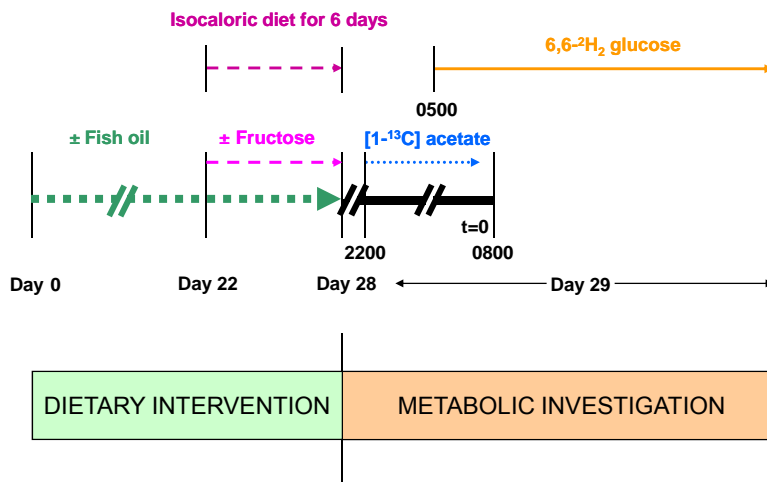
Study design



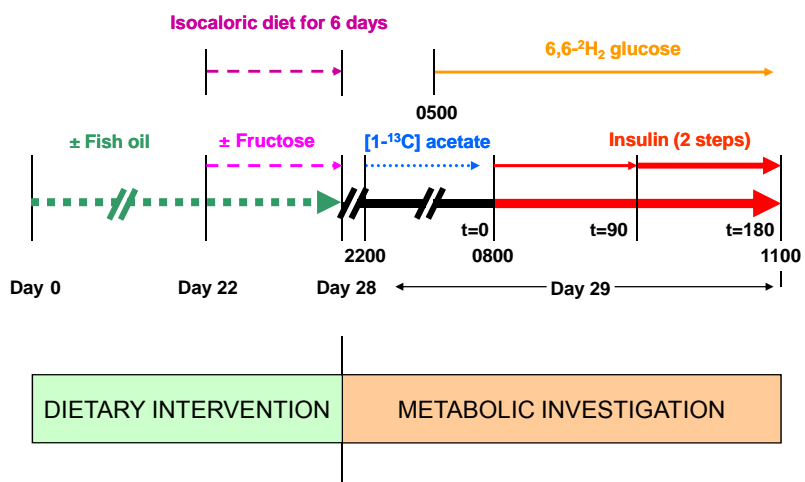
Study design

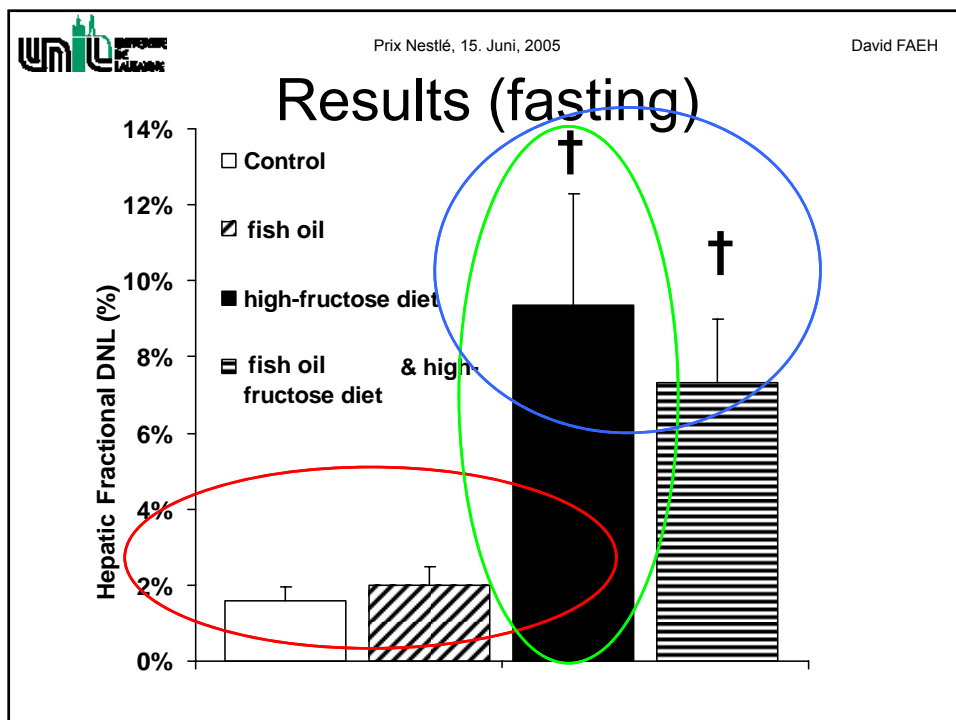
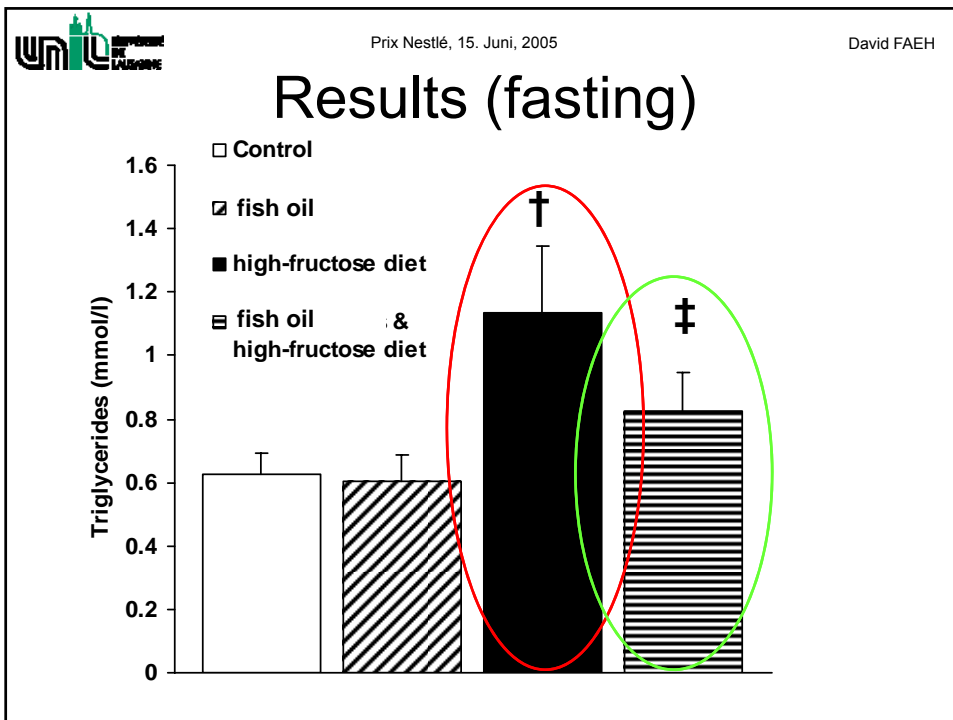


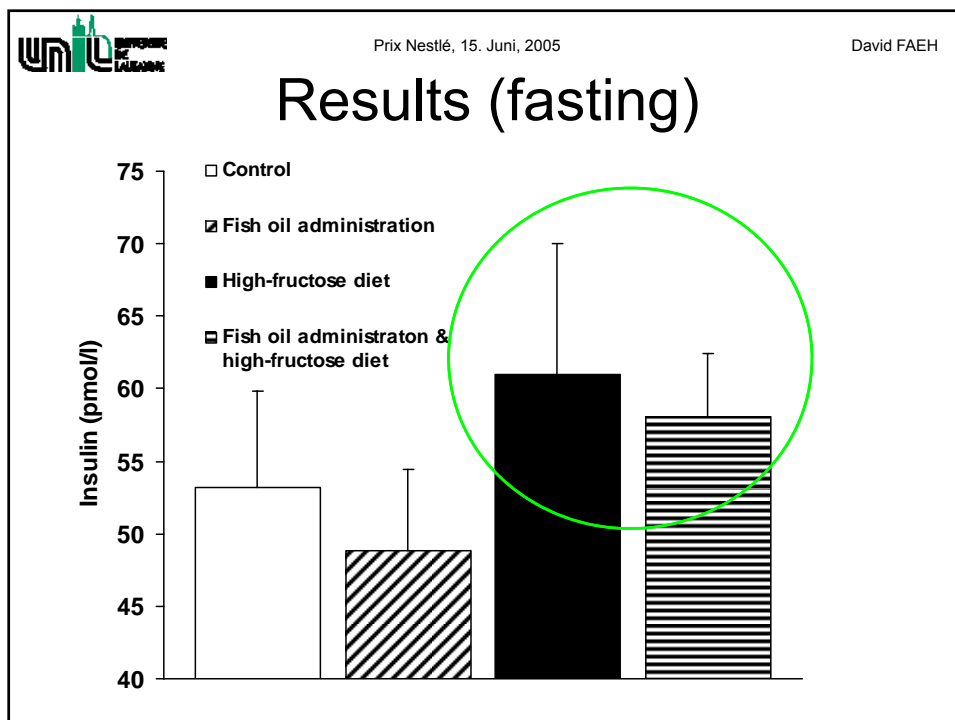
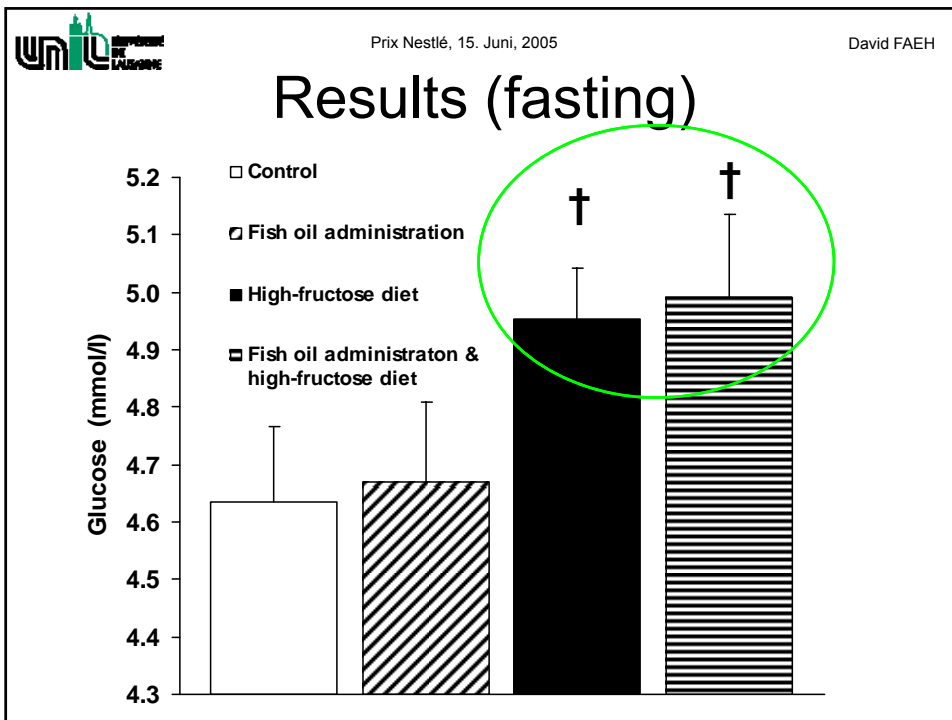
Study design

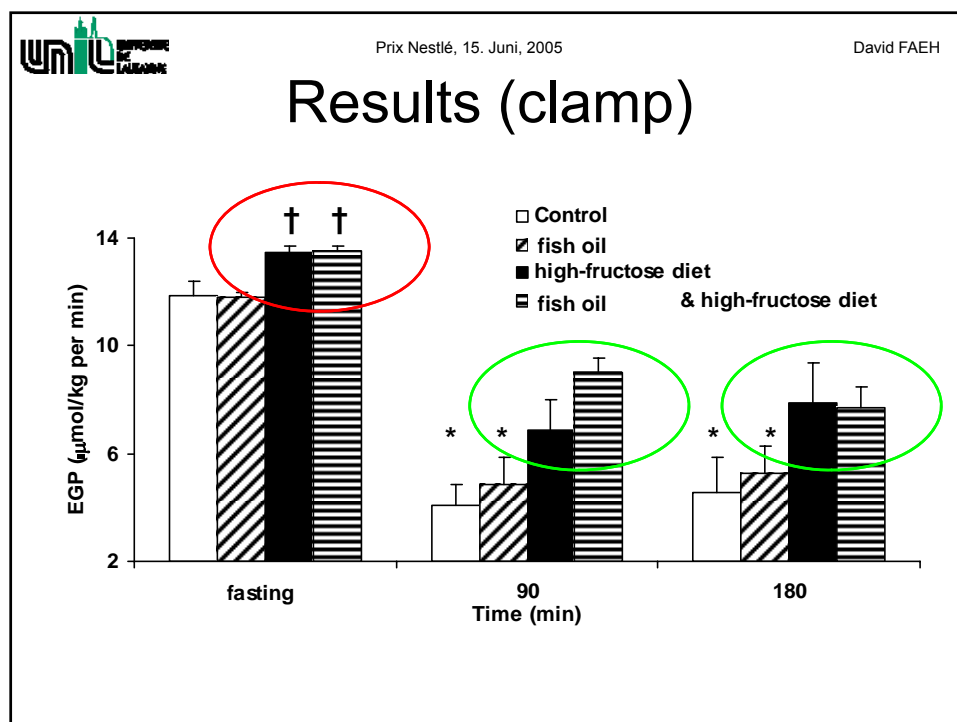
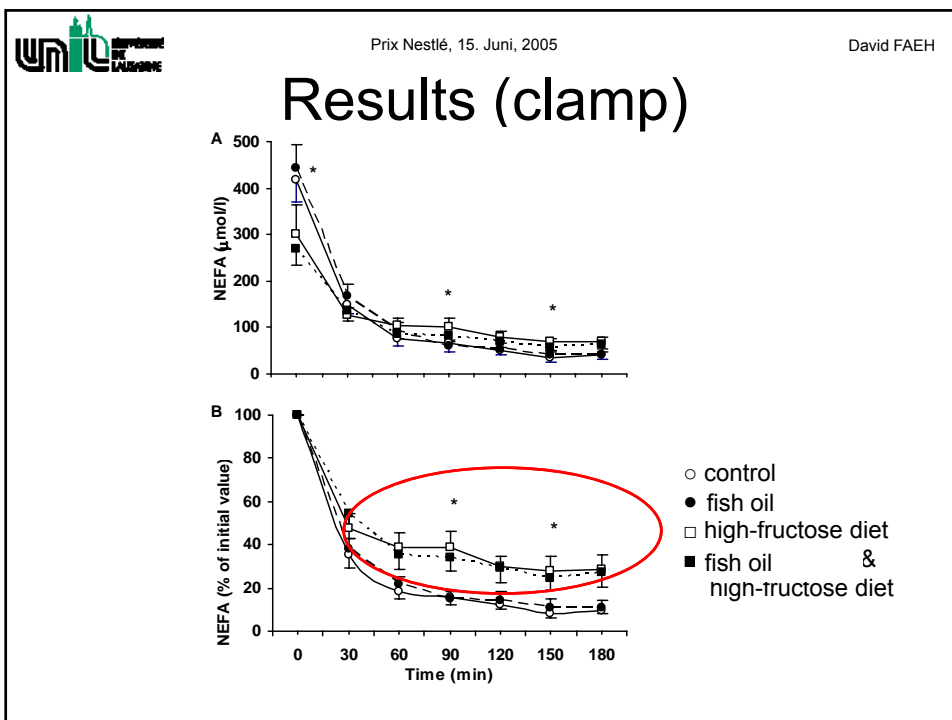


Study design

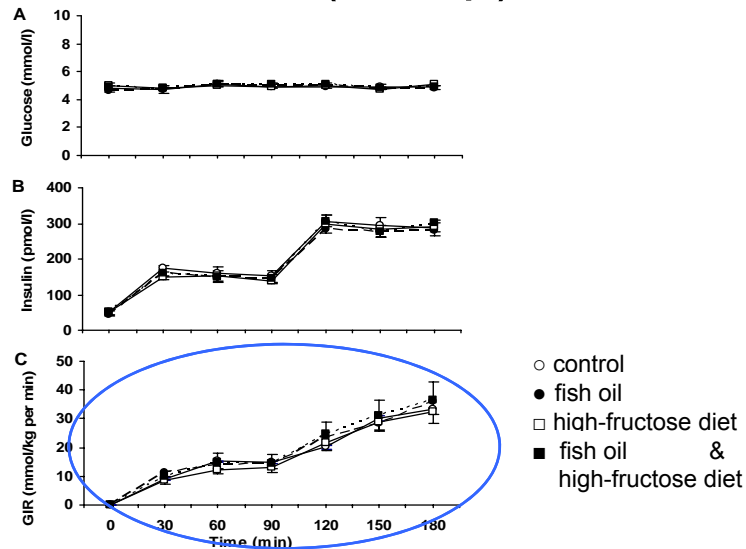








Results (clamp)



Conclusion

- After 6 days of fructose overfeeding,
 - ...mean fasting TG increased significantly by 79%
 - ...mean DNL increased significantly 6-fold
 - ...hepatic and adipose tissue insulin sensitivity decreased significantly
 - ...whole body insulin sensitivity was not affected

Conclusion

- Fish oil supplementation...
 - ...significantly attenuated fructose induced increase of blood TG and
 - ...tended to reduce fructose induced DNL (ns)
 - ...did not affect impaired insulin sensitivity associated to fructose overfeeding

Perspectives

- Long term (weeks) Fructose supplementation might...
 - ...increase Intra Myocellular (IMCL) and Intra Hepatocellular Lipids (IHCL)
 - ...impair muscle insulin sensitivity and cause hyperinsulinemia (as in rodents: Podolin et. al, 1998)



Thanks to

- Christine Cayeux**
- Françoise Secrétan**
- Rodrigue Stettler**
- Eunika Rossi**
- Nathalie Stefanoni**
- Valentine Rey**
- Philippe Schneiter**