

Effect of fructose overfeeding and fish oil administration on hepatic de novo lipogenesis and insulin sensitivity in healthy males

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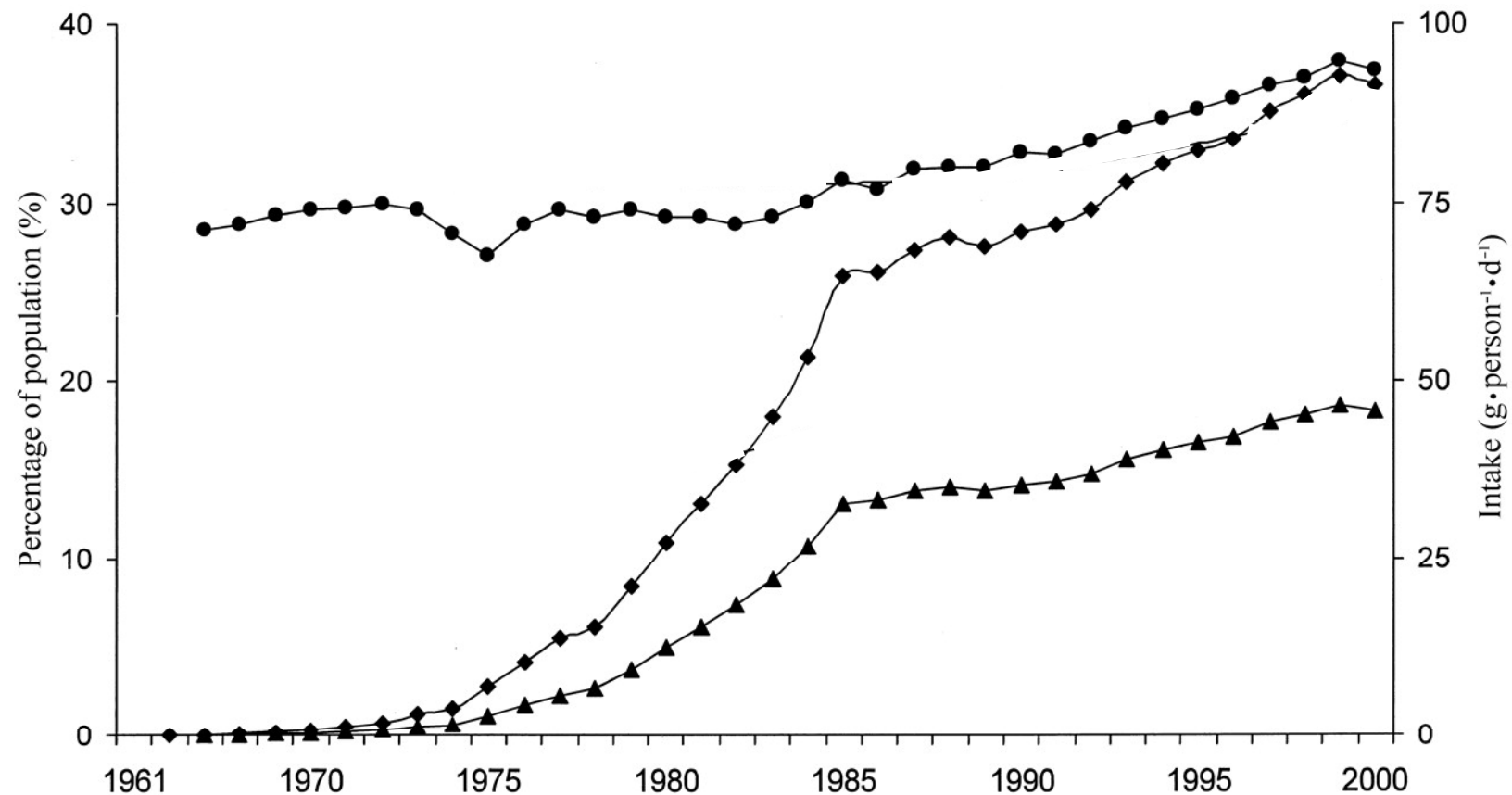
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Introduction

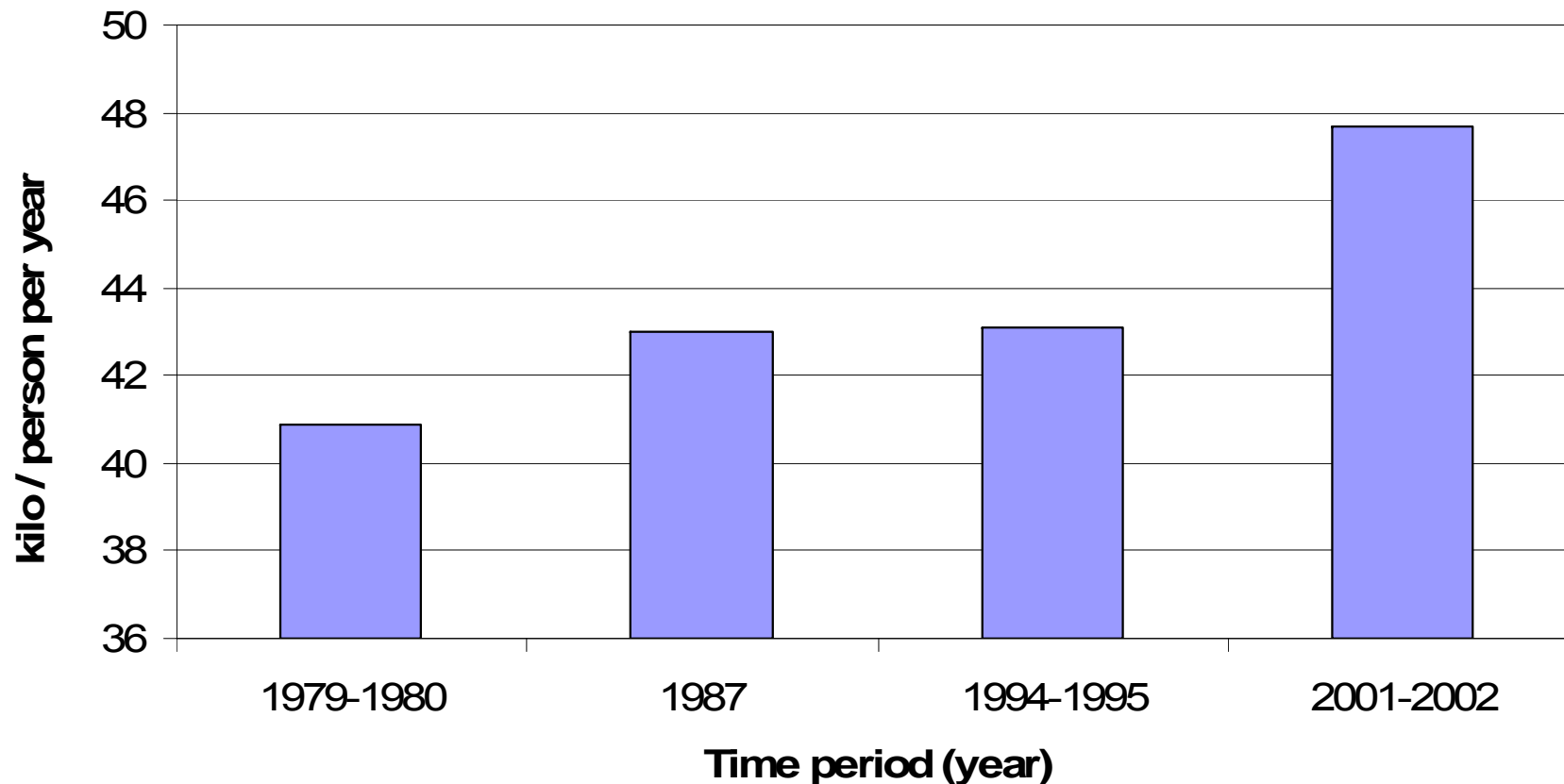


Estimated intakes of **total fructose (●)**,
high-fructose corn syrup (HFCS,◆) and
free fructose (▲).

Bray et al, 2004

Introduction

Sugar consumption in Switzerland



Sources: 1997-1995: 2., 3. & 4. CH Ernährungsbericht,
2001-2002: Schweizerischer Bauernverband

Introduction

Annual per capita consumption of sugar
sweetened drinks in Switzerland:

89.3 kilo*

*Source: Schweizerischer Bauernverband (2001-2002)

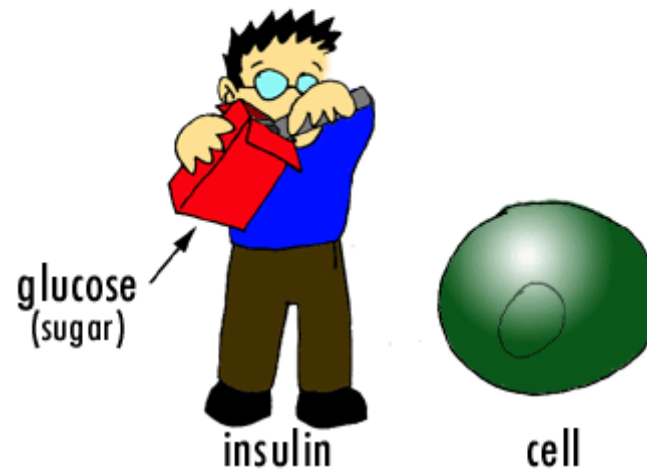
Background

Metabolic consequences of fructose overfeeding

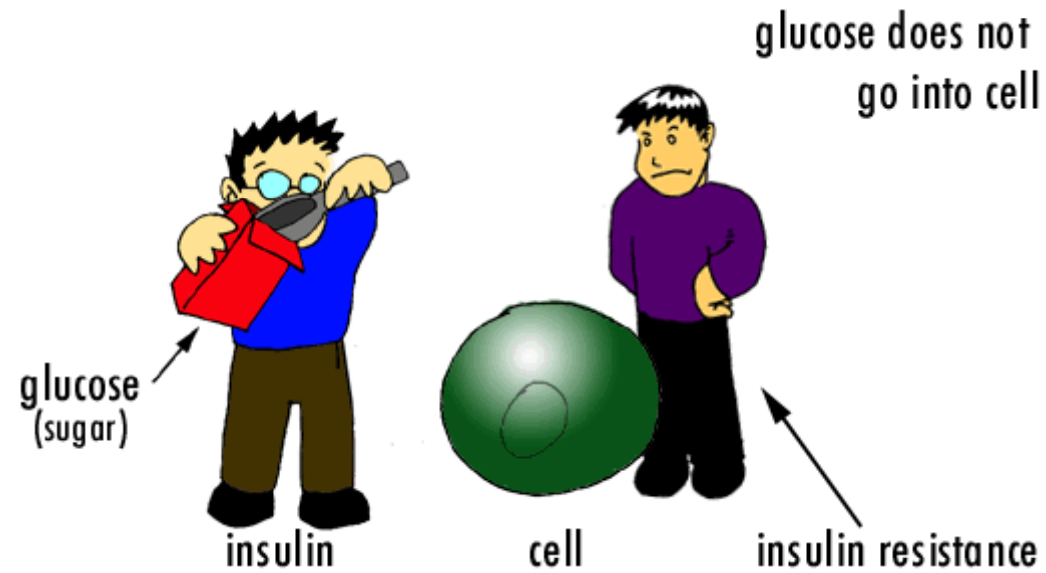
1. Hypertriglyceridemia (rodents & humans)
2. Increased hepatic de novo lipogenesis (DNL)
(rodents & humans)
3. Hepatic, adipose tissue and whole body insulin
resistance (rodents)

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

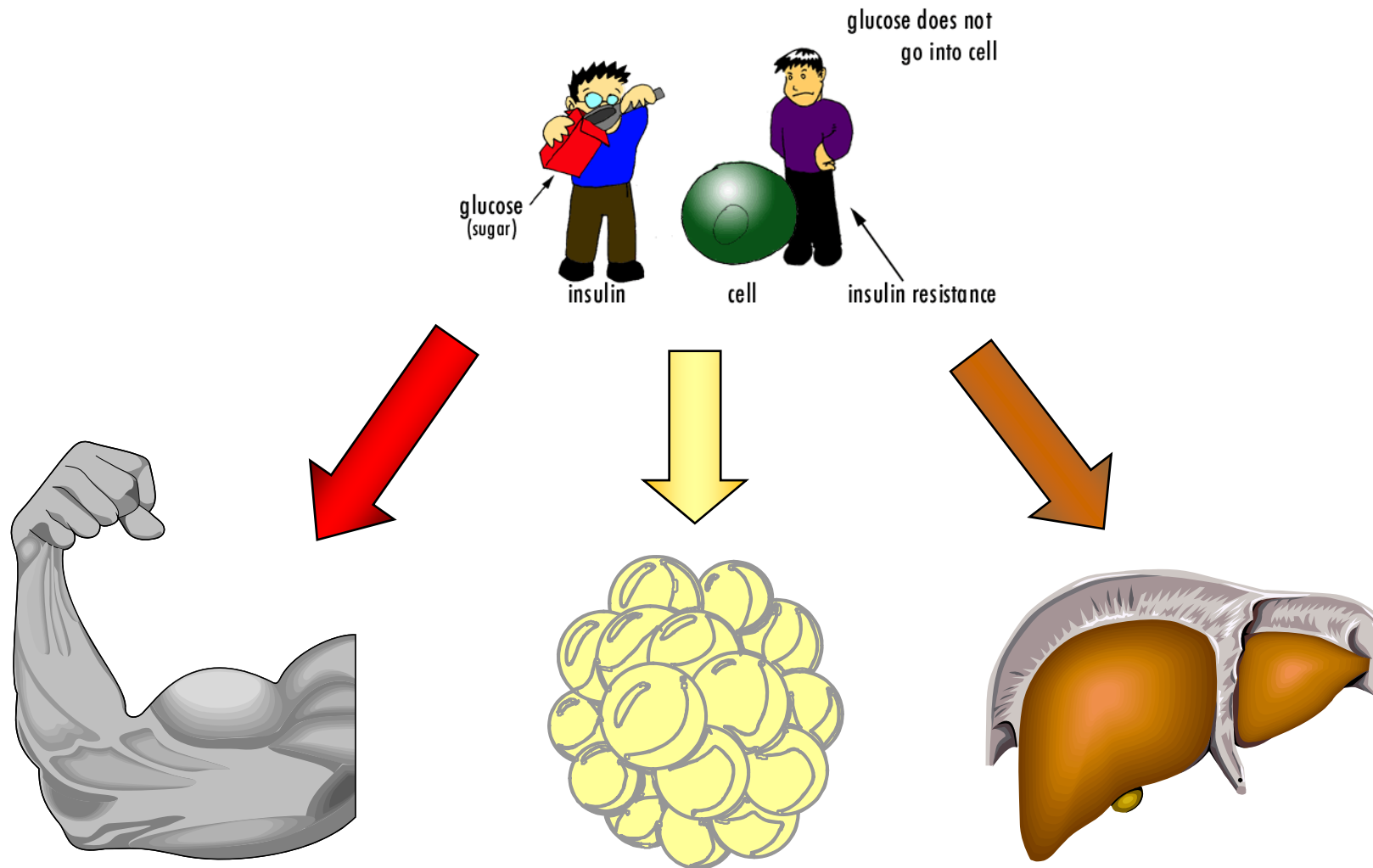
Action of insulin



Insulin resistance



Insulin resistance



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

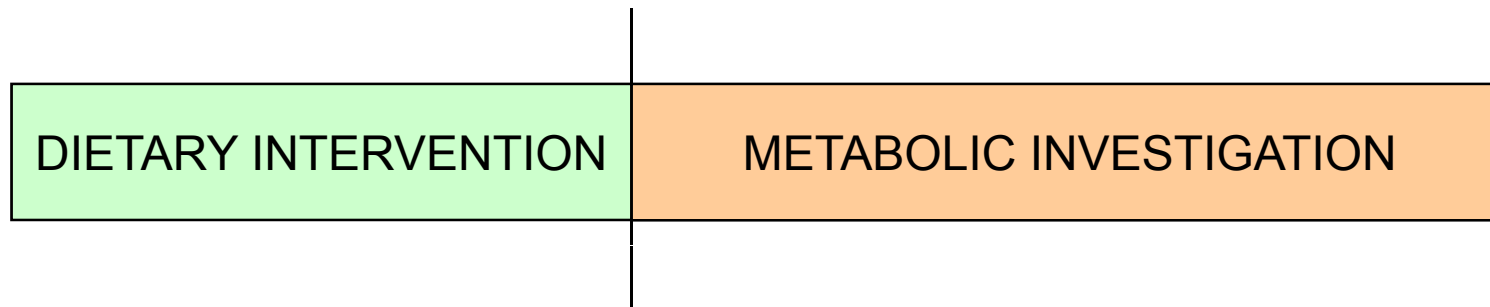
Seven healthy men

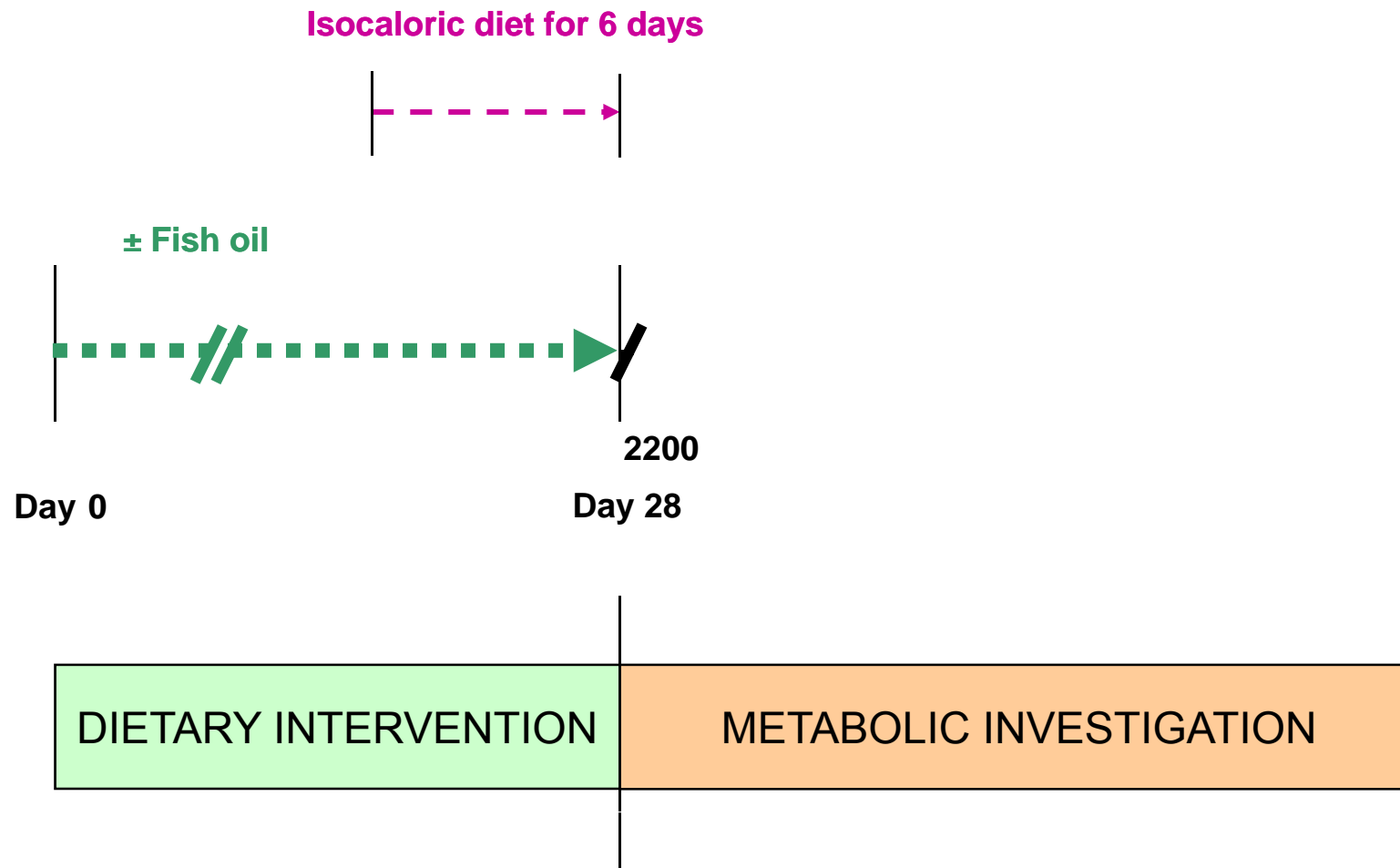
- Mean age: **24.7 \pm 1.3** years
- Mean BMI: **22.0 \pm 0.75** kg/m²
- Mean body fat: **16.5 \pm 0.7** %
- Mean waist circ.: **80 \pm 2.9** cm

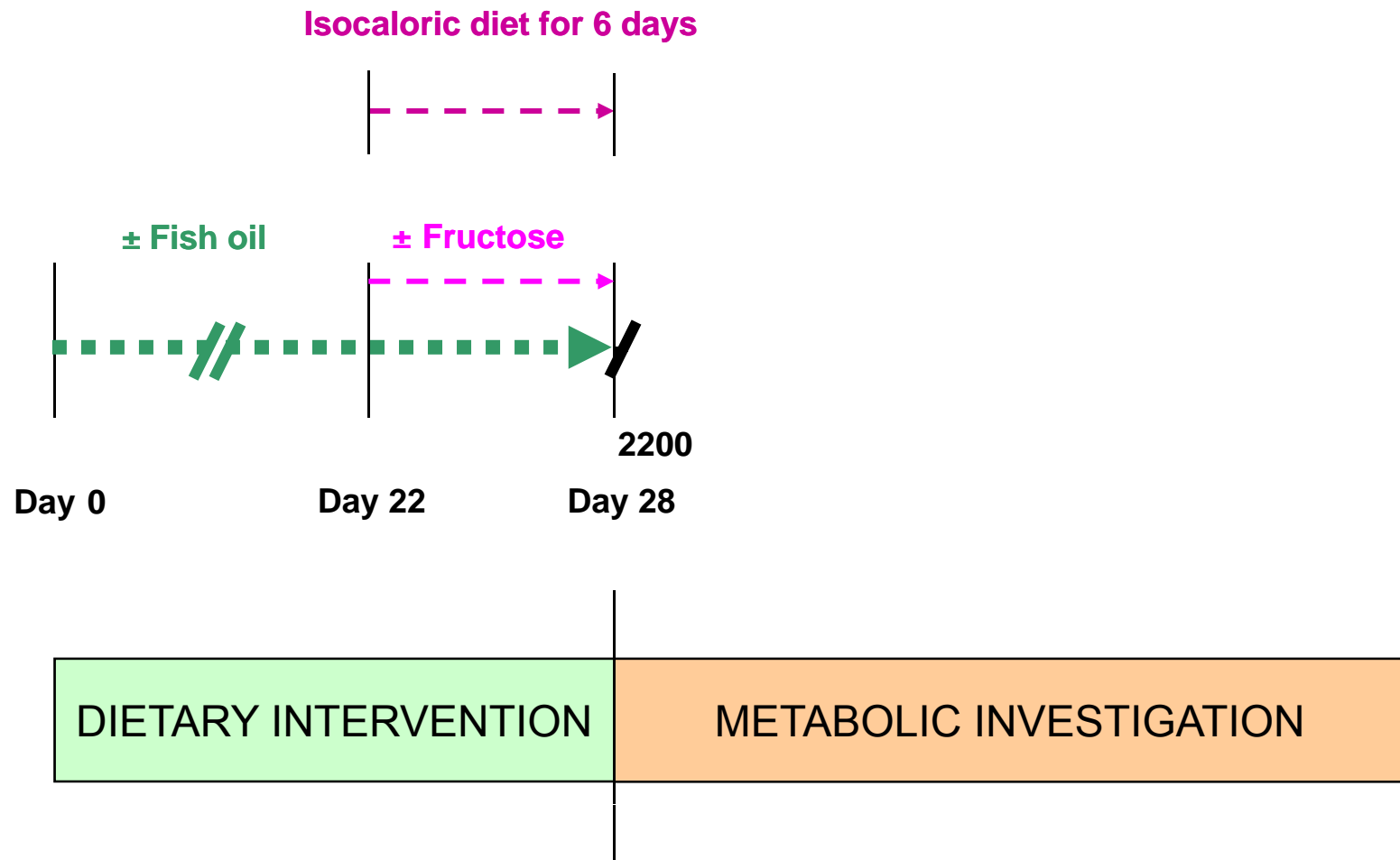
Study design

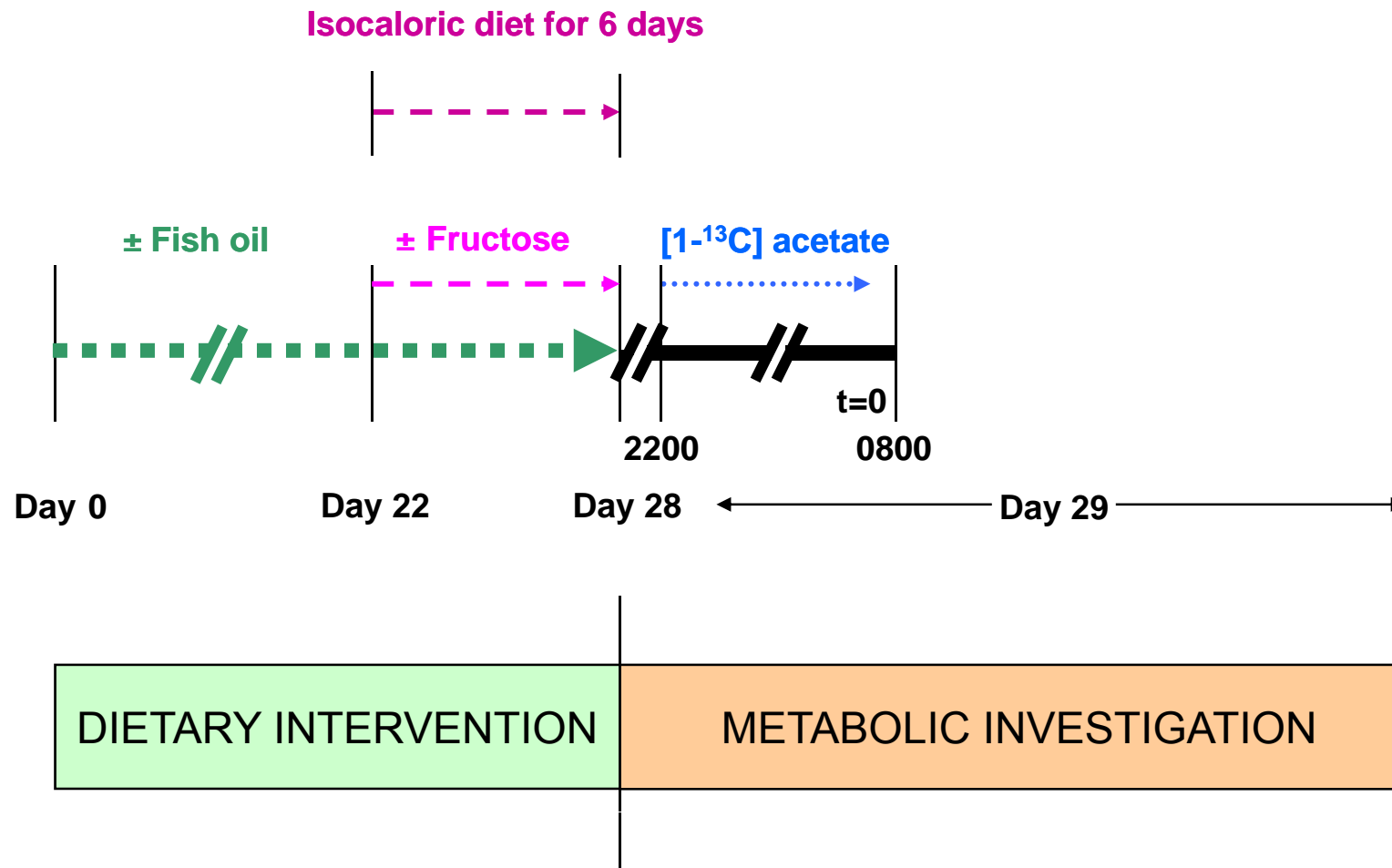
- Each subject was examined after every of the four conditions (randomized):
 - **Fish oil** (7.2 g per day for 4 weeks)
 - **Fructose** (3 g per kilo BW per day for 6 days = plus 30% of energy intake)
 - **Fish oil and Fructose**
 - **Control**

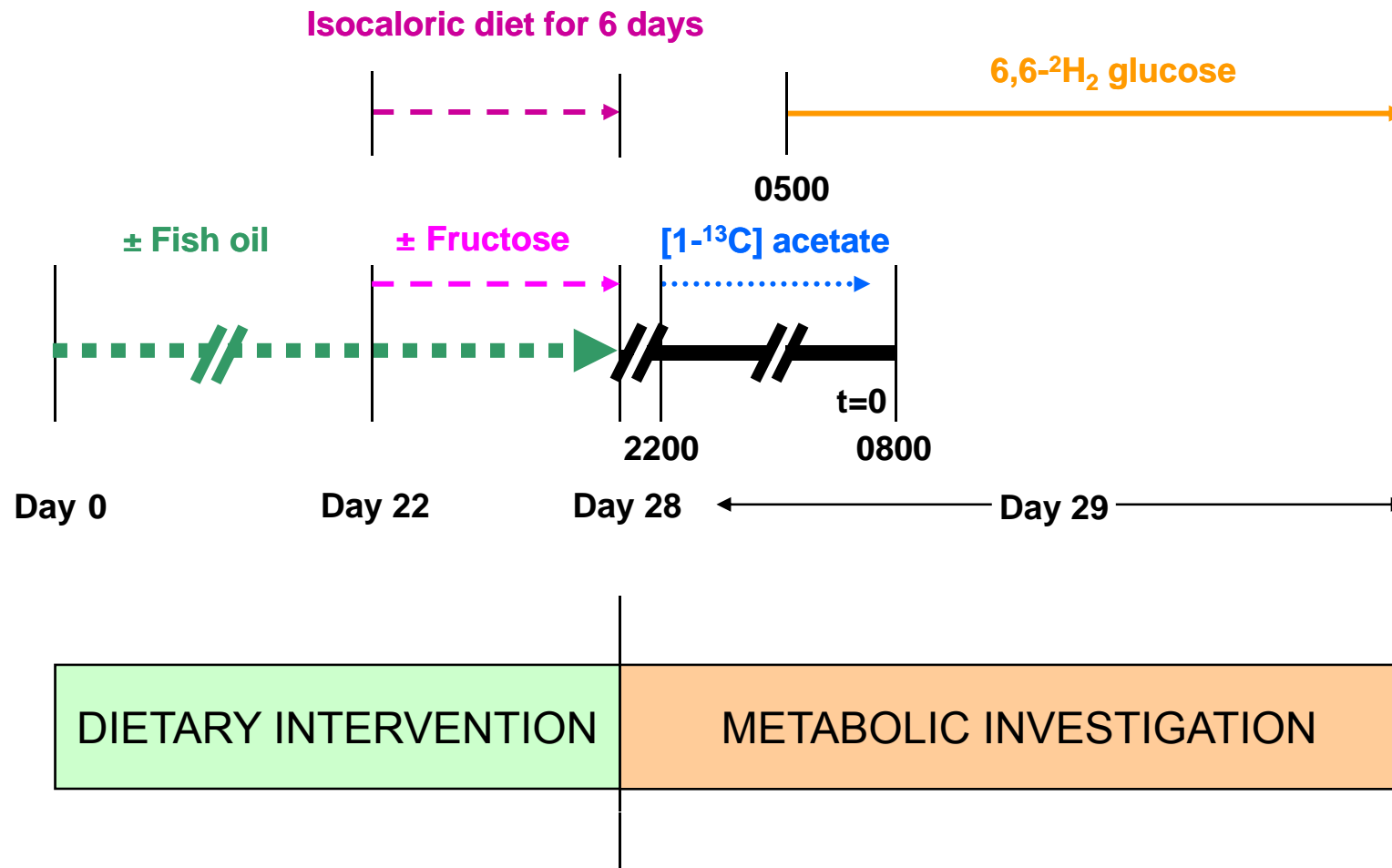
Isocaloric diet for 6 days

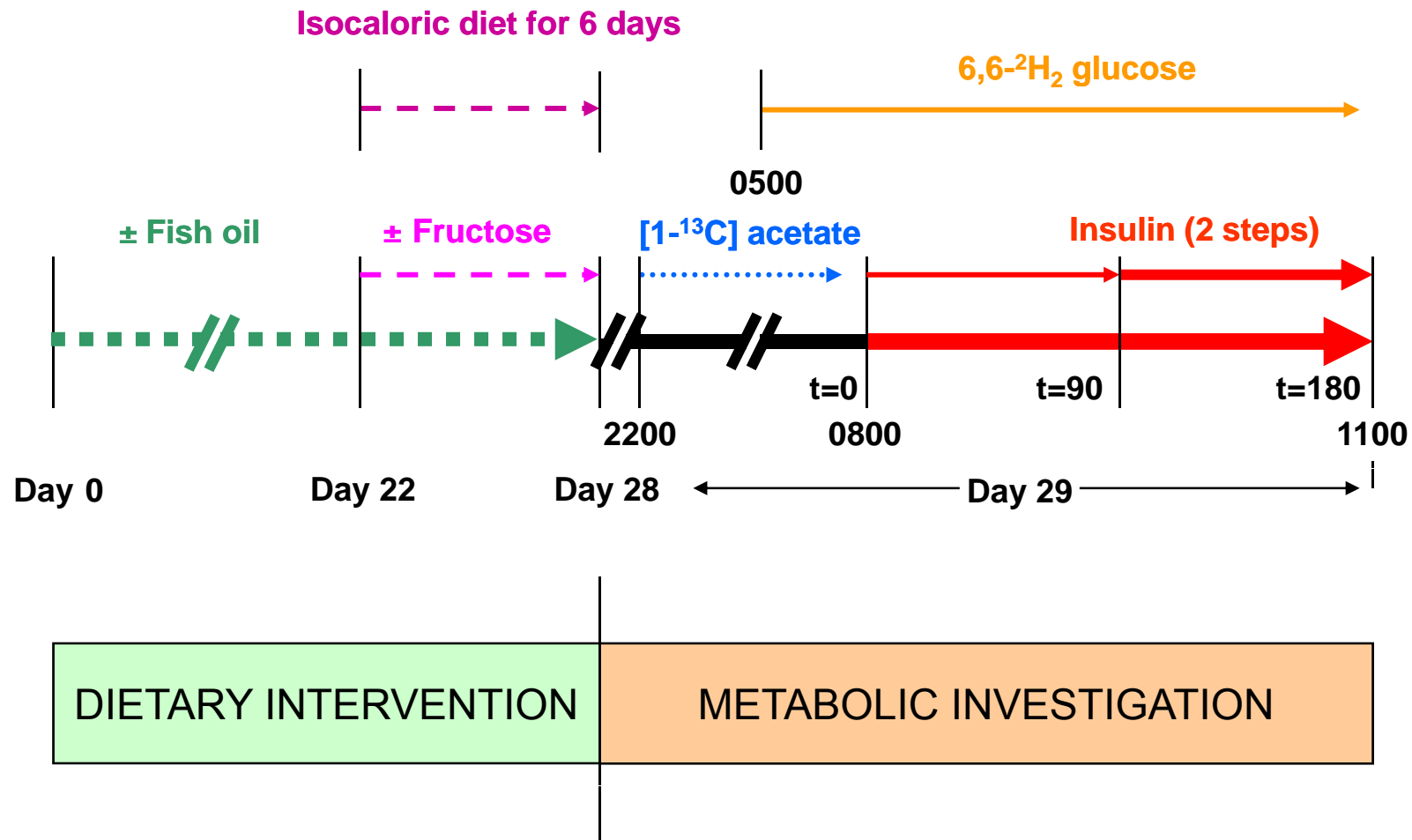












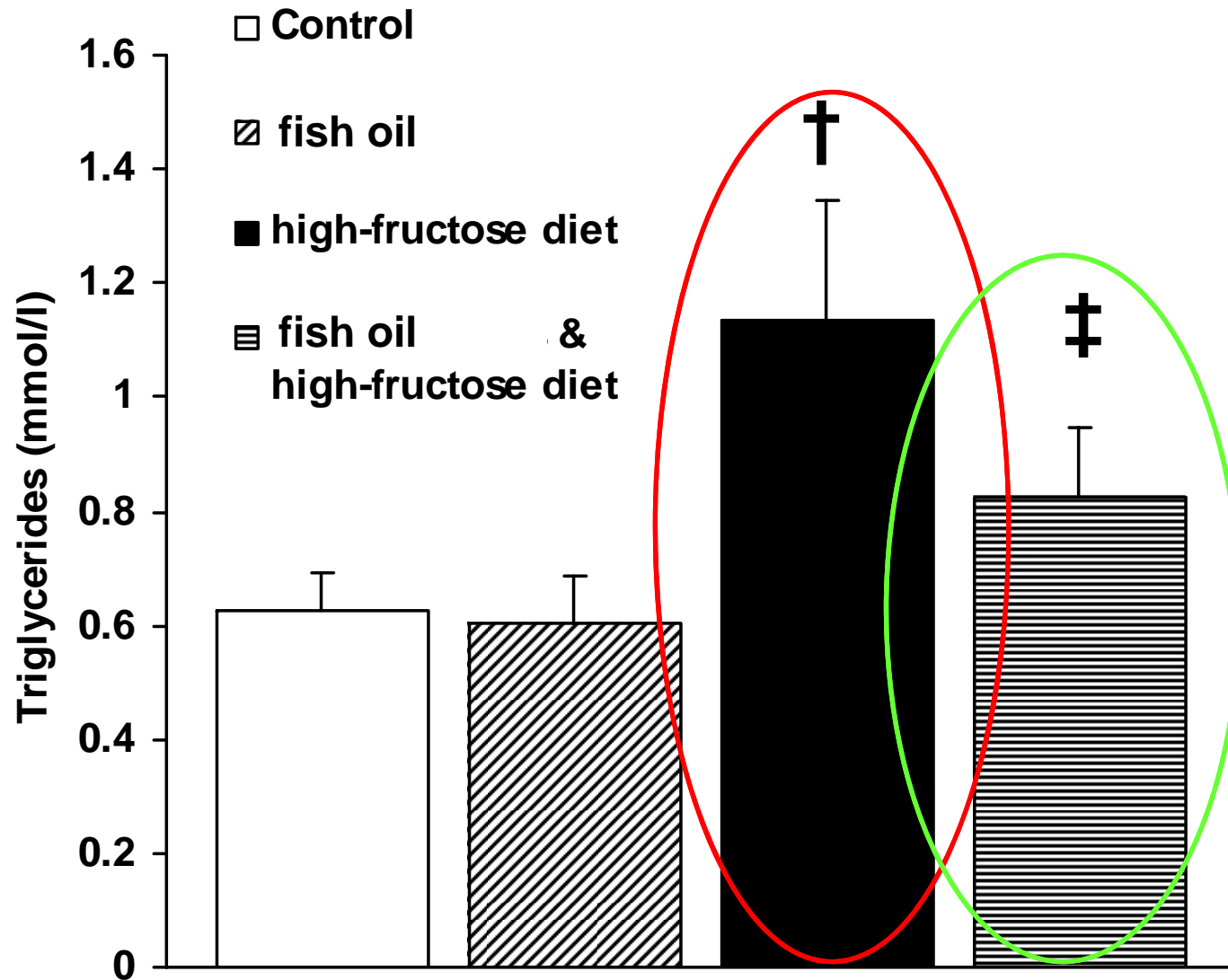




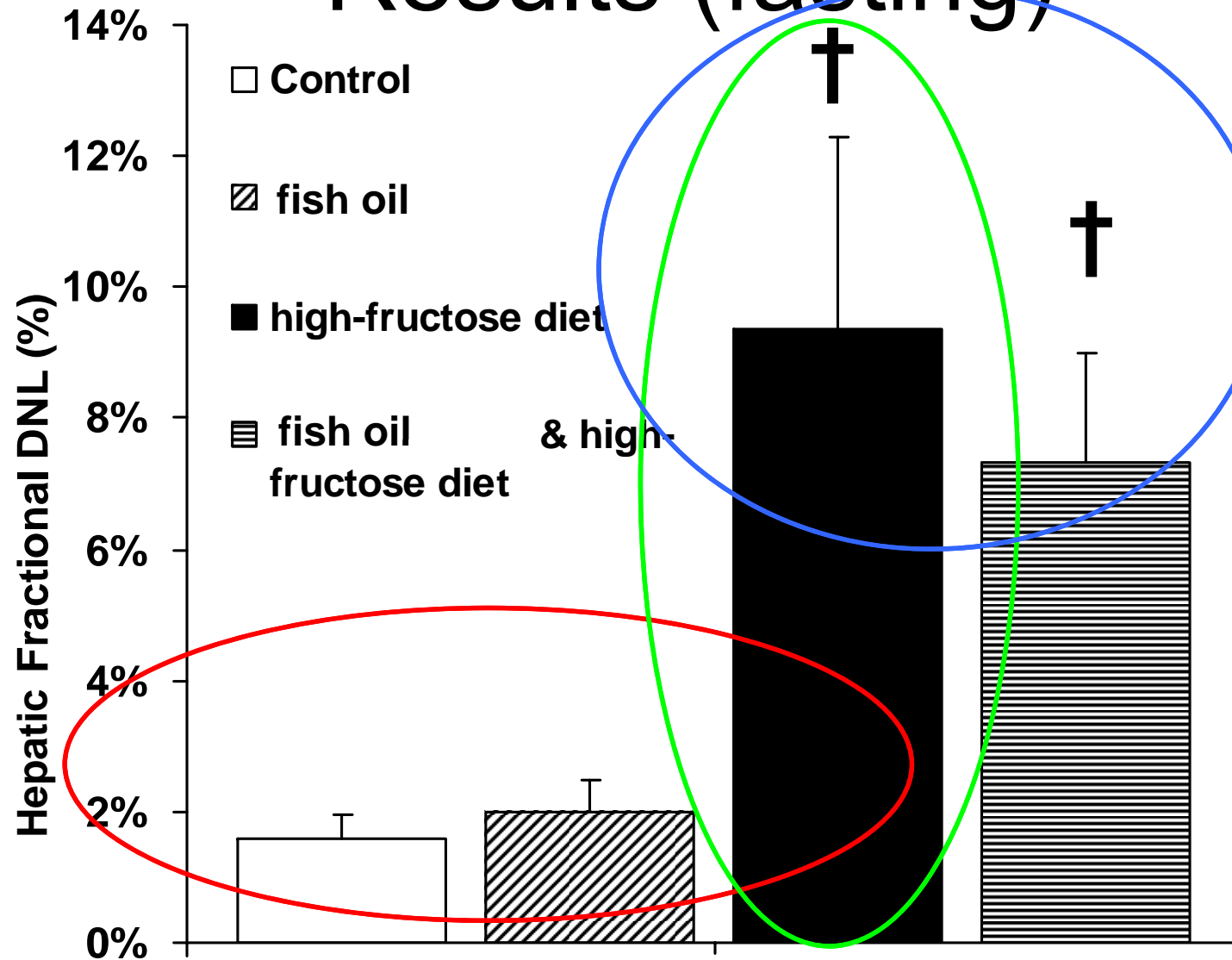




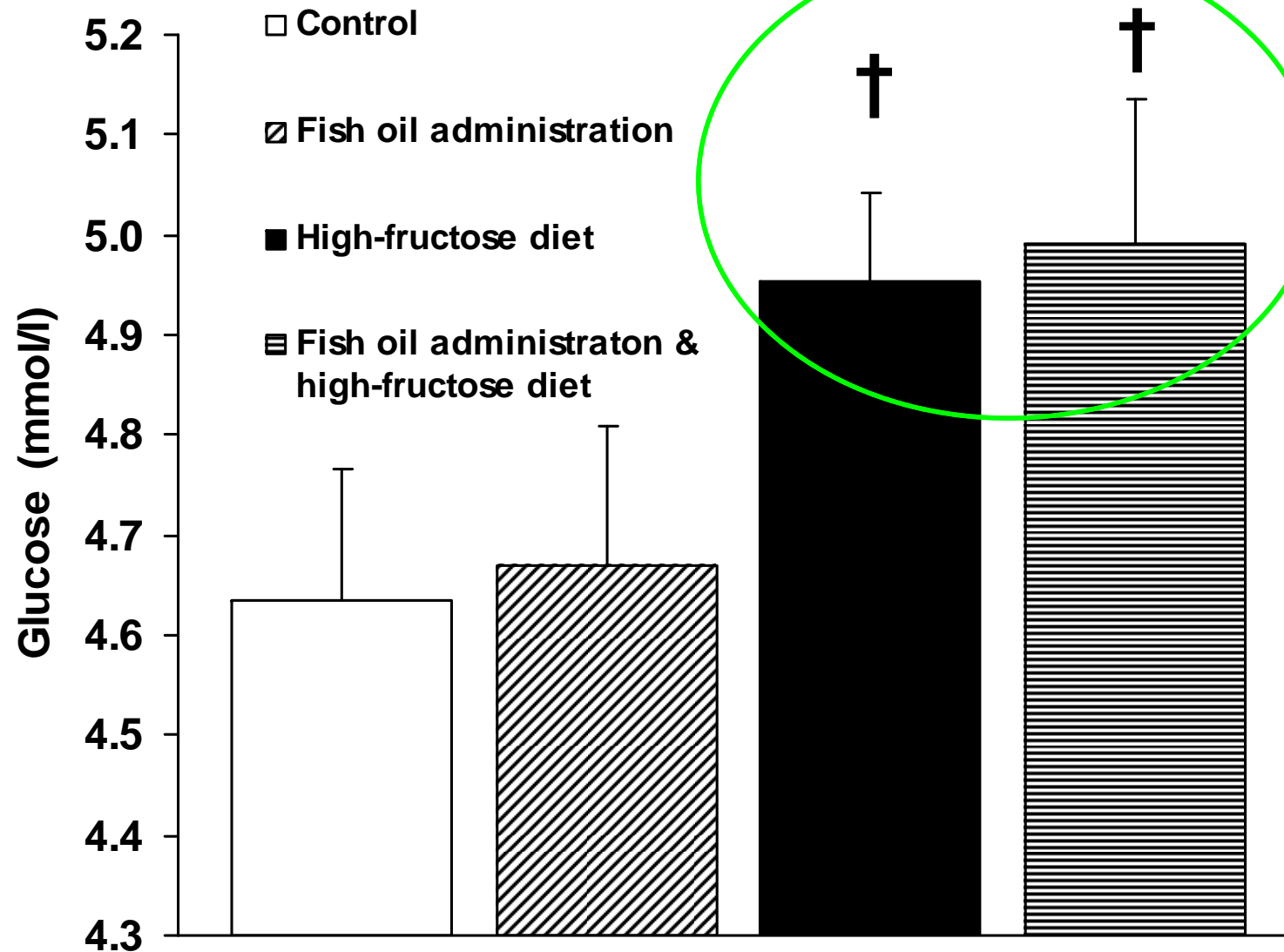
Results (fasting)



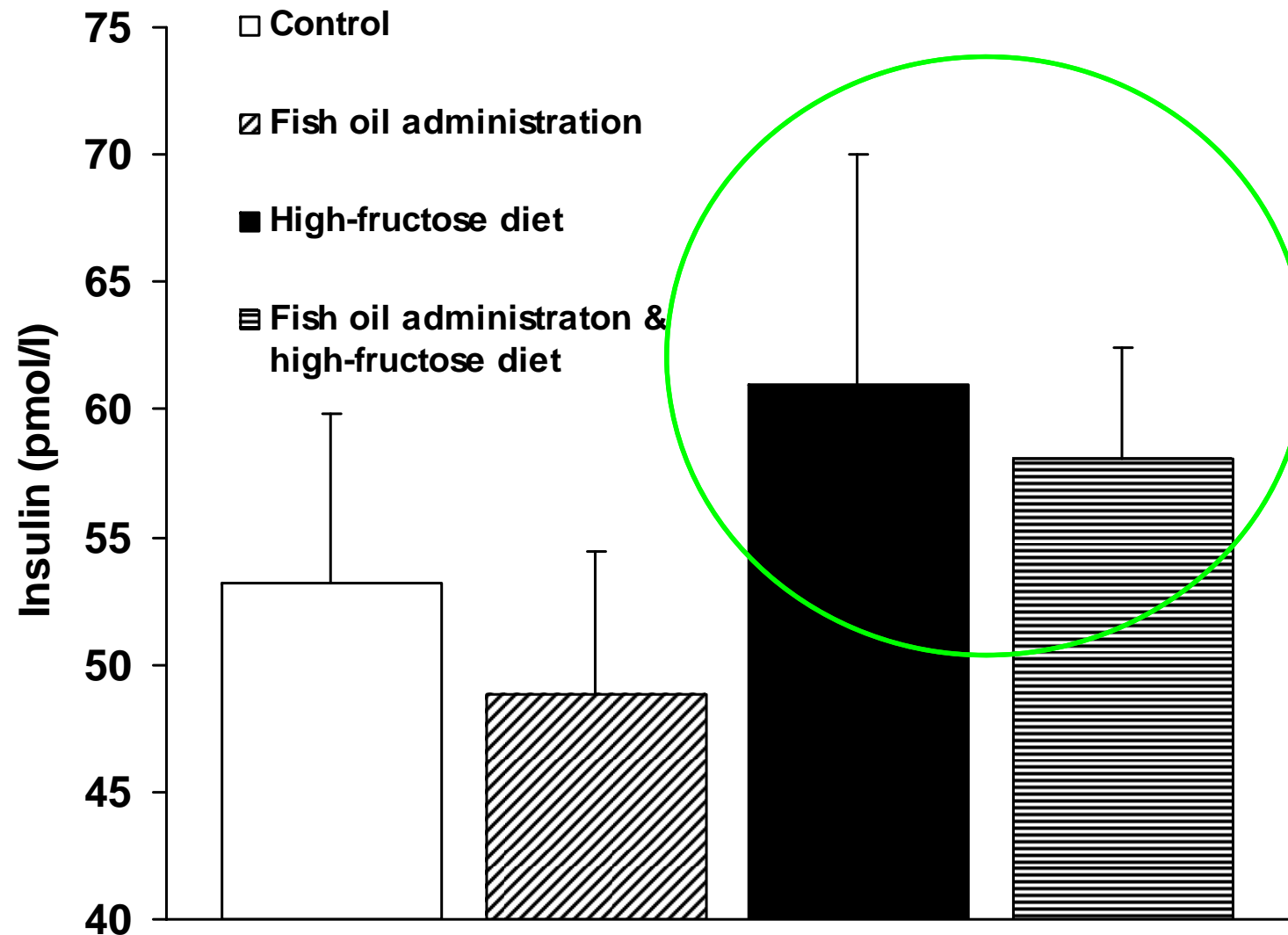
Results (fasting)



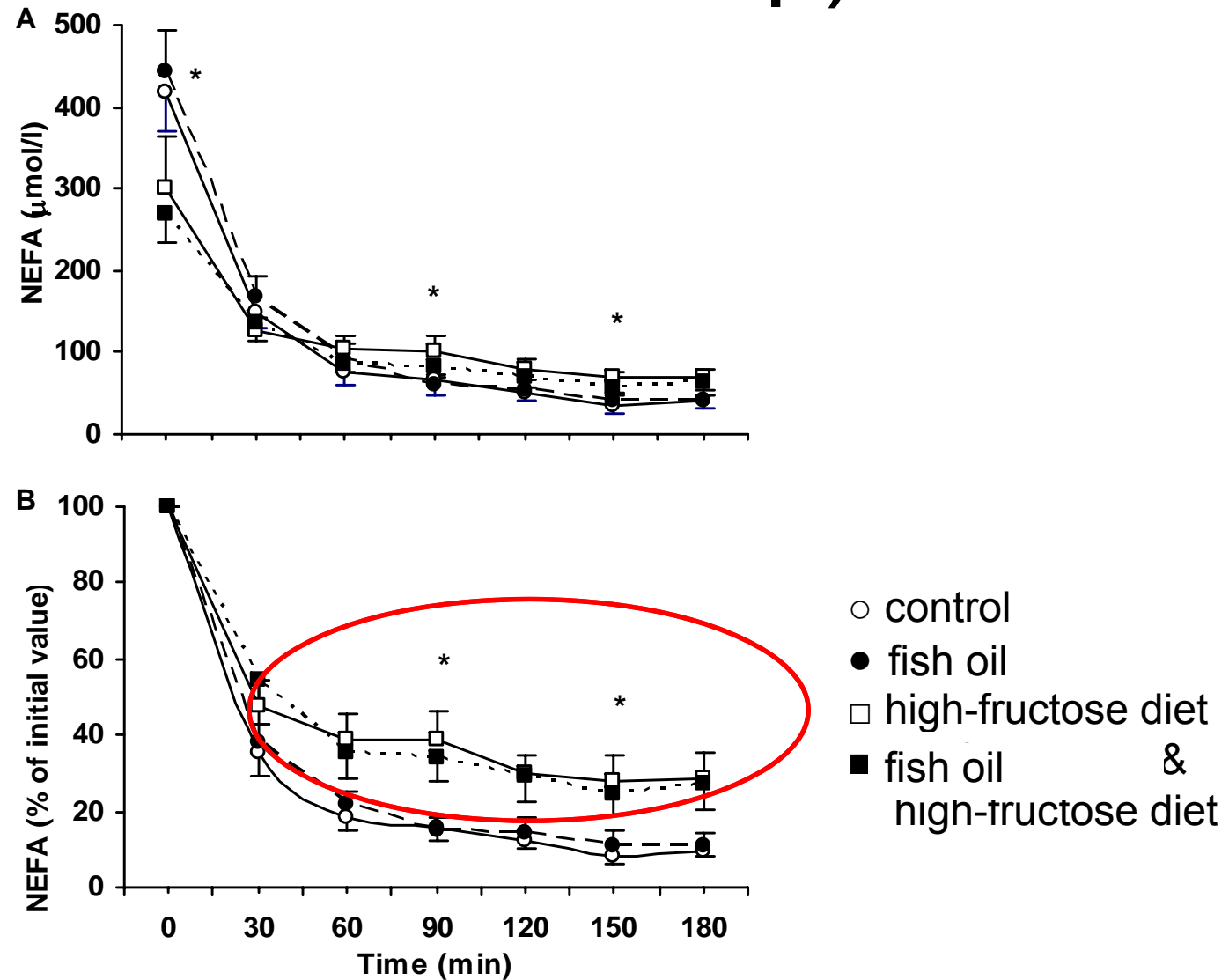
Results (fasting)



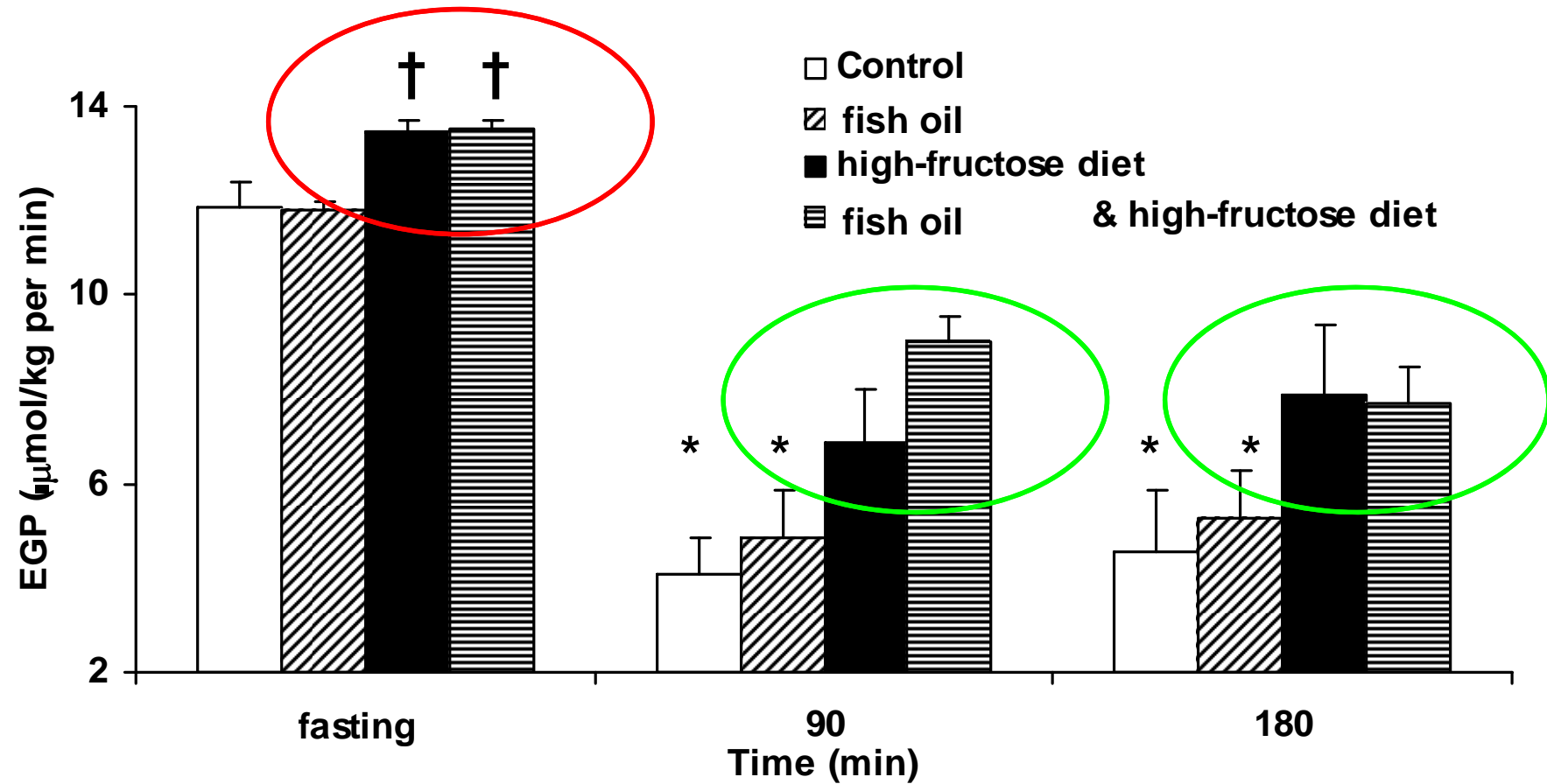
Results (fasting)



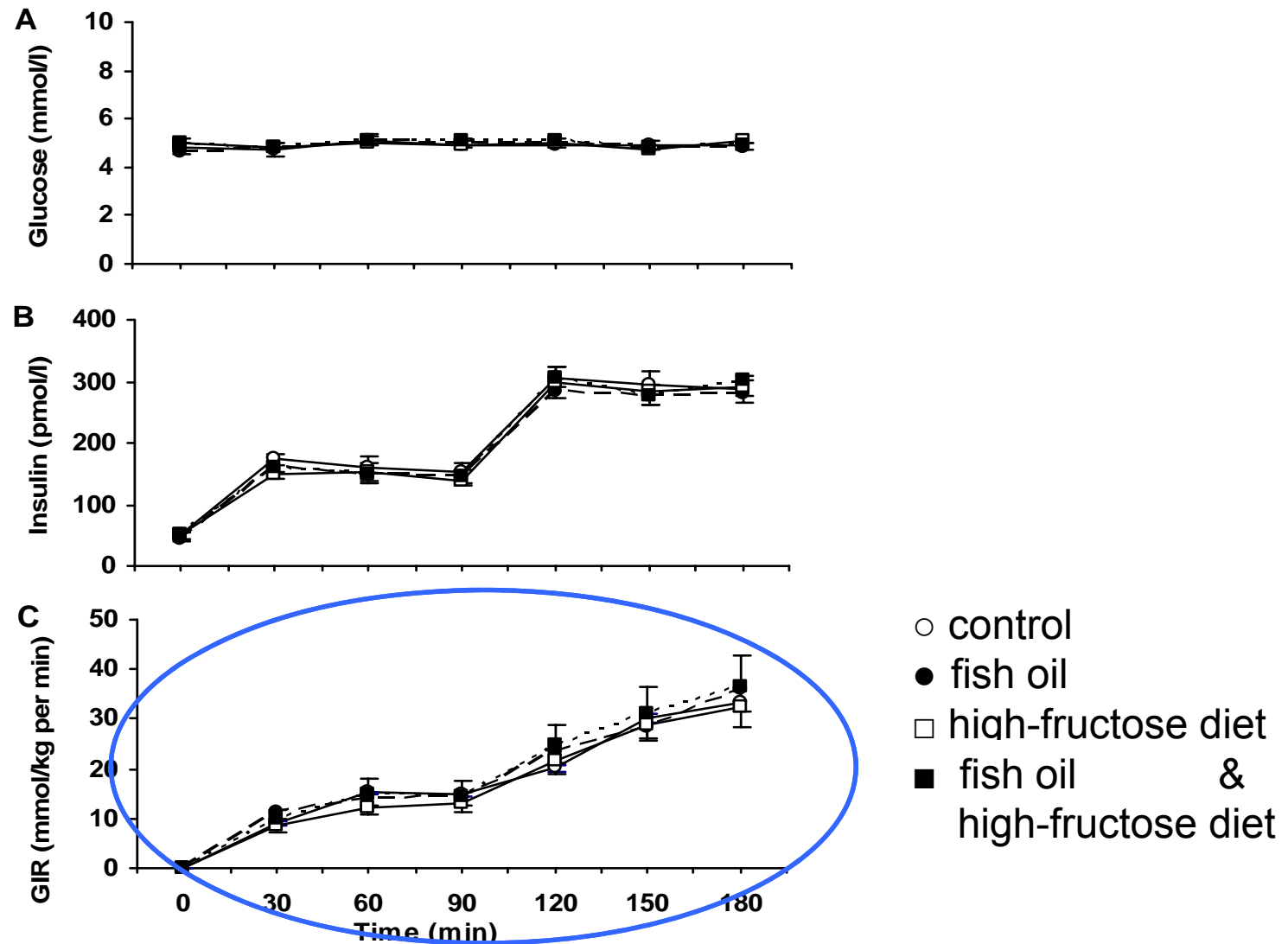
Results (clamp)



Results (clamp)



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)

Further aspects of fructose

- Fructose can lead to increased food intake because unlike glucose, it
 - 1. does not cross the blood-brain barrier
 - 2. does not increase insulin and leptin concentrations and decreases ghrelin

Havel, 2001; Teff, et al., 2004

Further aspects of fructose

- Subjects consuming fructose or sucrose-sweetened beverages did not compensate additional energy intake by those drinks by reducing their energy intake from other sources

Tordoff, et al., 1990; Anderson et al., 1989; Raben et al., 2002

Further aspects of fructose

- Prolonged ad libitum consumption of fructose can increase body weight
- Nurses' Health Study: consumption of larger amounts of soft drinks was associated with greater weight gain and increased risk for diabetes

Tordoff, et al., 1990; Anderson et al., 1989; Schulze et al., 2004

Further aspects of fructose

- Children, who consume more than 265ml of soda /day had a 15% higher energy intake than those who did not consume soft drinks
- For each soda beverage BMI and frequency of Obesity increased in children

Harnack, et al., 1999; Ludwig, et al. 2001

Further aspects of fructose

- Education program aimed to reduce soda intake prevented further weight gain in school children
- A 3-year intervention aimed at reducing soft drink intake lowered fasting insulin levels in students

James, et al., 2004; Ritenbaugh et al., 2003



A scenic view of a lake with mountains in the background. The water is a deep blue with gentle ripples. In the distance, a range of mountains is visible, with the highest peaks covered in snow and bathed in a warm, golden light, suggesting a sunset or sunrise. A small town or village is nestled at the foot of the mountains, and a single sailboat is visible on the water.

Thanks to

- Christine Cayeux**
- Françoise Secrétan**
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- Philippe Schneider**

- <http://www.nutriconsult.ch/fructose.pdf>