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

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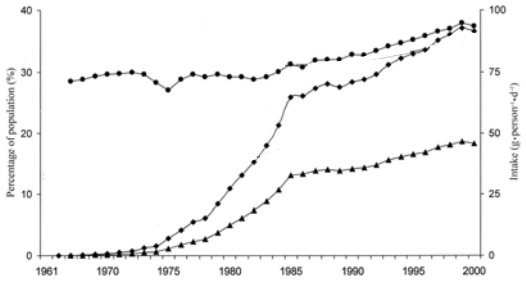
Introduction



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

Bray et al, 2004

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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

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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

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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)

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Subjects

Seven healthy men

- Mean age: **24.7** ± **1.3** years
- Mean BMI: **22.0** ± **0.75** kg/m^2
- Mean body fat: **16.5** ± **0.7** %
- Mean waist circ.: **80** ± **2.9** cm

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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**

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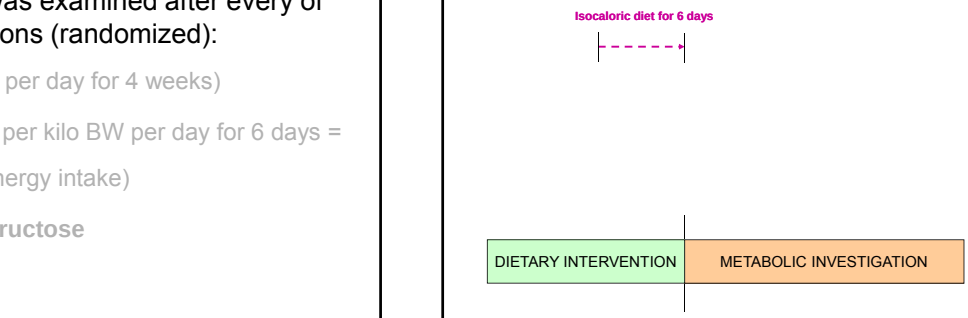
Study design



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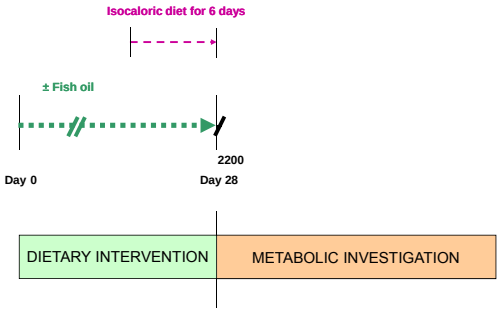

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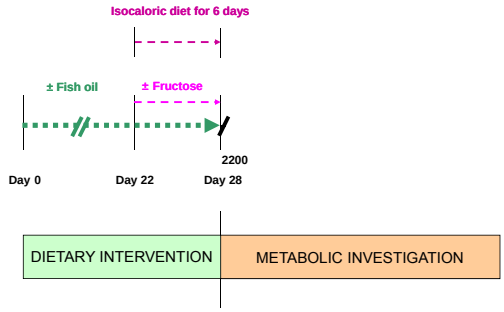

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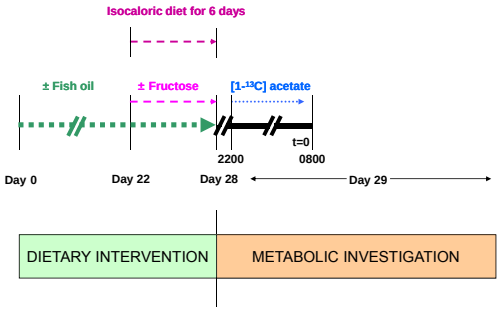

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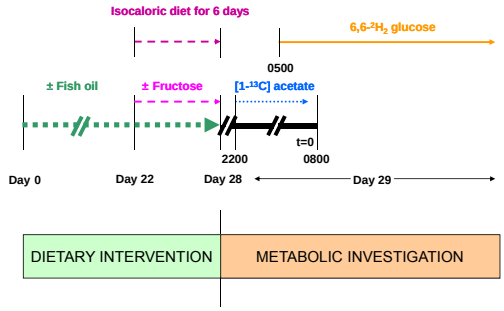

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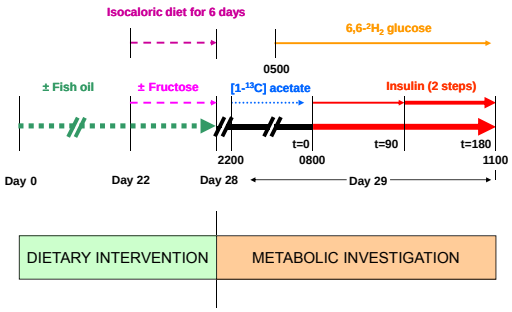

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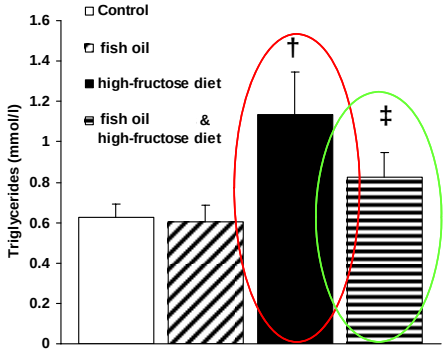
Results (fasting)



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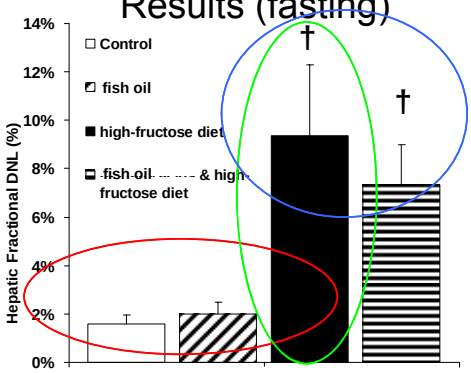

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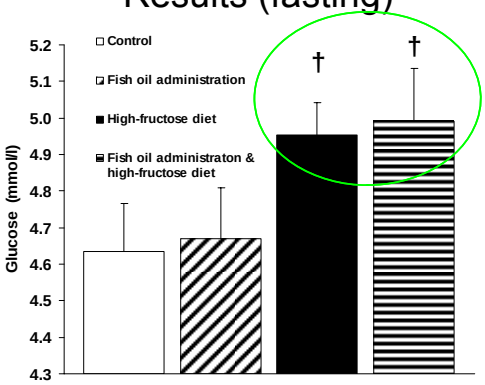

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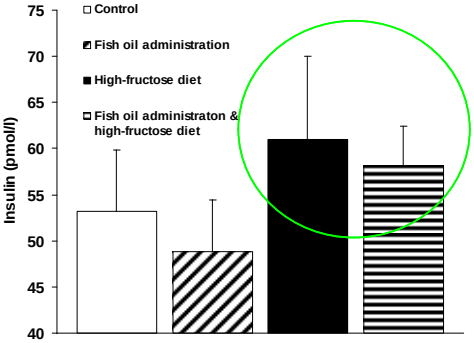

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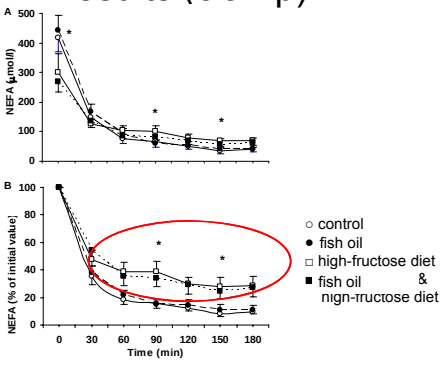
Results (clamp)



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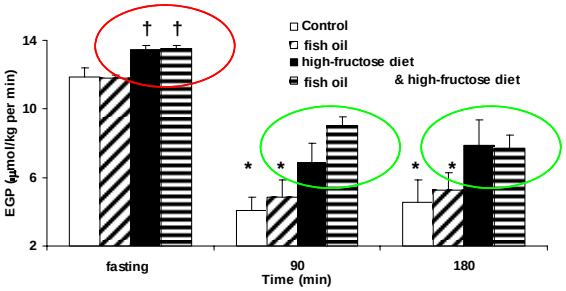

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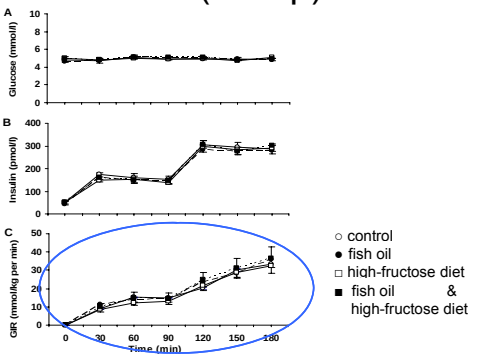

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Conclusion

- 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

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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

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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)