

Glucose et insuline

Rôle des incrétines

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Contexte

- Glucose oral vs parentéral
- Support entéral vs parentéral
- Désordres métaboliques: hyperglycémie, hypertriglycéridémie, stéatose hépatique
- Efficacité de la renutrition: contexte inflammatoire, cycles futiles métaboliques



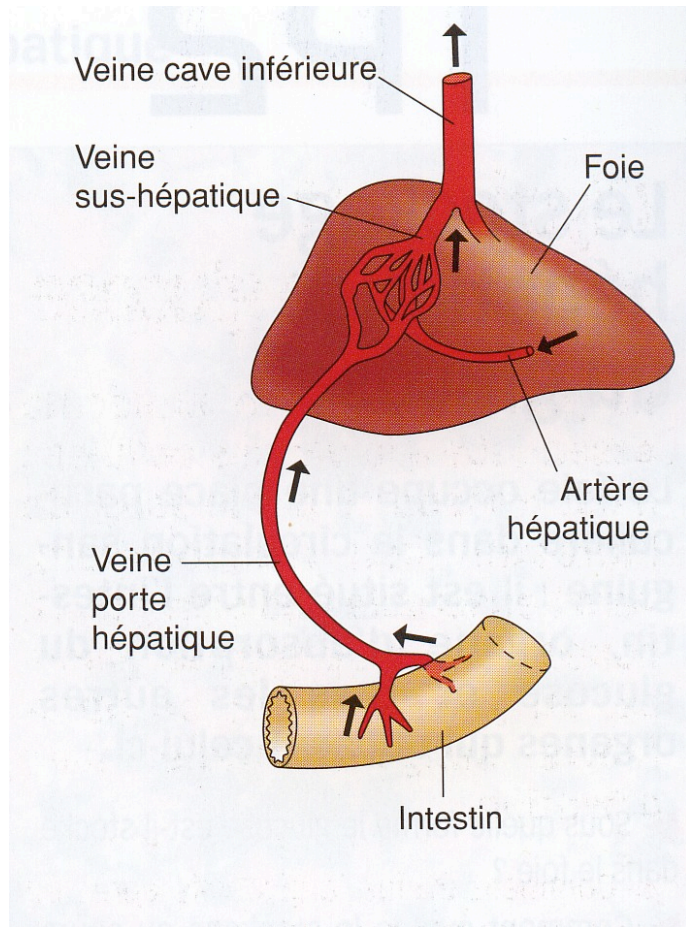
INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.Sc., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., PH.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.

Conclusions Intensive insulin therapy to maintain blood glucose at or below 110 mg per deciliter reduces morbidity and mortality among critically ill patients in the surgical intensive care unit. (N Engl J Med 2001;345:1359-67.)

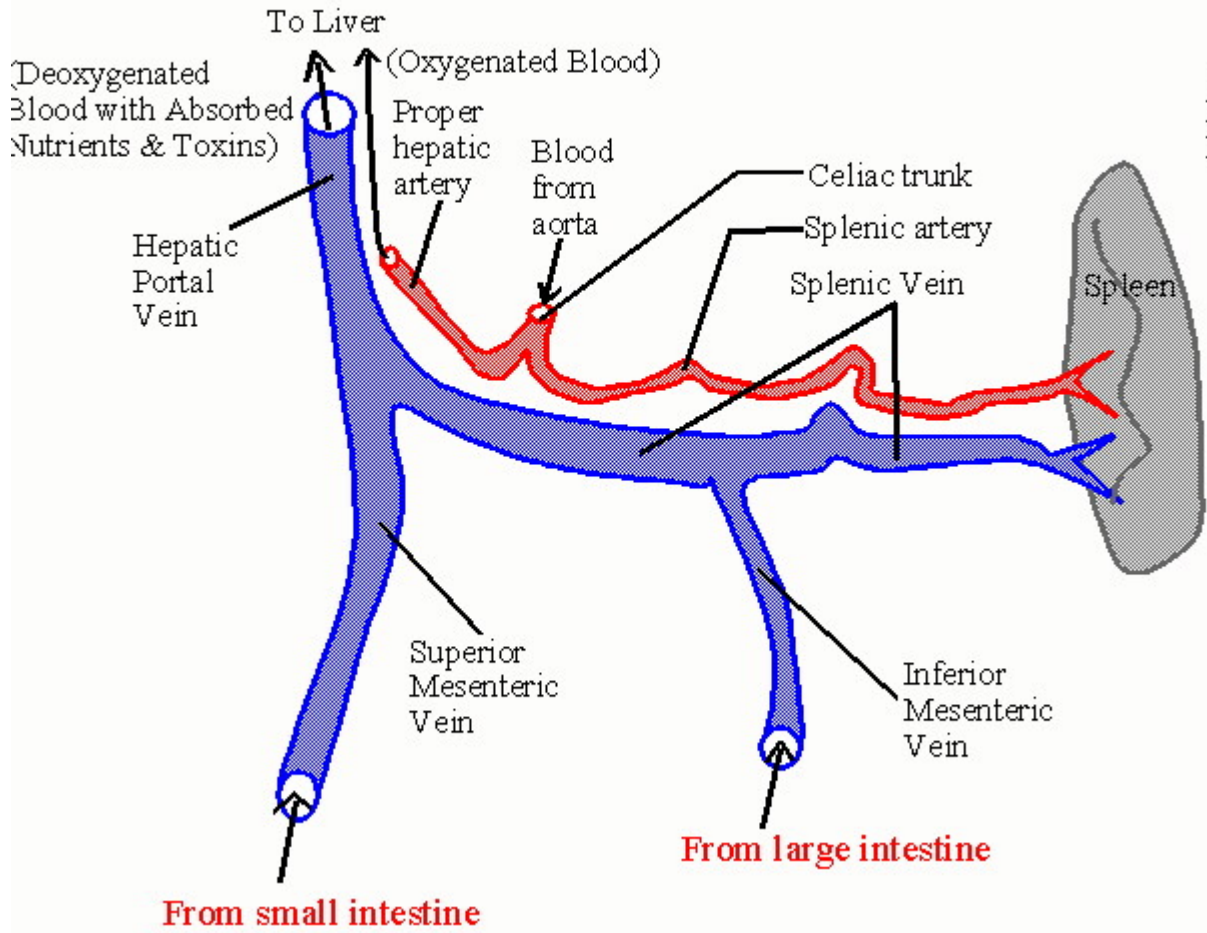
Insuline portale vs insuline périphérique

Méthodes



Comment explorer la voie portale ?

Major Vessels of the Hepatic Portal System

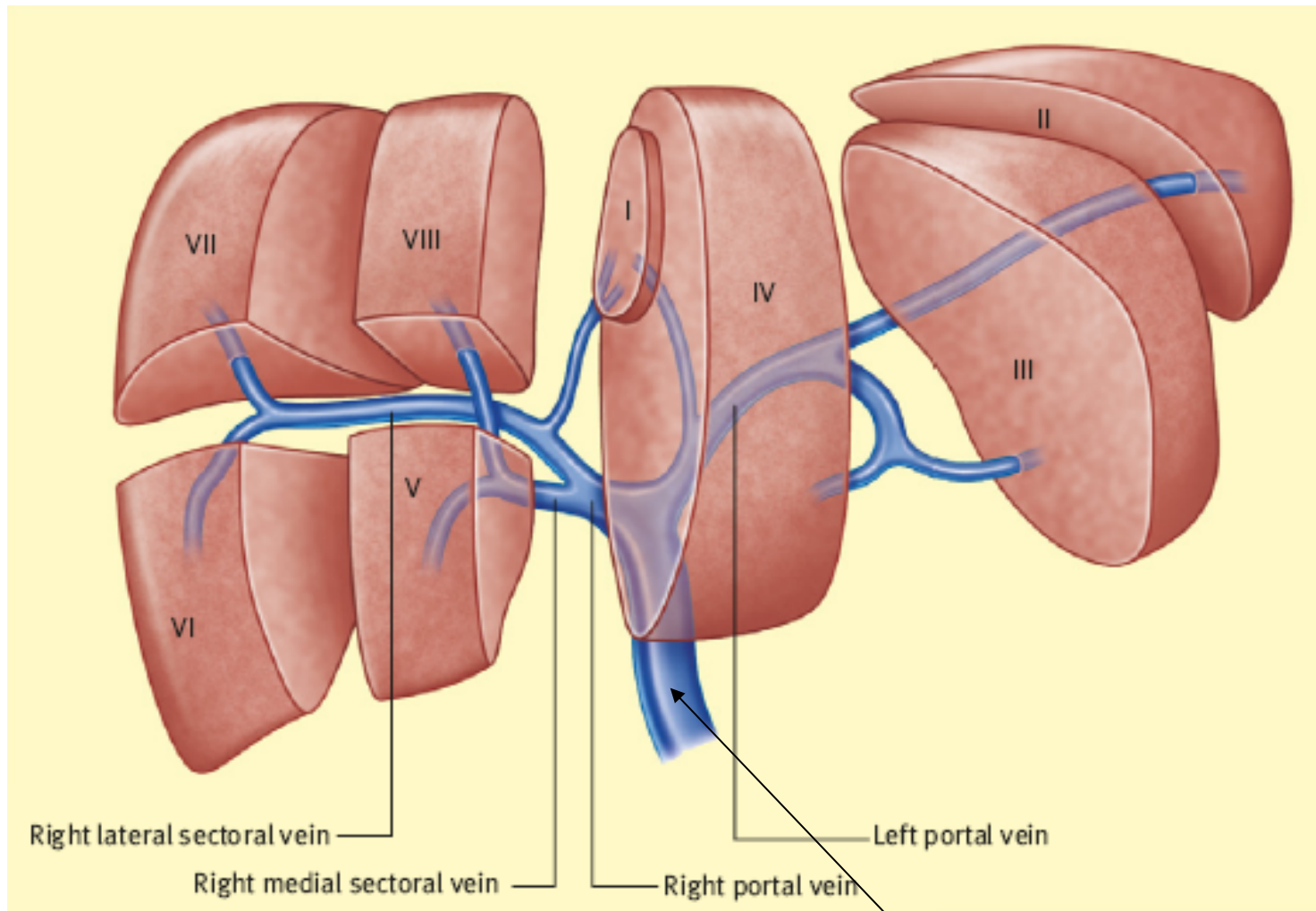




Ellis H, Surgery 2011

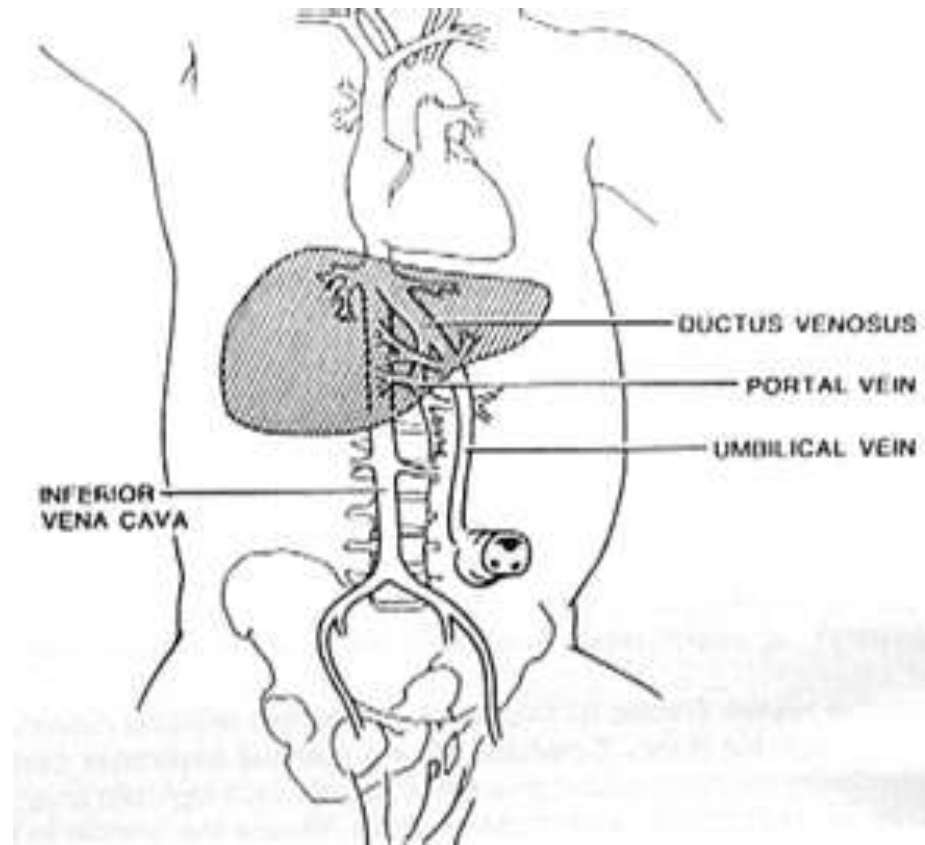
Méthodes

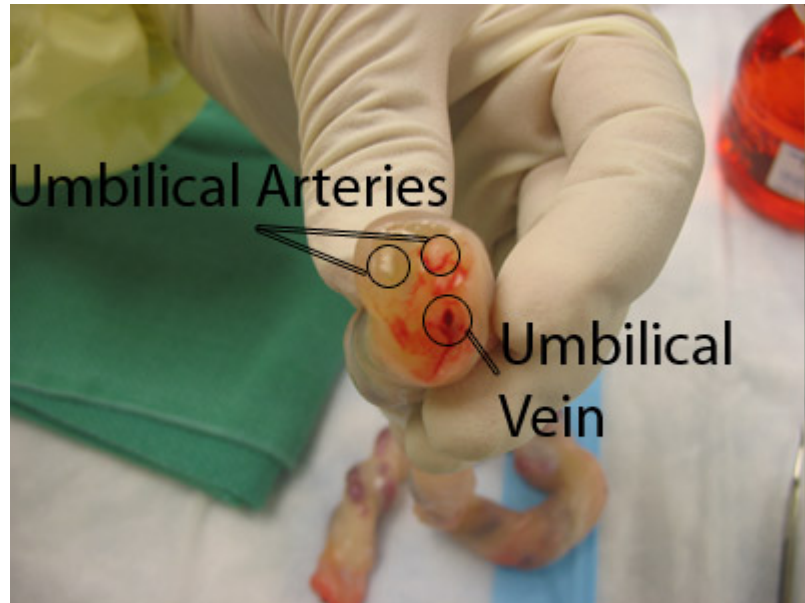
- **Modèles animaux:**
 - Ponction veine porte
 - Perfusion veine porte
 - Dénervation de la veine porte
- **Homme:**
 - Ponction de la veine porte
 - Chimiothérapie
 - Greffe d' îlots
 - Sulfamides hypoglycémiants
 - Voie péritonéale
 - Reperméabiliser la veine ombilicale



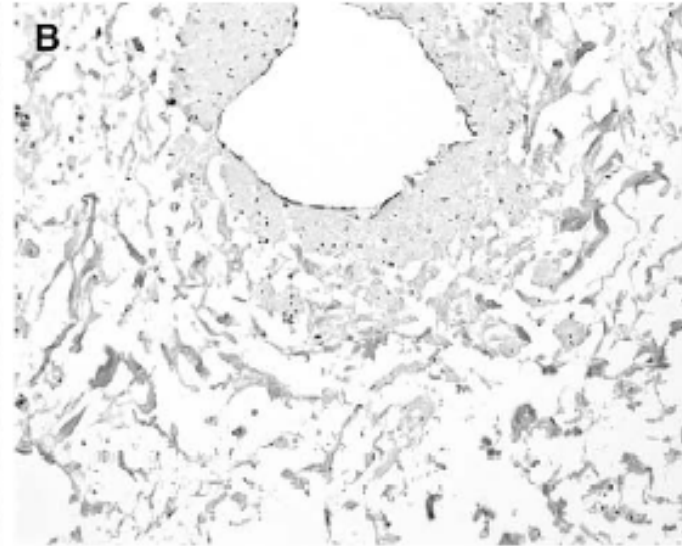
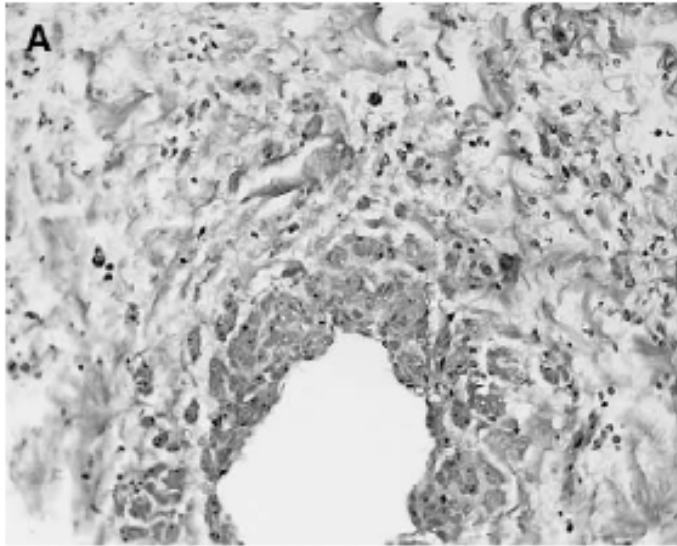
Ponction

Anat veine ombilicale









Insuline portale vs insuline périphérique

Comparison of peripheral and portal (via the umbilical vein) routes of insulin infusion in IDDM patients.

Shishko PI, Kovalev PA, **Goncharov** VG, Zajarny IU. Diabetes. 1992 Sep;41(9):1042-9.

J Clin Endocrinol Metab. 1993 Sep;77(3):738-42.

Peritoneal and subcutaneous absorption of insulin in type I diabetic subjects.

Giacca A, Caumo A, Galimberti G, Petrella G, Librenti MC, Scavini M, Pozza G, Micossi P.

Comparison of the action of insulin according to its administration by the portal route or the humeral vein.

Gilsanz V, **Merino C, Barrio E**, Sánchez Creus P.
Rev Clin Esp. **1968** Aug 15;110(3):203-10.

Administration portale d'insuline:

Meilleur contrôle glycémique
Meilleure freination du glucagon
Meilleur contrôle de la PHG

Insuline portale vs insuline périphérique

Pour les mêmes effets de l'administration portale d'insuline:

plus fortes doses d'insuline périphérique
tous les DT1 sont sur-insulinés
certains DT2 nécessitent de fortes doses d'insuline SC

Conséquences:

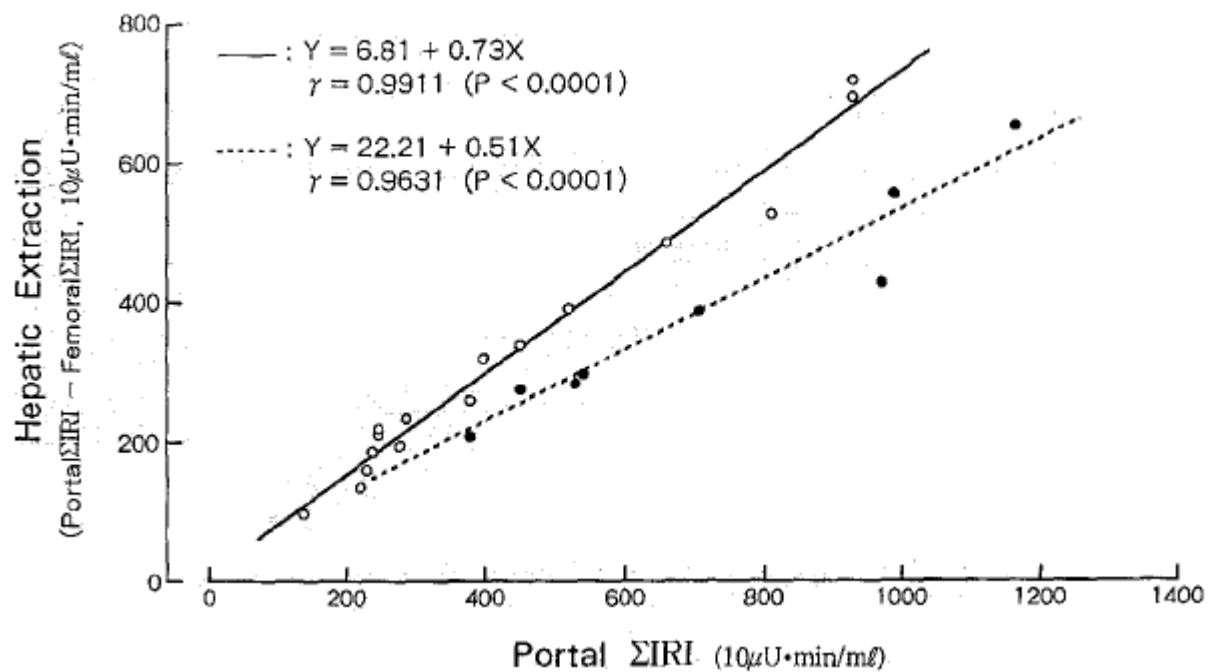
développement d'insuline à tropisme hépatique

développement des pompes implantables
utilisation de la voie péritonéale

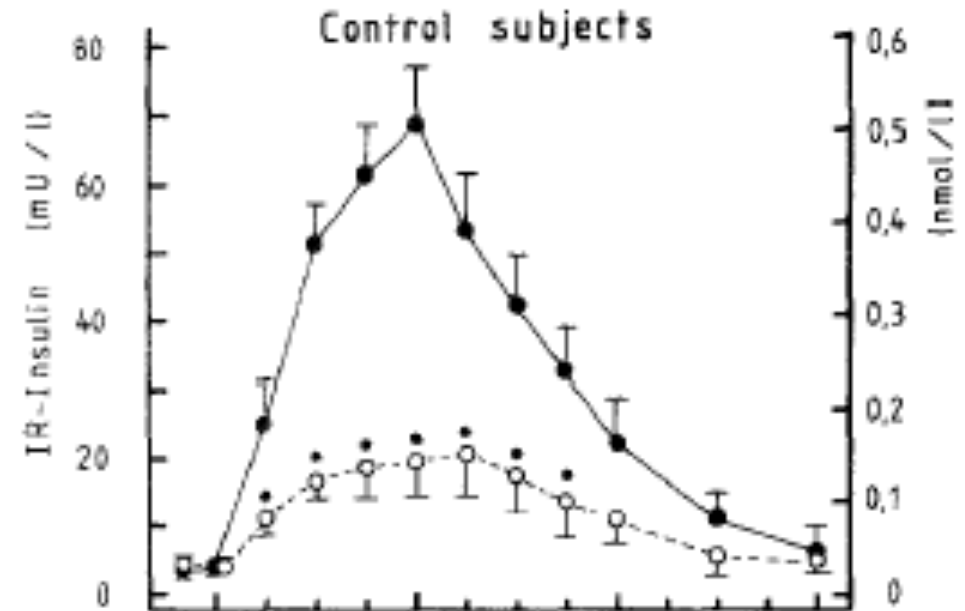
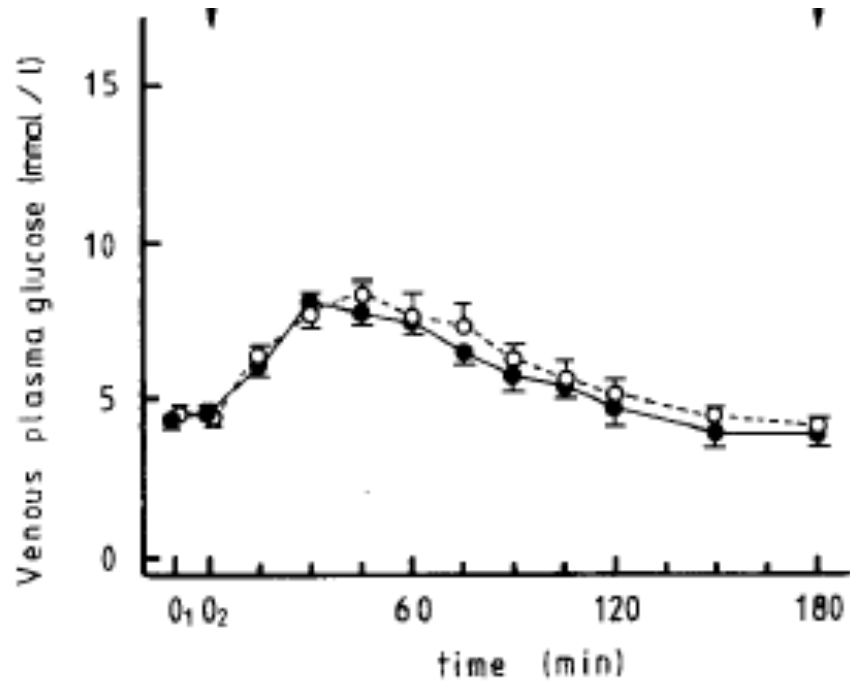
pulsatilité de la sécrétion d'insuline

phase précoce de la sécrétion d'insuline +++

Fig. 2. Correlation between portal Σ IRI and hepatic insulin extraction (portal Σ IRI minus femoral Σ IRI).
 ○, Group A; ●, group B. Solid line, regression line for group A; dotted line, regression line for group B.

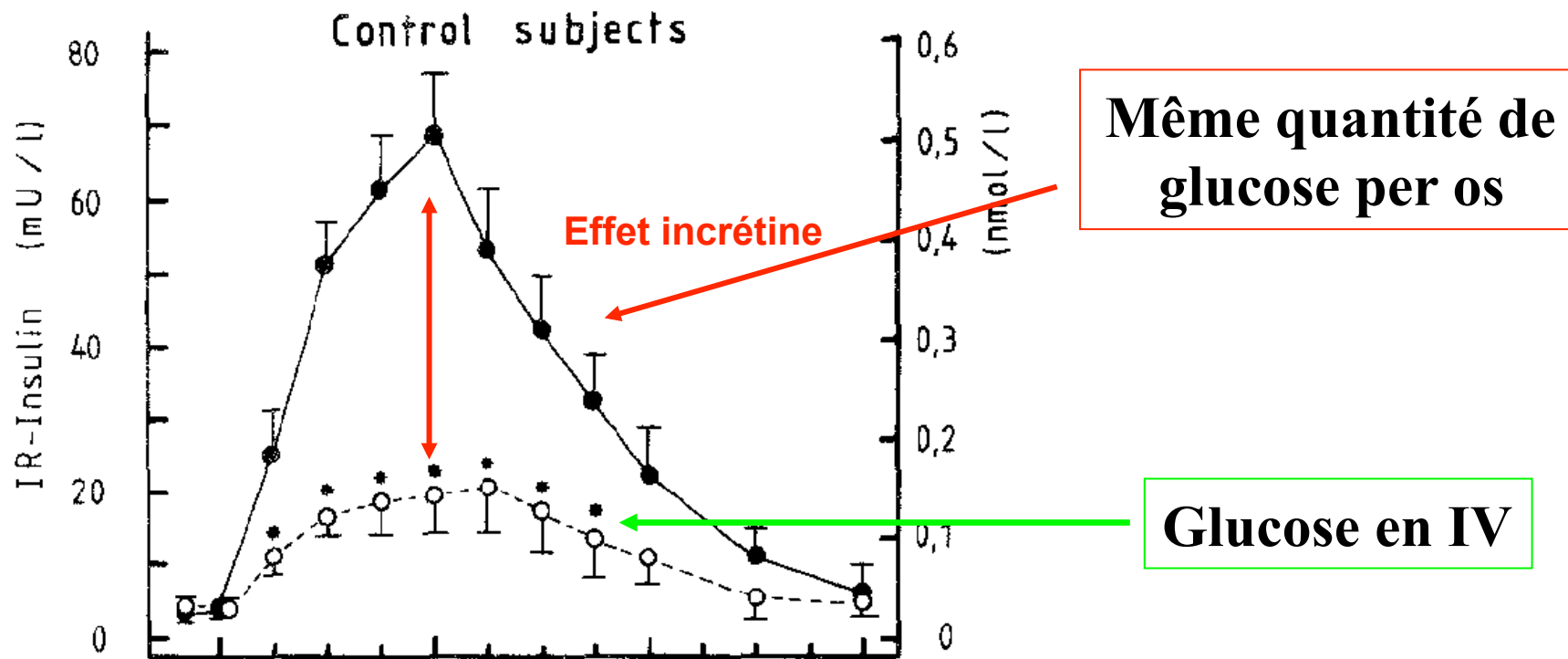


Modes d'administration du glucose



Nauck M et al, Diabetologia 1986.

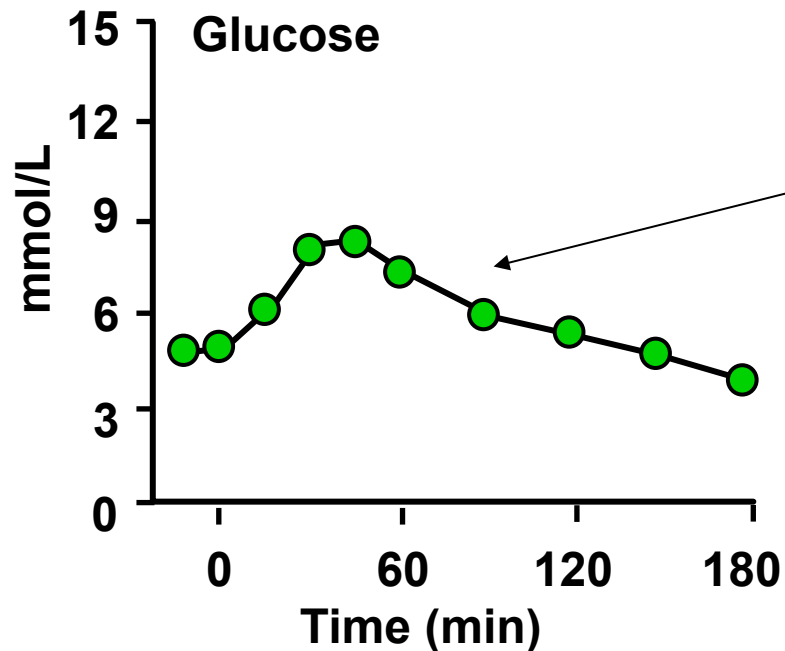
La démonstration de l'effet incrétine



Le glucose per os stimule plus fortement l'insulinosécrétion qu'en IV

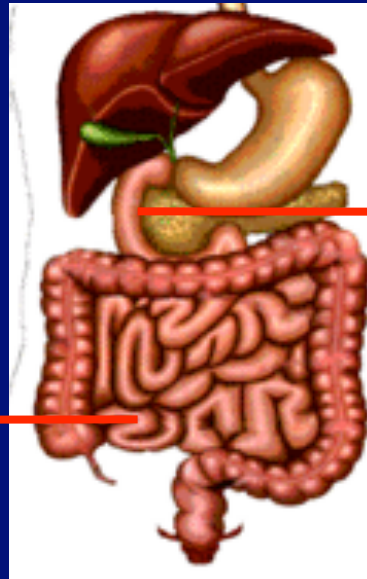
Nauck M et al, Diabetologia 1986.

Rôle essentiel du couple Foie / glucagon



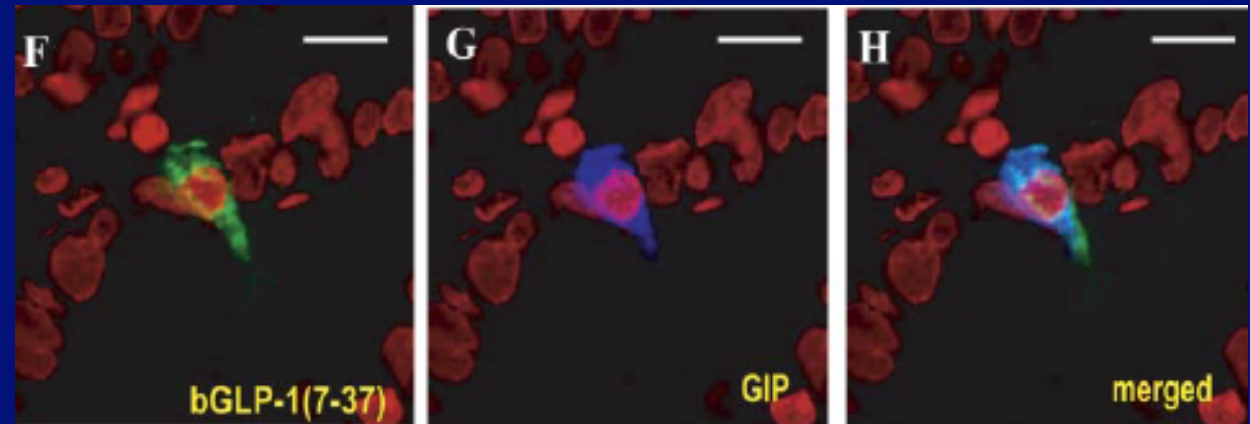
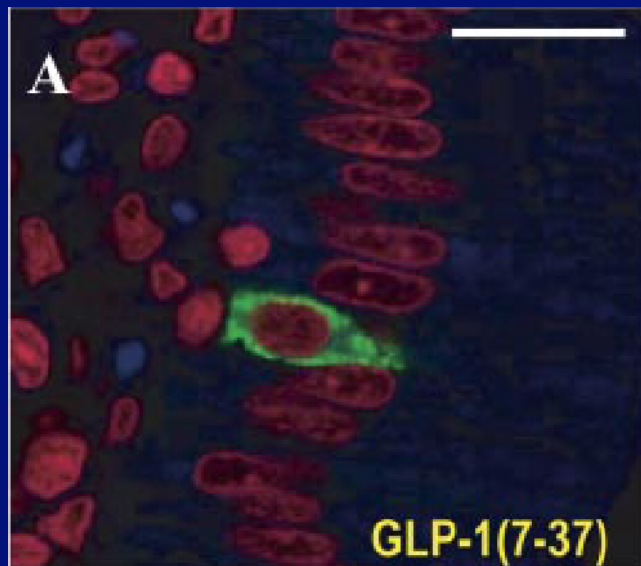
Les 60% de contrôle de la glycémie post-prandiales sont liés à:

- la freination de la PHG
- la freination du glucagon



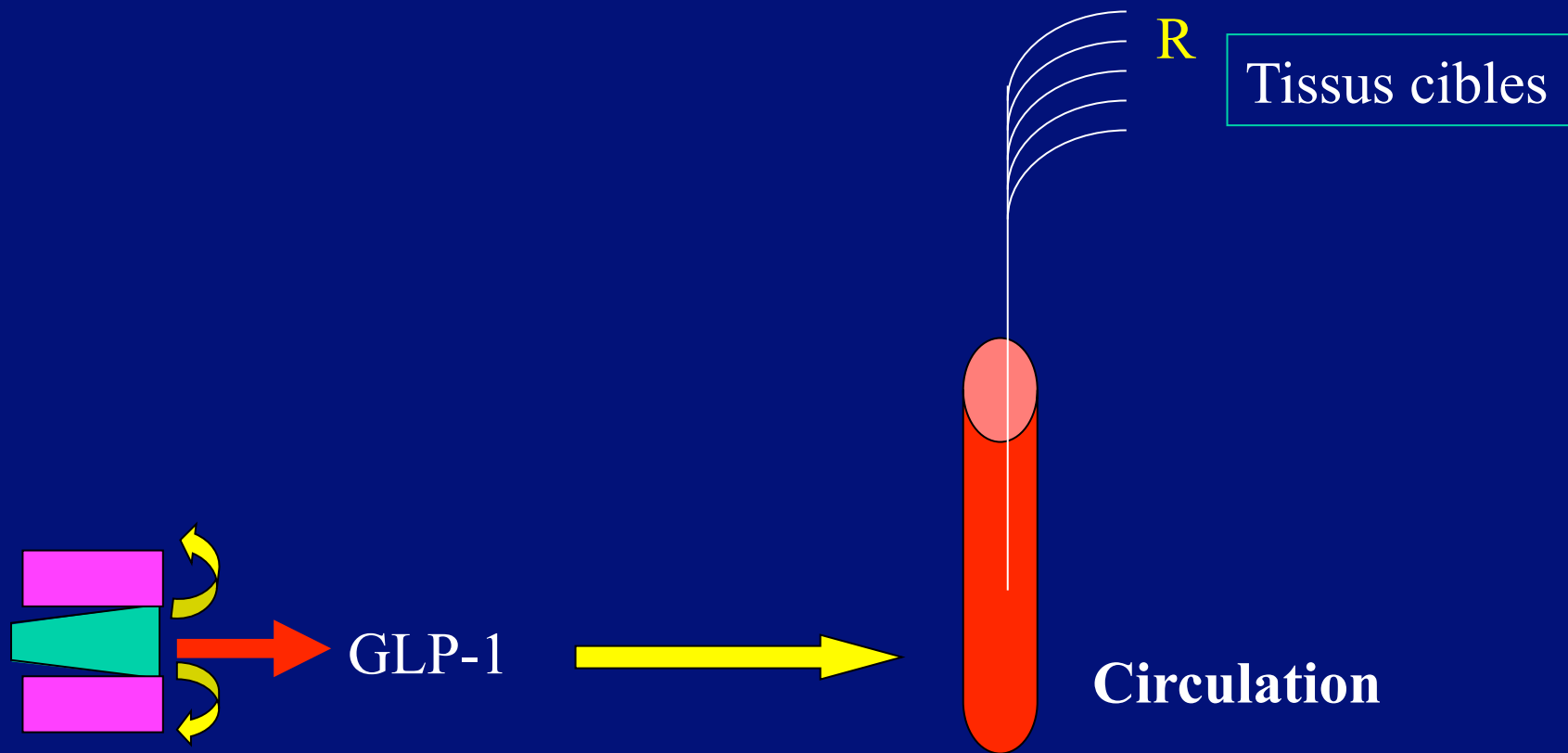
Cellules K du duodénum
et du jéjunum : GIP

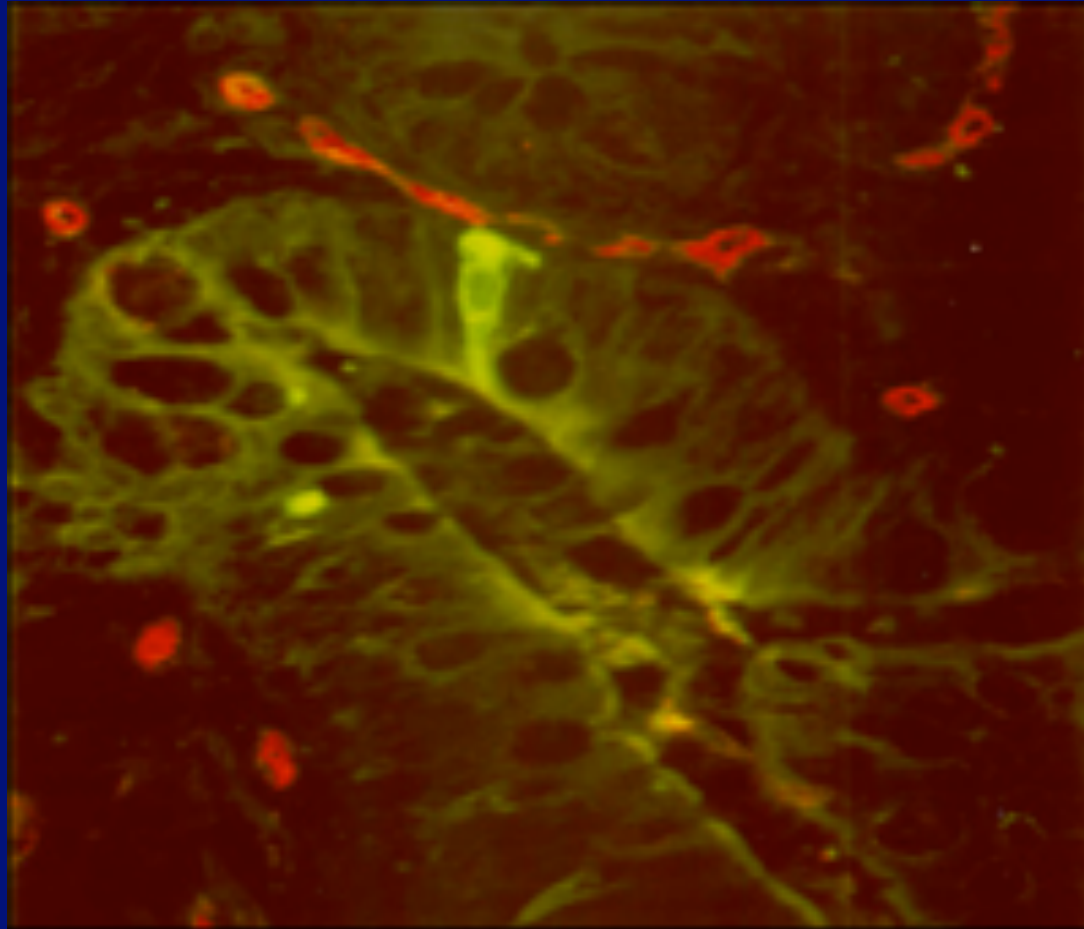
Cellules
L de
l' iléon
distal :
GLP-1



Theodorakis MJ et al, Am J Physiol 2006

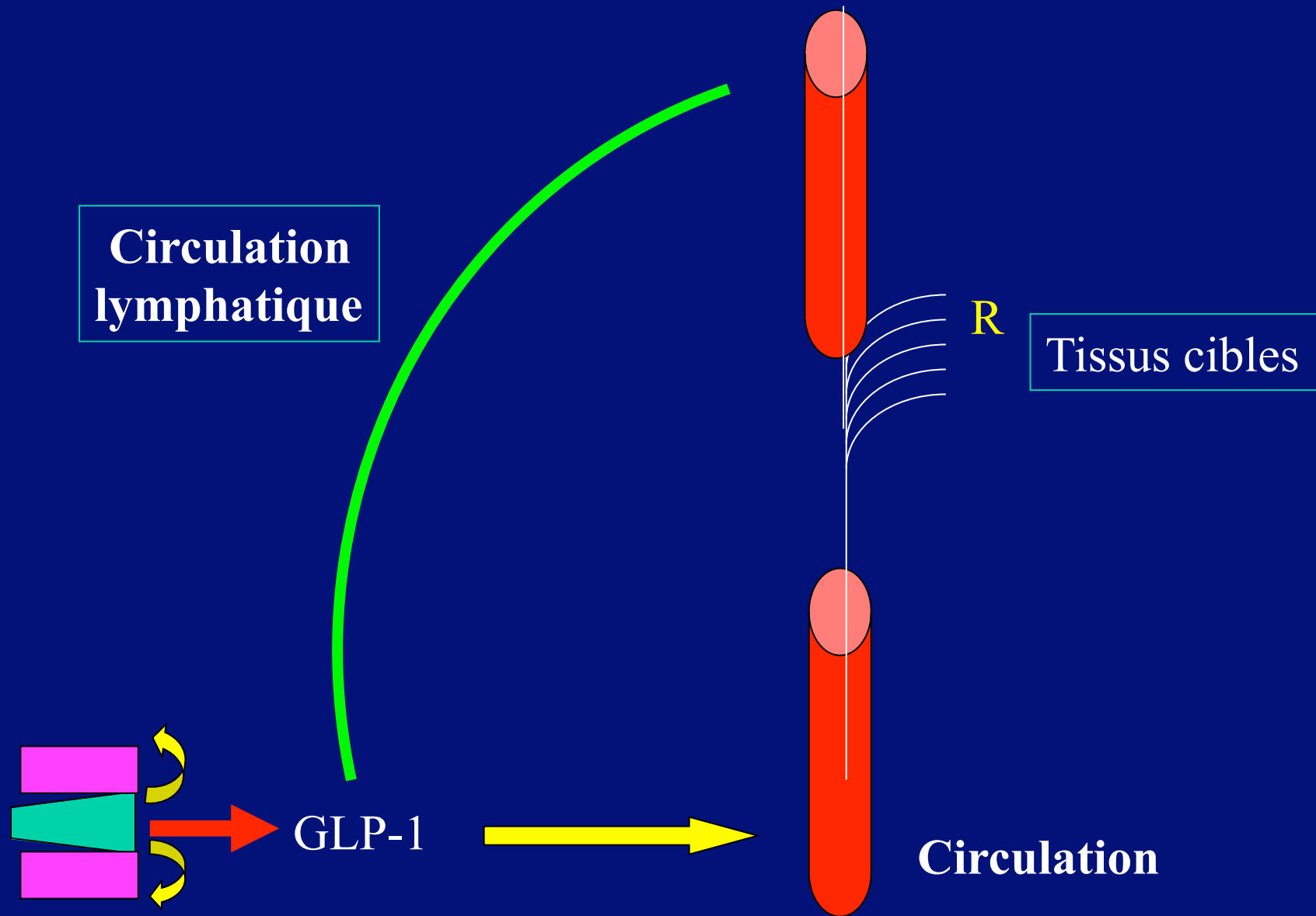
Diffusion directe du GLP-1 vers la circulation



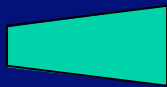
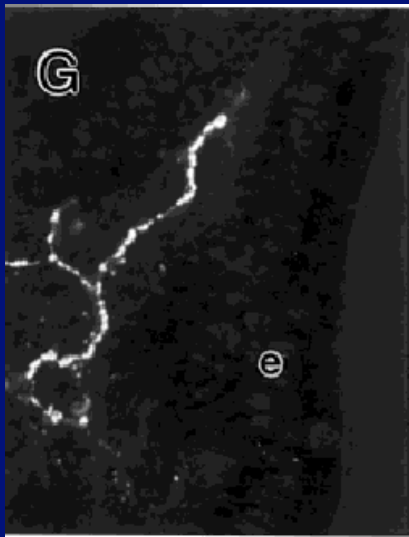
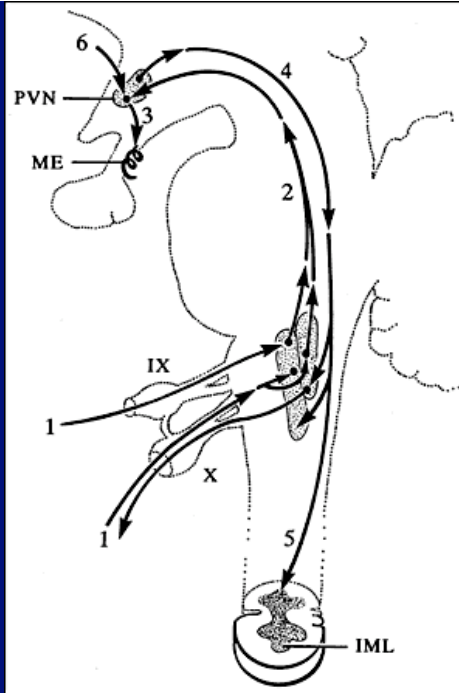


When GLP-1 (green) is released into the intestinal capillaries, it is immediately exposed to DPP-4 (red)

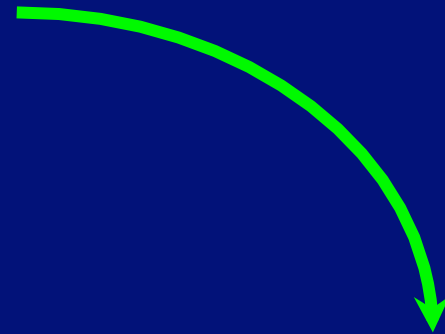
Diffusion indirecte du GLP-1 via la lymphe



GLP-1 en tant que neurotransmetteur

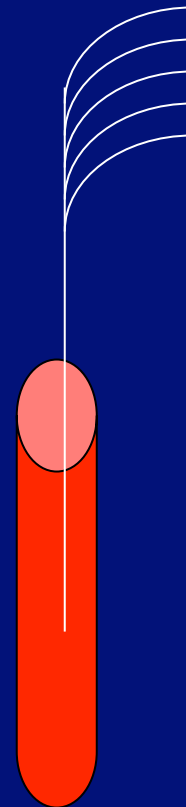


GLP-1



R

Tissus cibles



Facteurs régulant la sécrétion de GLP-1

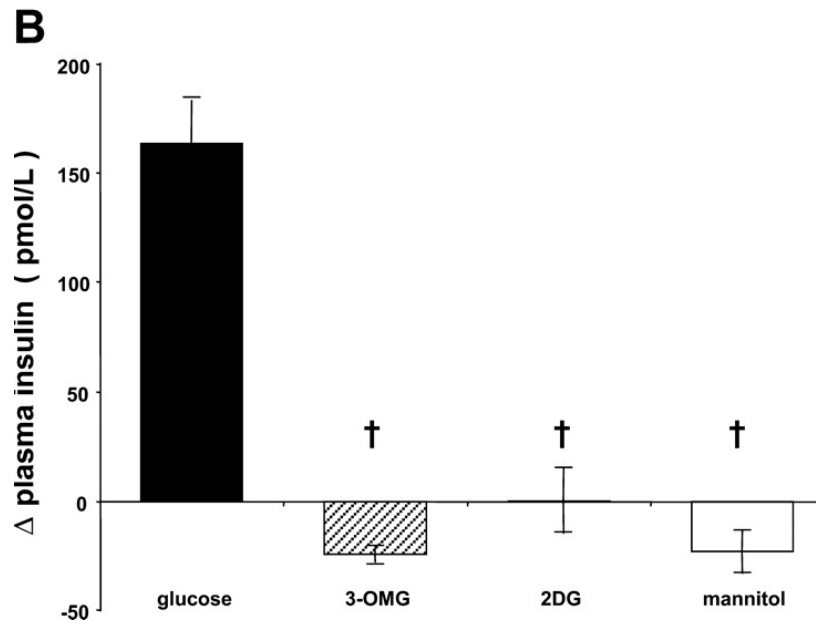
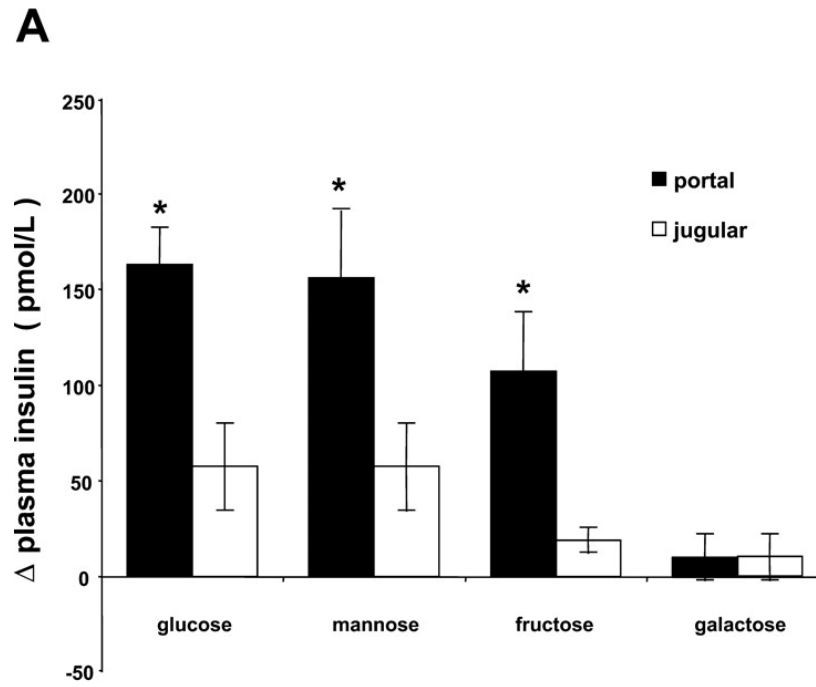
-sécrétion stimulée par

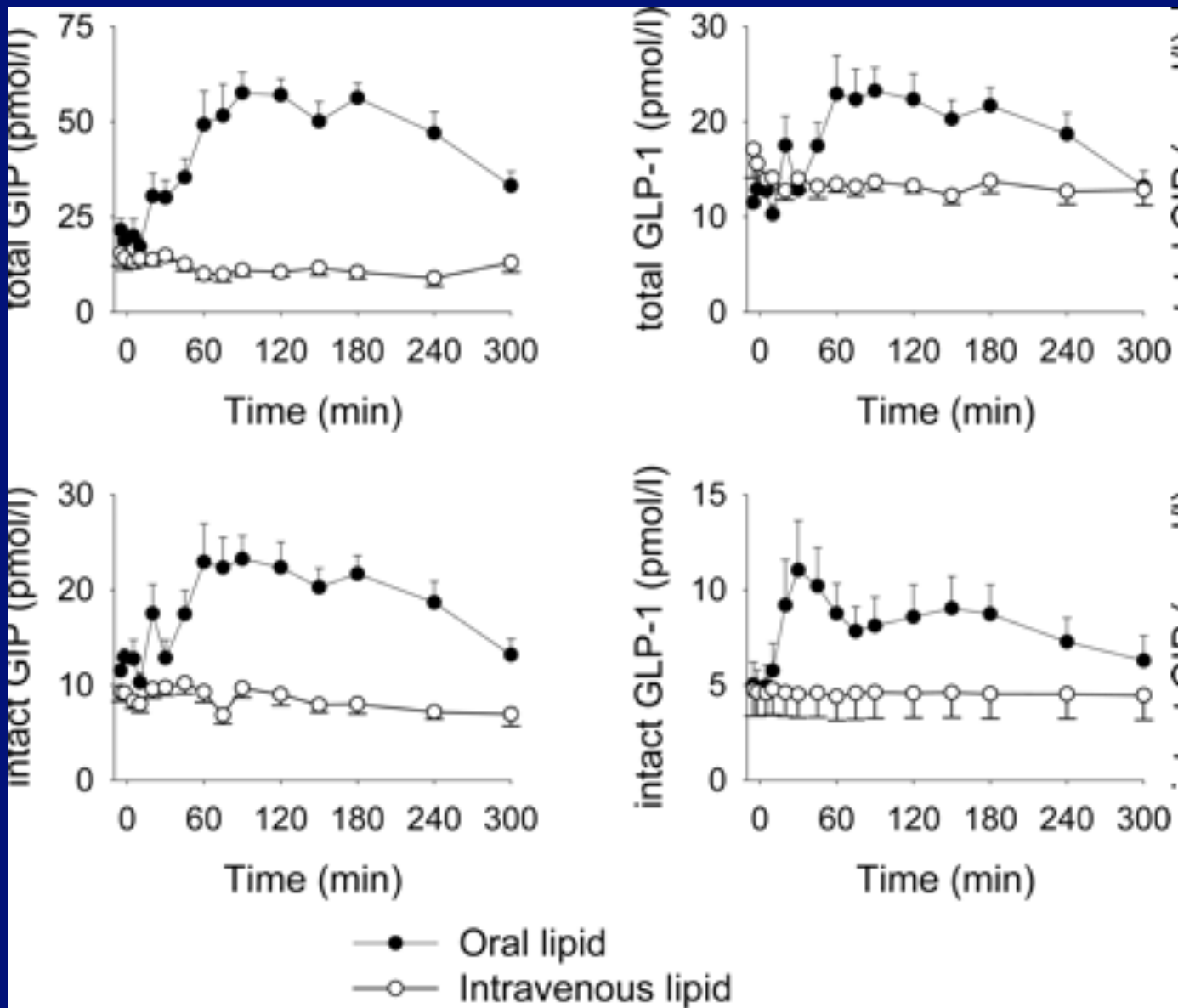
- glucides
- lipides
- régime riche en oligofructose
- chirurgie de by-pass gastrique

-sécrétion réduite par

- régime gras
- restriction calorique

Fukaya M et al, AJP 2007

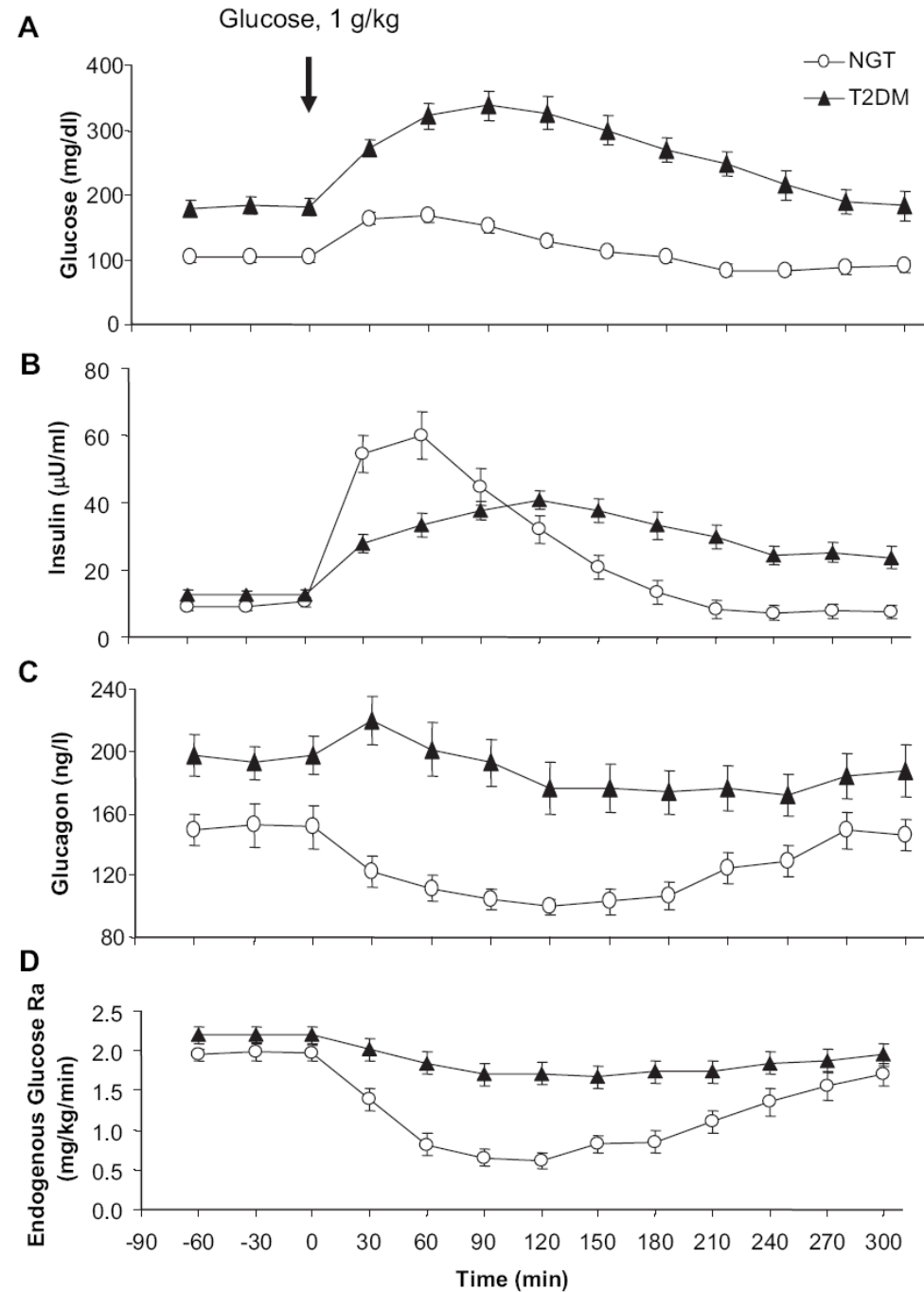




Lindgren O et al, JCEM 2011

Hyperglucagonémie du patient DT2

Dunning BE et al,
Endocrine Rev, 2007

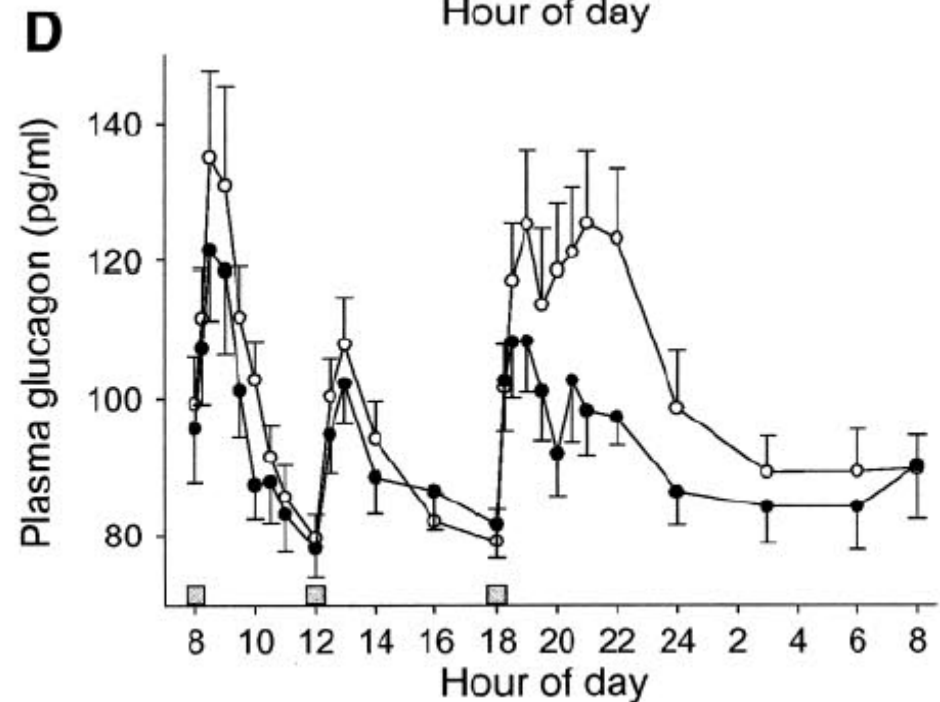
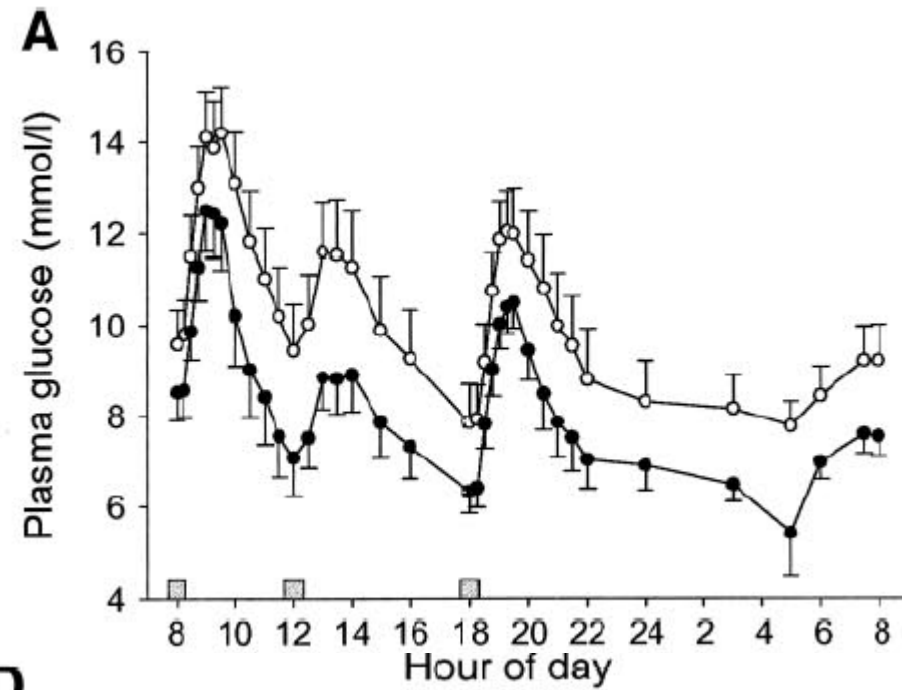


Actions du GLP-1 sur la cellule α

-réduction de la sécrétion de glucagon

*par voie directe

*par voie indirecte (via l'insuline)



Degn KB et al, Diabetes 2004

Glucose oral



incrétines



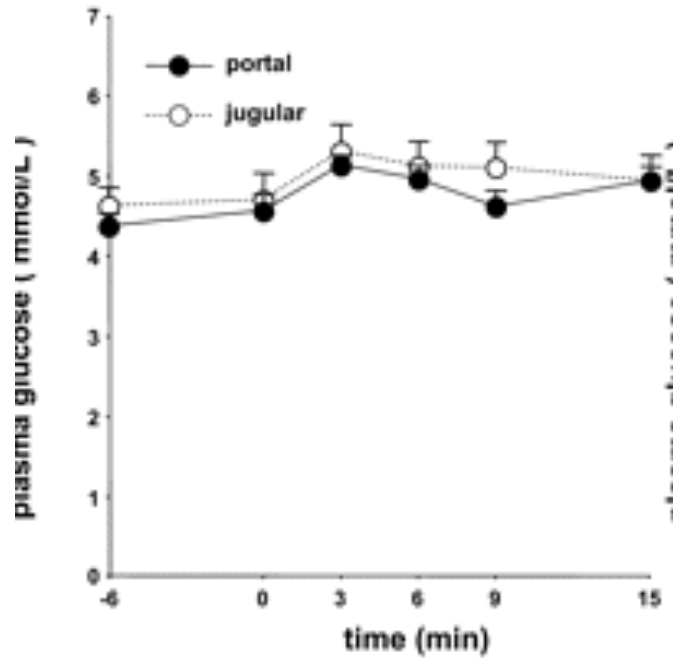
Stimule l'insulinosécrétion endogène
Contrôle le glucagon



Meilleur contrôle de la PHG



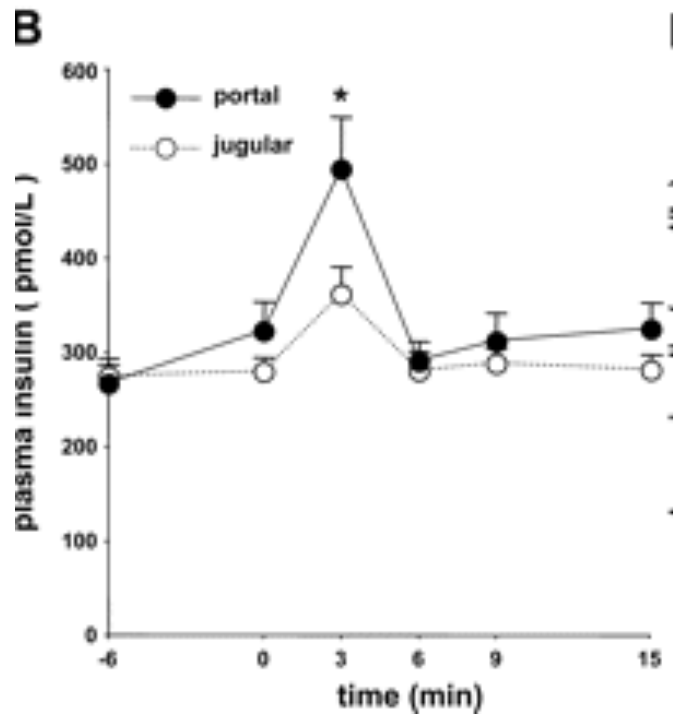
Statut métabolique préservé



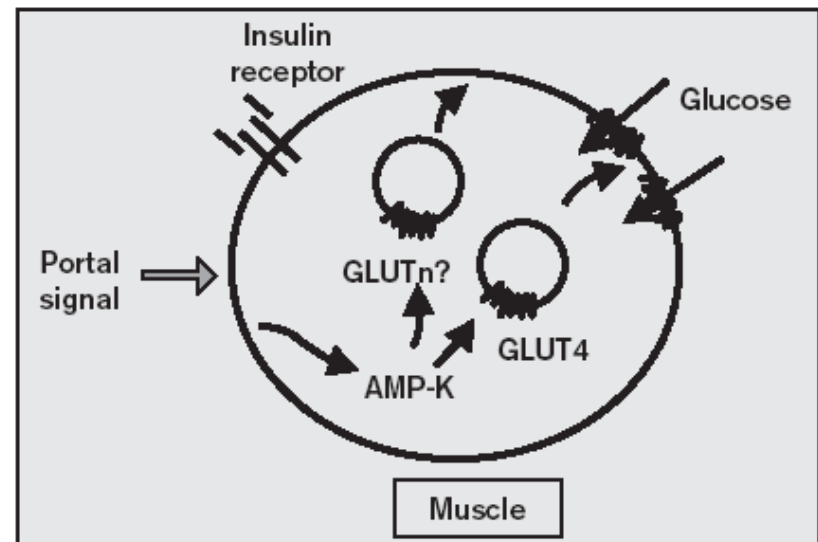
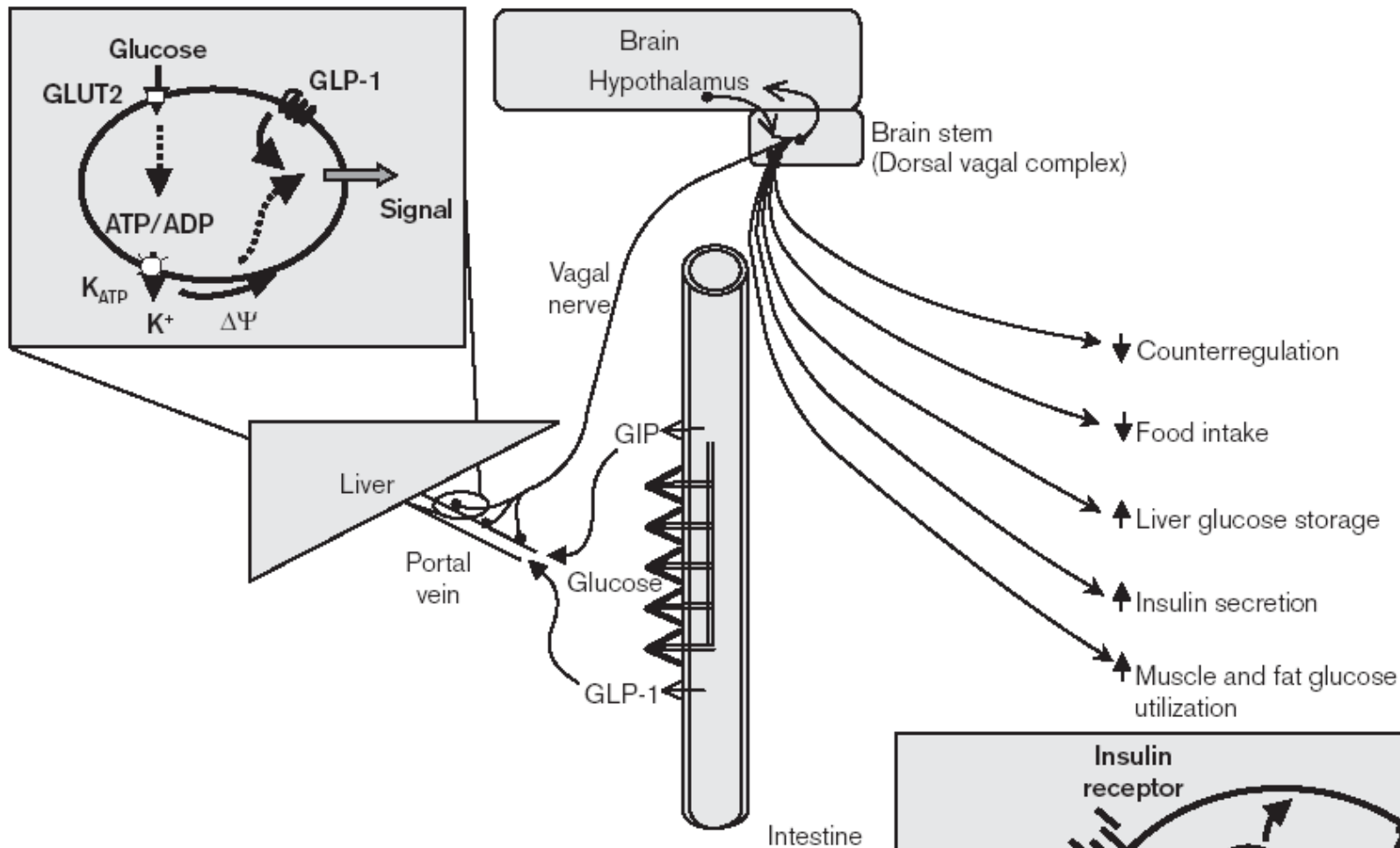
The Cephalic Insulin Response to Meal Ingestion in Humans Is Dependent on Both Cholinergic and Noncholinergic Mechanisms and Is Important for Postprandial Glycemia

Bo Ahrén¹ and Jens J. Holst²

Diabetes 2001

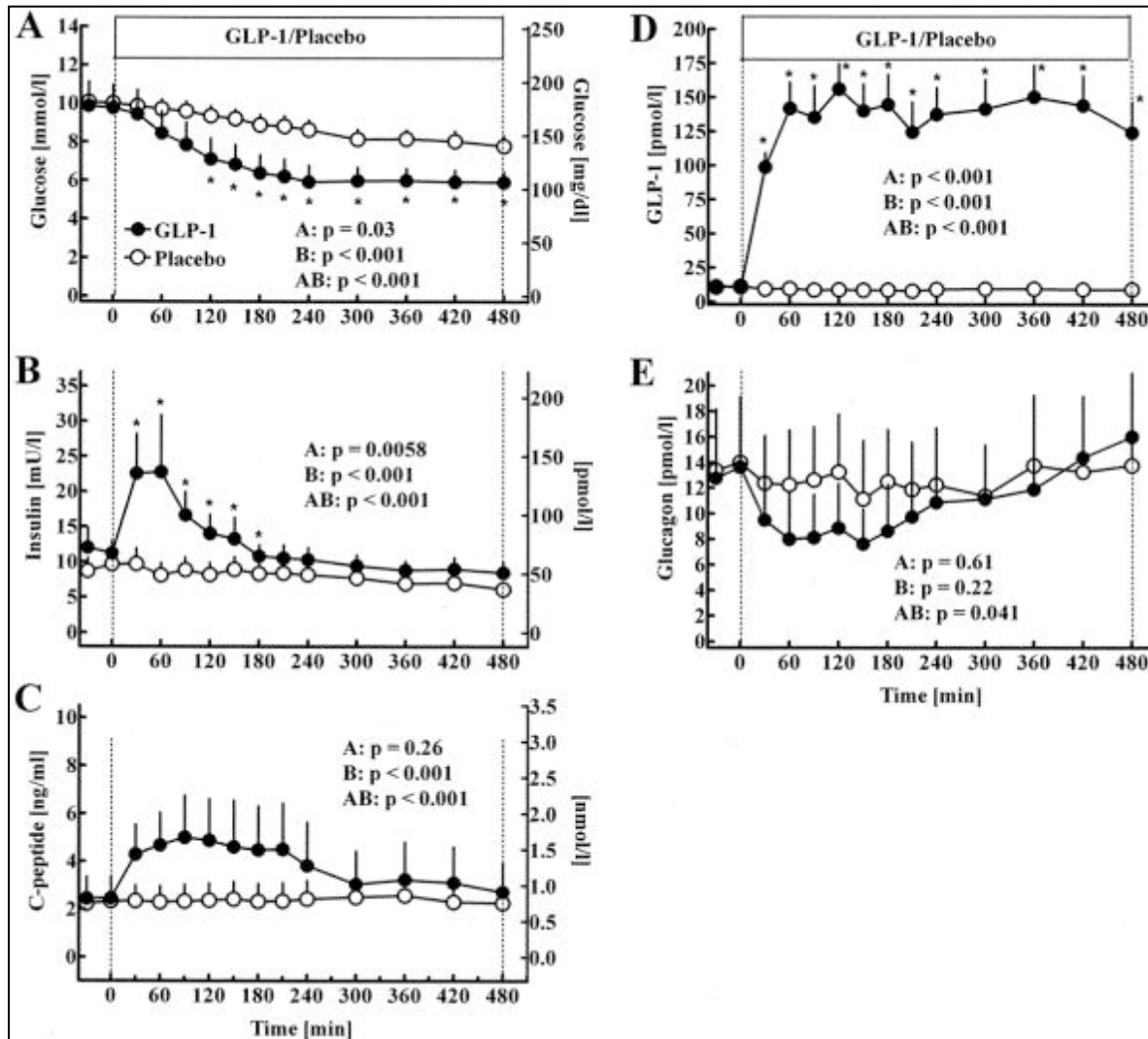


Fukaya M et al, AJP 2007



Thorens B, 2004

Figure 1.

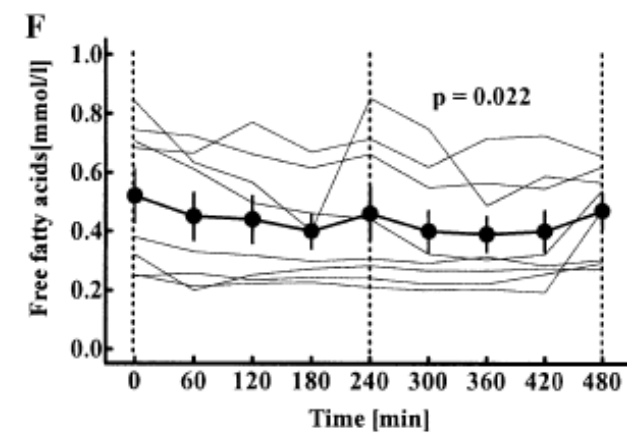
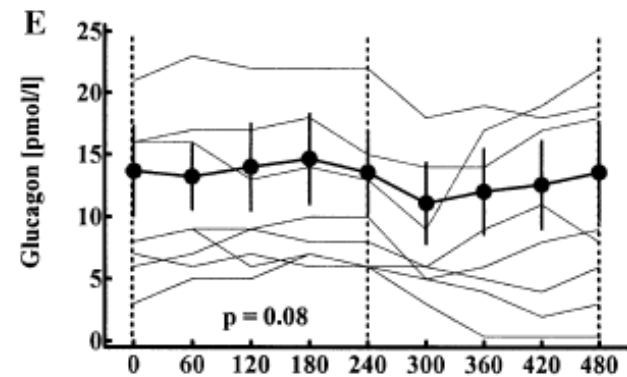
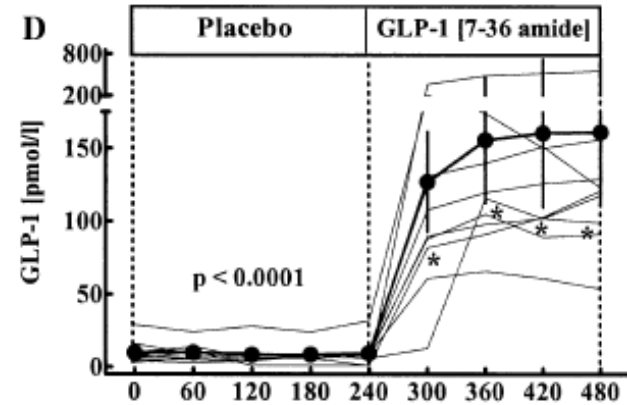
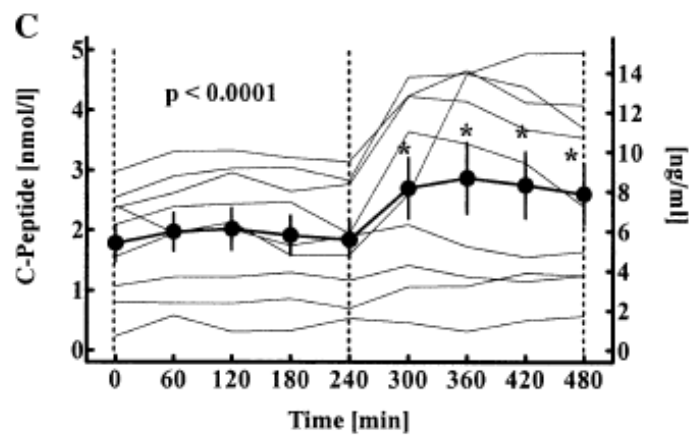
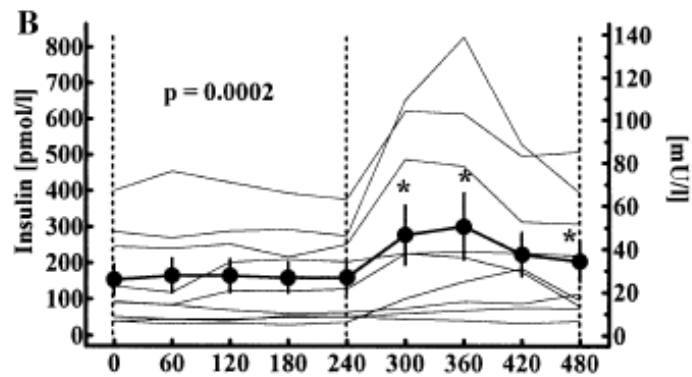
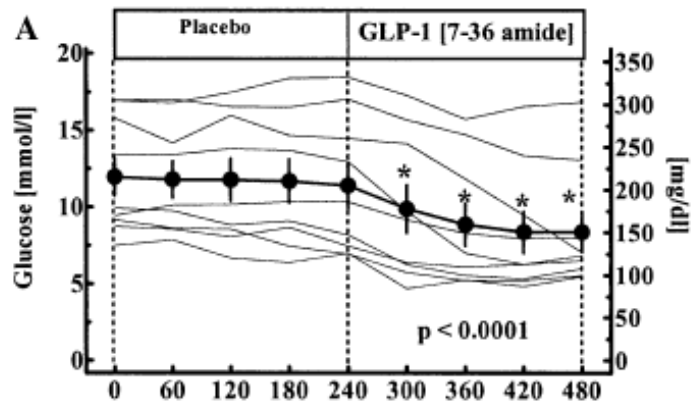


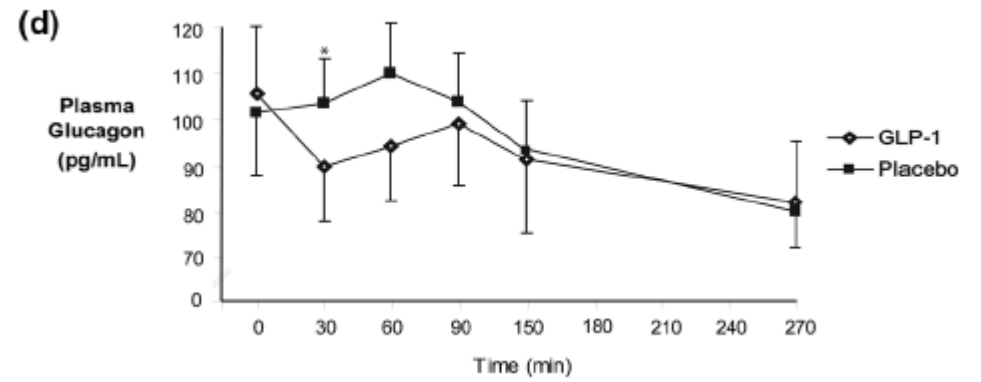
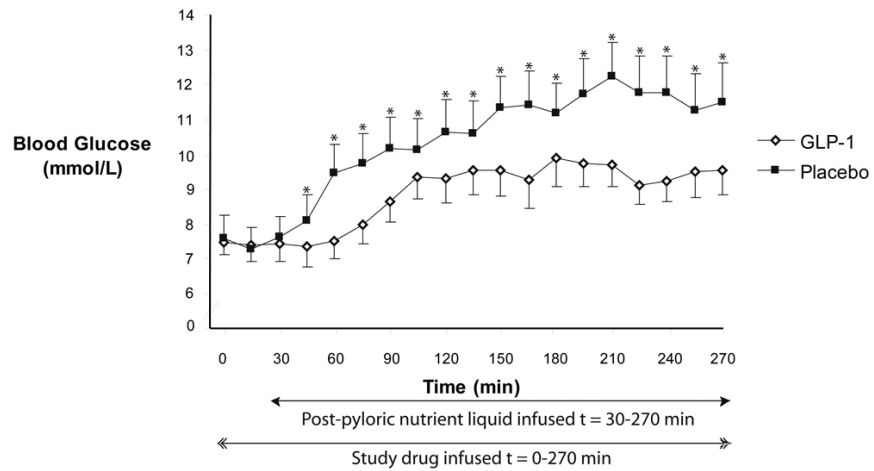
Intravenous glucagon-like peptide 1 normalizes blood glucose after major surgery in patients with type 2 diabetes.

Meier, Juris; Weyhe, Dirk; Michaely, Mark; Senkal, Metin; MD, PhD; Zumtobel, Volker; MD, PhD; Nauck, Michael; MD, PhD; Holst, Jens; MD, PhD; Schmidt, Wolfgang; MD, PhD; Gallwitz, Baptist; MD, PhD

Critical Care Medicine. 32(3):848-851, March 2004.
DOI: 10.1097/01.CCM.0000114811.60629.B5

Figure 1. Plasma concentrations of glucose (A), insulin (B), C-peptide (C), glucagon-like peptide 1 (GLP-1, D), and glucagon (E) during the intravenous administration of GLP-1 (1.2 pmol·kg⁻¹·min⁻¹, filled circles) or placebo (open circles) administered in the fasting state over 480 mins in eight patients with type 2 diabetes who had undergone major surgical procedures. Data are presented as mean ± sem. p Values were calculated using repeated-measures analysis of variance and denote A, differences between the groups; B, differences over time; and AB, differences due to the interaction of experiment and time. Asterisks indicate significant differences (p < .05) vs. placebo at single time points (one-way analysis of variance).





Adam M dean et al, Crit Care 2009

