

4° Congresso SIO – Sezione Regionale Triveneto
Udine, 4 Ottobre 2008

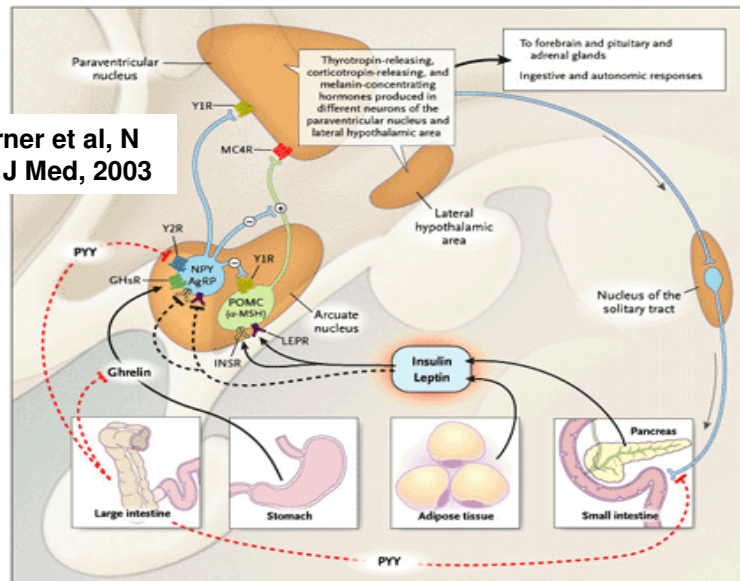
Regolazione ipotalamica dell'appetito Rocco Barazzoni

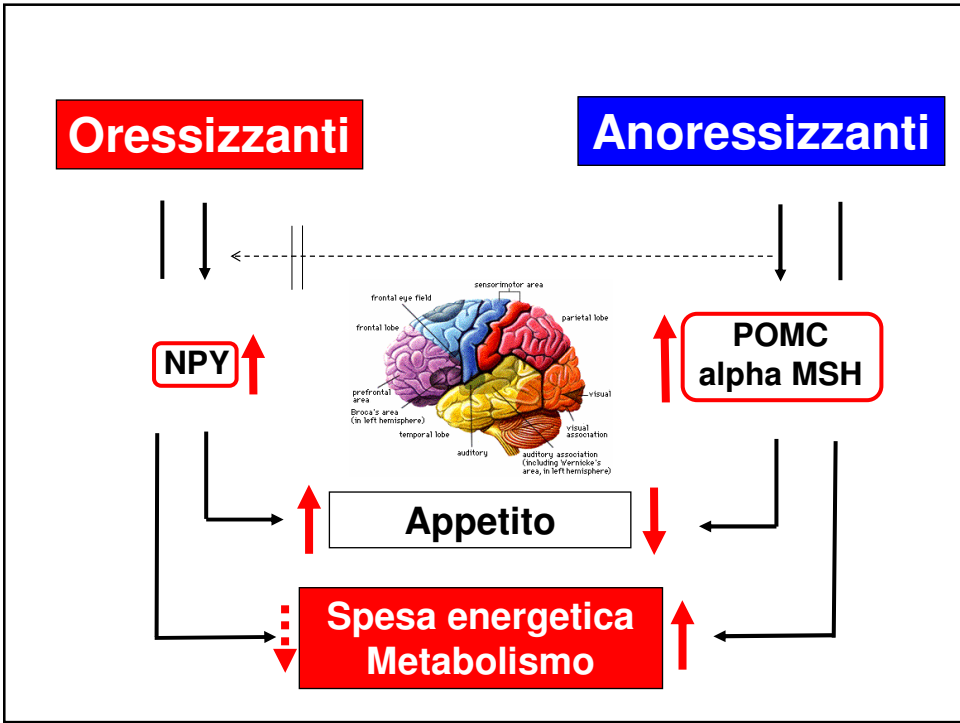
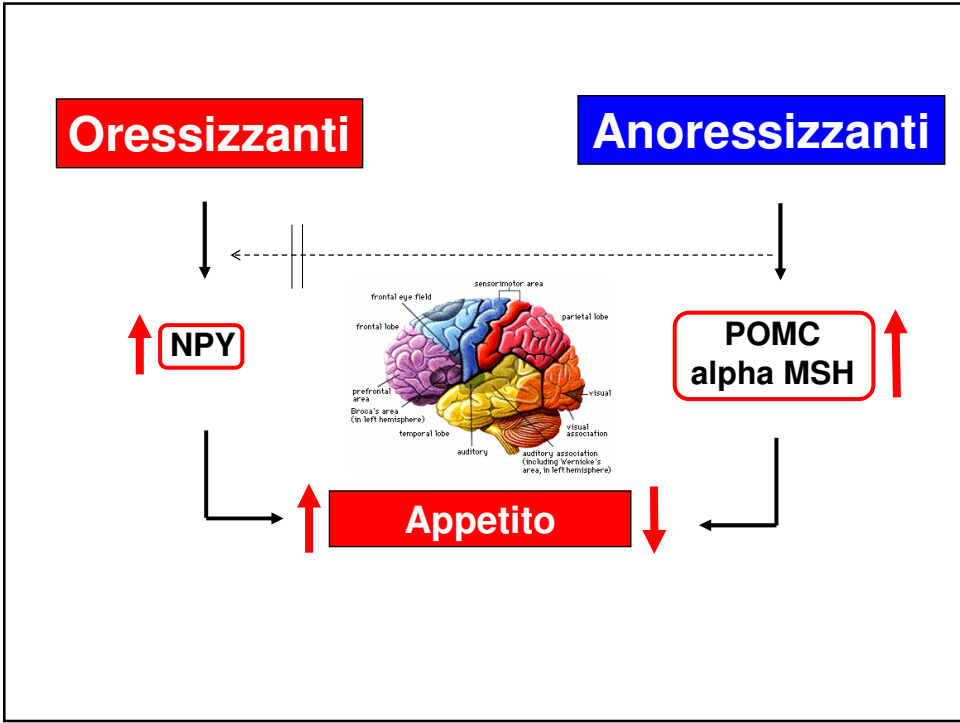


University of Trieste
Department S.C.M.T.
Clinica Medica Generale
e Terapia Medica

Comportamento alimentare: Integrazione centrale di stimoli periferici

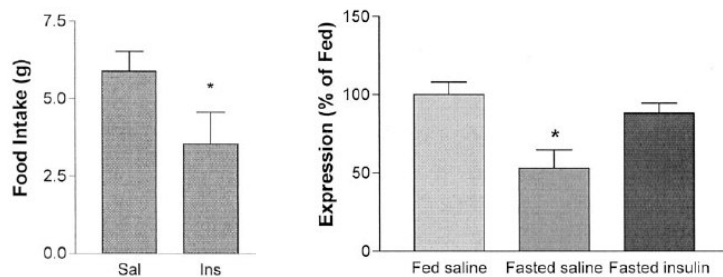
Korner et al, N
Eng J Med, 2003





Regolazione ormonale dell'appetito

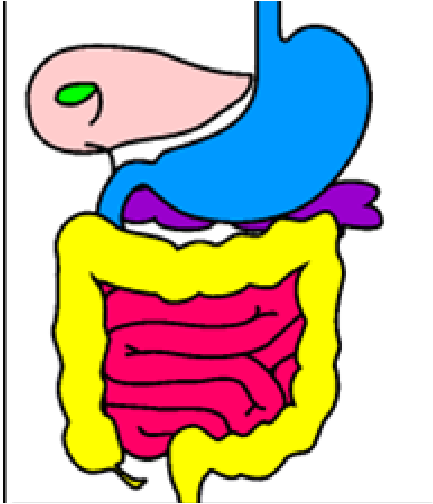
CENTRAL ADMINISTRATION OF **INSULIN** INCREASES EXPRESSION OF **POMC** RELATIVE TO FASTING



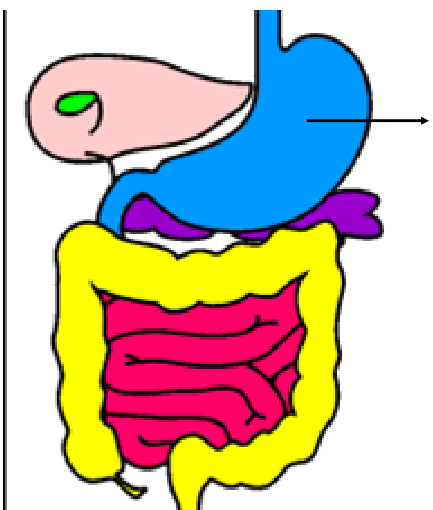
Benoit et al, J Neurosci 2002

Regolazione a feedback Asse enterico

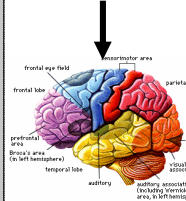
CCK
GLP-1
PYY
Enterostatin
Oxyntomodulin
Bombesin /GRP



Regolazione a feedback Asse enterico

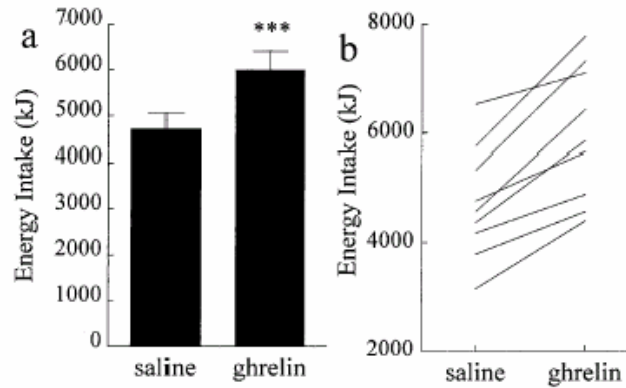


Ghrelin



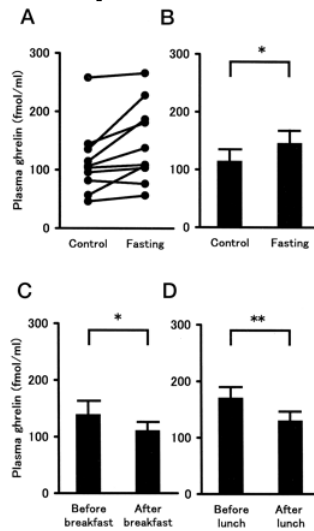
↑ **Appetite**
Weight gain

La ghrelina aumenta l'introito calorico spontaneo in vivo nell'uomo



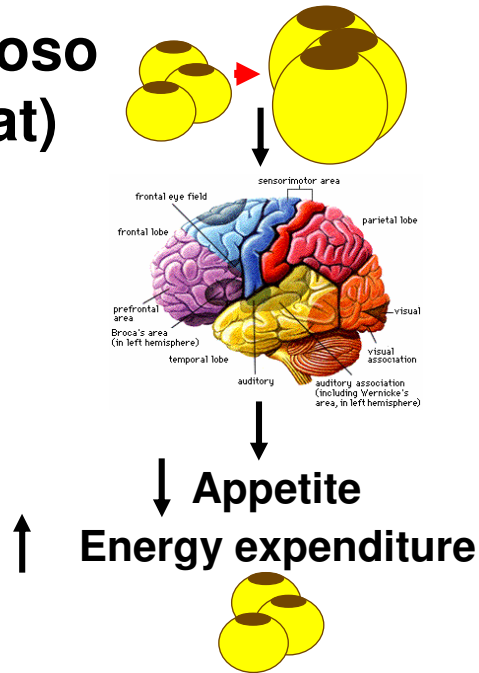
Wren et al, J Clin Endocrinol Metab, 2001

La ghrelina aumenta con il digiuno ed è soppressa dal pasto in vivo nell'uomo

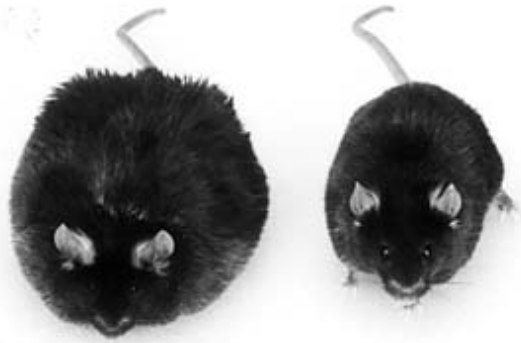


Ariyasu et al, J Clin Endocrinol Metab, 2001

Asse adiposo (adipostat)



Leptina



Topo Ob/Ob

Halaas et al,
Science, 1995

↓
Appetito
Peso-Grasso Corporeo

Leptina: mutazioni umane causano obesità

No Leptina

Leptina



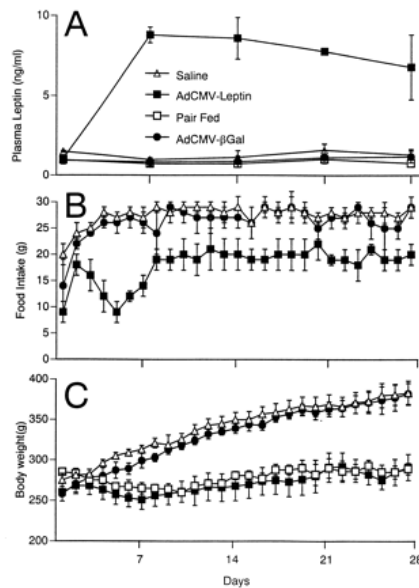
Farooqi et al, J Clin Invest, 2002

La leptina riduce l'introito calorico in modelli animali non-obesi

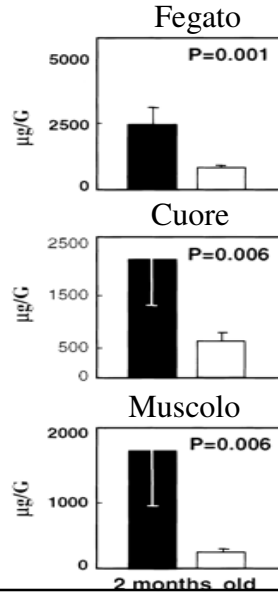
Introito Calorico

Peso Corporeo

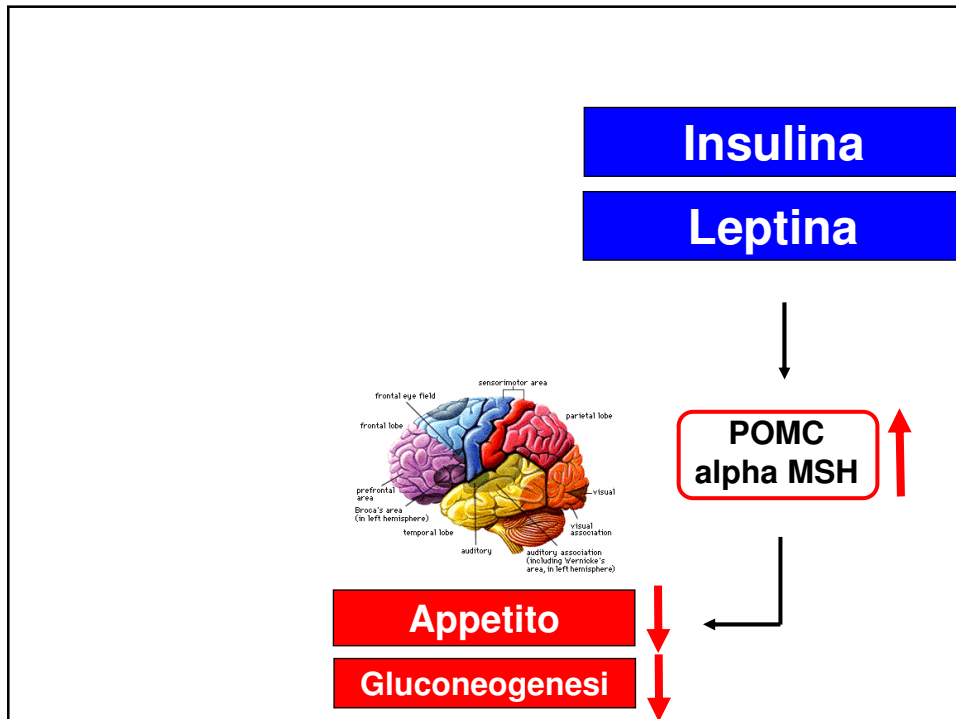
Chen et al, PNAS, 1996

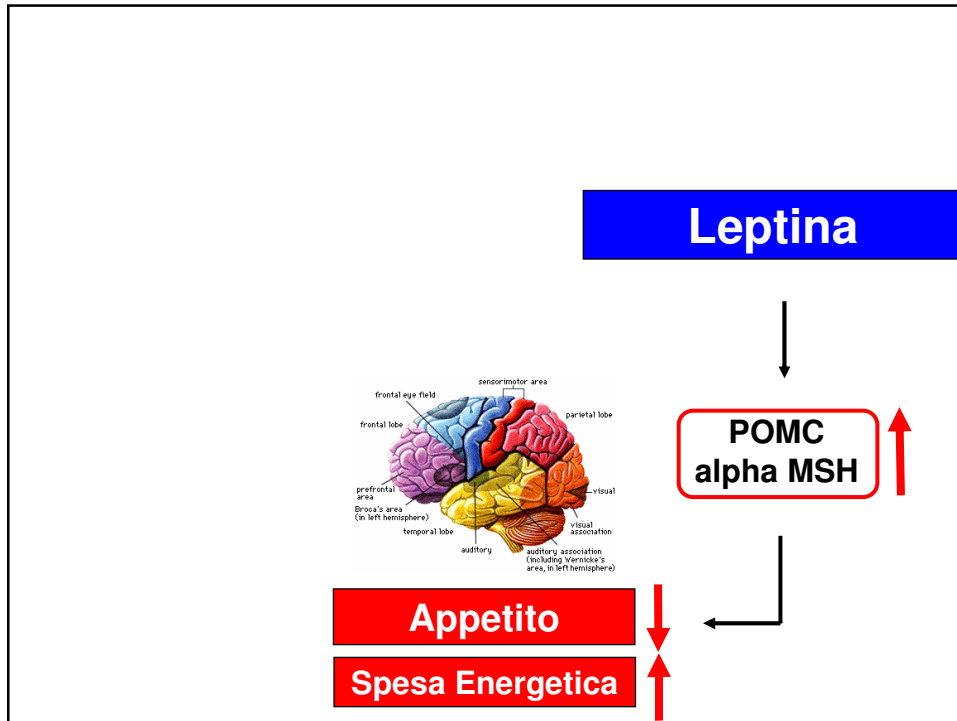


La leptina riduce il contenuto lipidico tissutale in vivo in modelli sperimentali



Unger et al, FASEB J, 2000





Regolazione ormonale dell'appetito

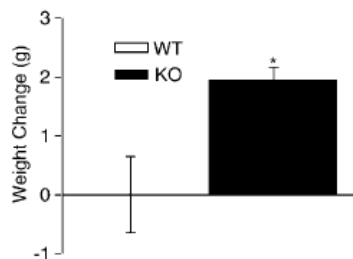
Causa di alterazioni patologiche del peso corporeo?

Leptina e ghrelina nell'insufficienza renale cronica

In pazienti con insufficienza renale cronica sono state descritte:

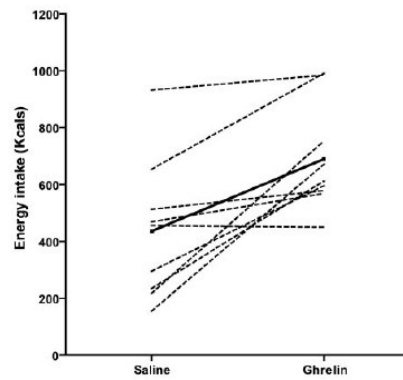
- concentrazioni plasmatiche di leptina elevate in misura sproporzionata al contenuto di grasso corporeo (Merabet et al, J Clin Endocrinol Metab 1997)
- associazioni negative tra leptinemia e introito calorico (Bossola et al, Nephron 2004; Daschner et al, J Am Soc Nephrol 1999) o introito proteico (Young et al, Nephrol Dial Transplant 1997)
- associazioni negative tra leptinemia e massa muscolare (Stenvinkel et al, J Am Soc Nephrol 2000; Castaneda-Sceppa C et al, JREN, 2007)
- associazioni positive tra ghrelinemia e albuminemia, prealbuminemia, transferrinemia e appetito (Aguilera et al, Adv Perit Dial 2004)

L'assenza del gene MCR-4 protegge dal calo ponderale in modelli renali di cachessia



Marks et al, J Clin Invest 2005

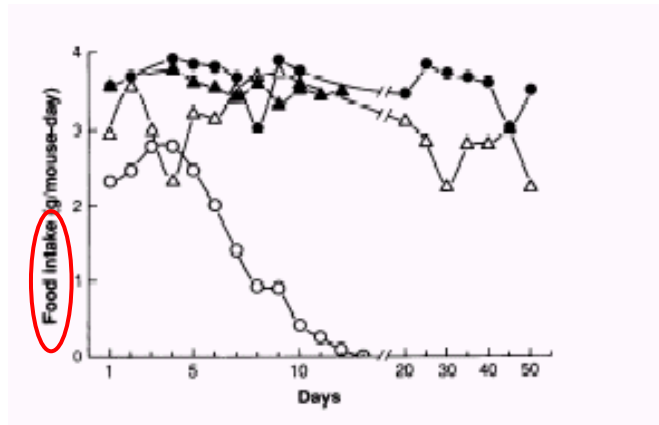
Subcutaneous Ghrelin Enhances Acute Food Intake in Malnourished Patients Who Receive Maintenance Peritoneal Dialysis: A Randomized, Placebo-Controlled Trial



Wynne et al, J Am Soc Nephrol 2005

Infiammazione e appetito
Ruolo delle citochine

Proinflammatory cytokines reduce food intake through central effects in experimental models



- Carrier-CNS
- ▲ Carrier-muscle
- TNF-CNS
- △ TNF-muscle

Tracey et al, JCI 1990

Low-grade chronic systemic inflammation

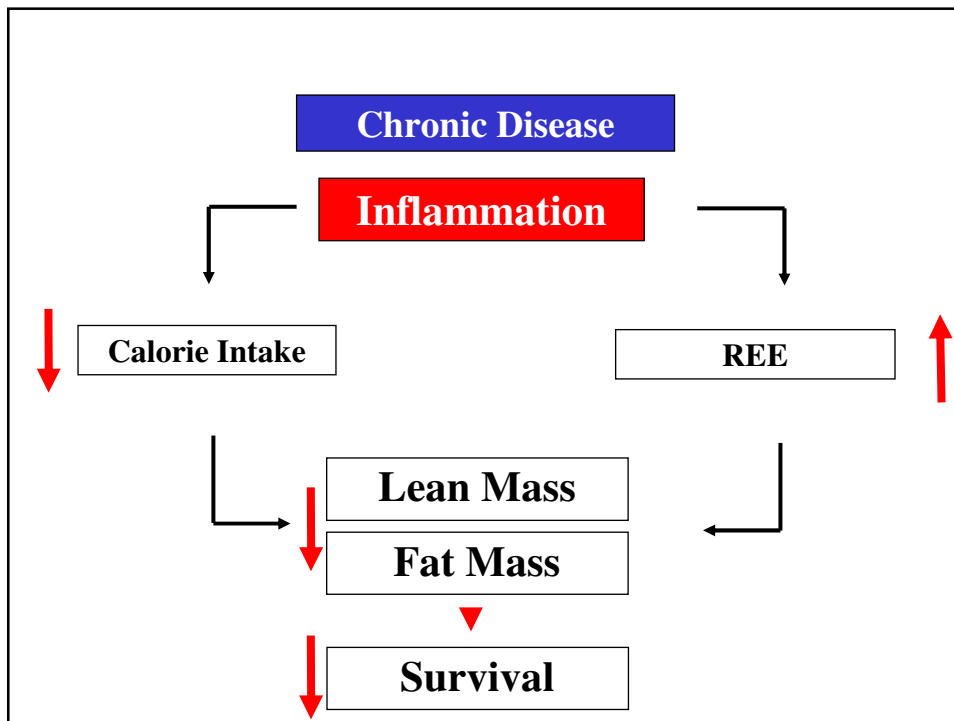
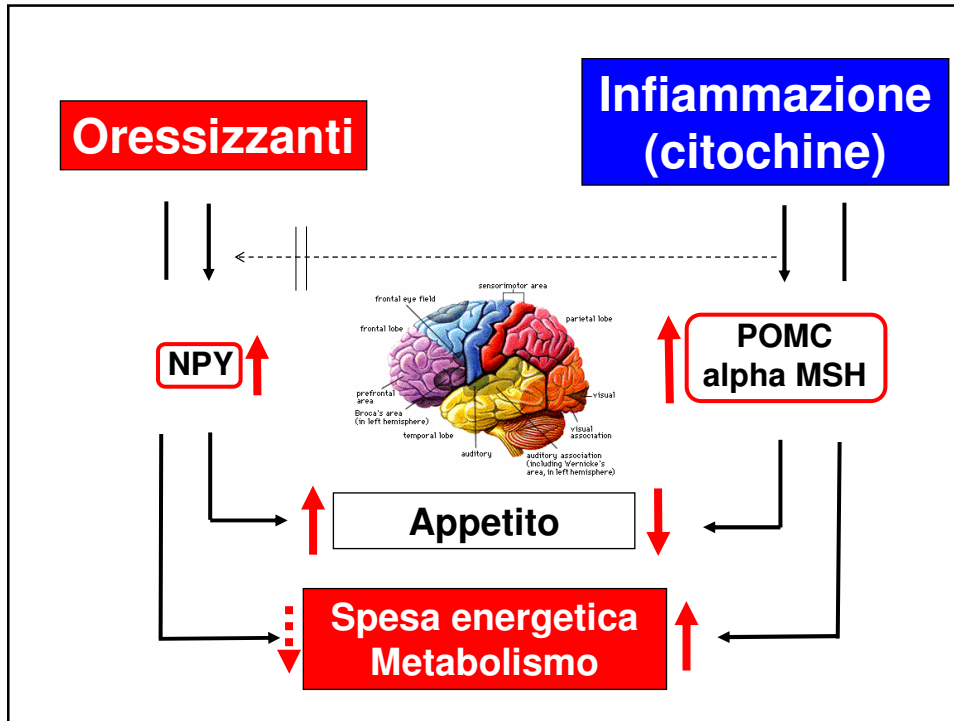
Aging (frail elderly)

Cancer

Chronic Heart Failure

Chronic Kidney Disease

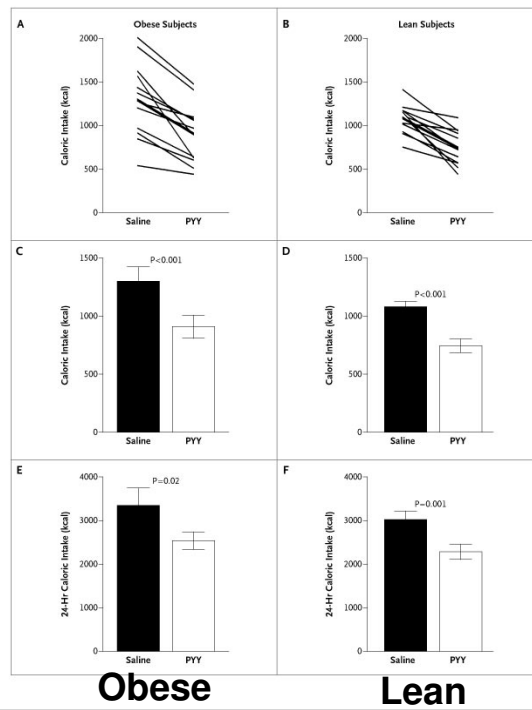
Chronic Obstructive Pulmonary Disease



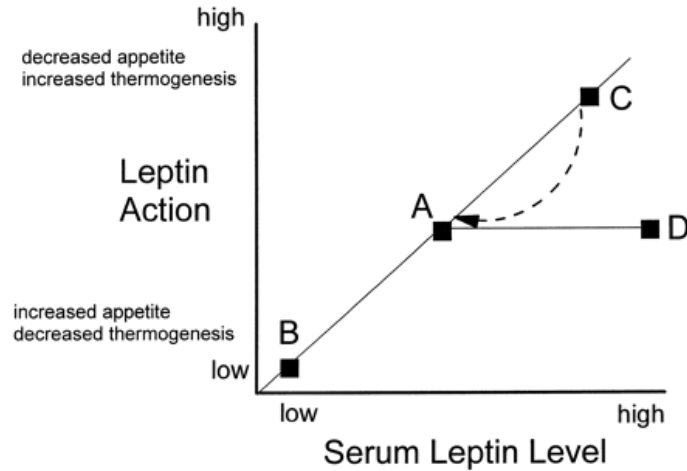
Obesità

Peptide YY

Batterham, RL et al, N Eng J Med, 2003

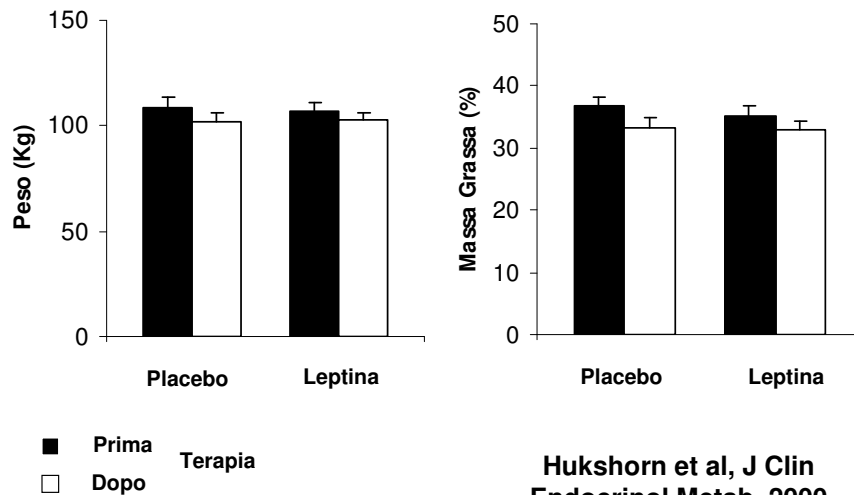


Leptino-resistenza nell'obesità



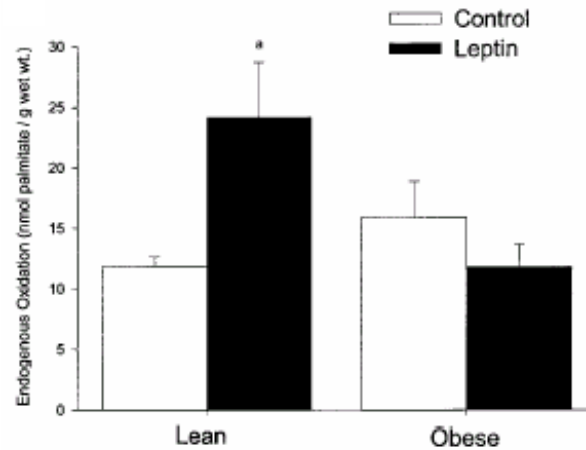
Flier JS, J Clin Endocrinol Metab, 2000

La leptina non riduce peso corporeo e massa grassa in pazienti obesi

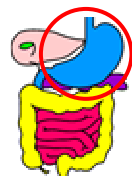


Hukshorn et al, J Clin Endocrinol Metab, 2000

Leptino-resistenza nell'obesità – La leptina stimola l'ossidazione degli acidi grassi nel muscolo scheletrico in soggetti normopeso ma non obesi



Steinberg et al, Am J Physiol Endocrinol Metab, 2002



Barazzoni et al, Gastroenterology 2003

Leptina
Insulina

Saad et al, JCEM 2002

..... -

Ghrelina

Nakazato et al, Nature 2001

↓ +

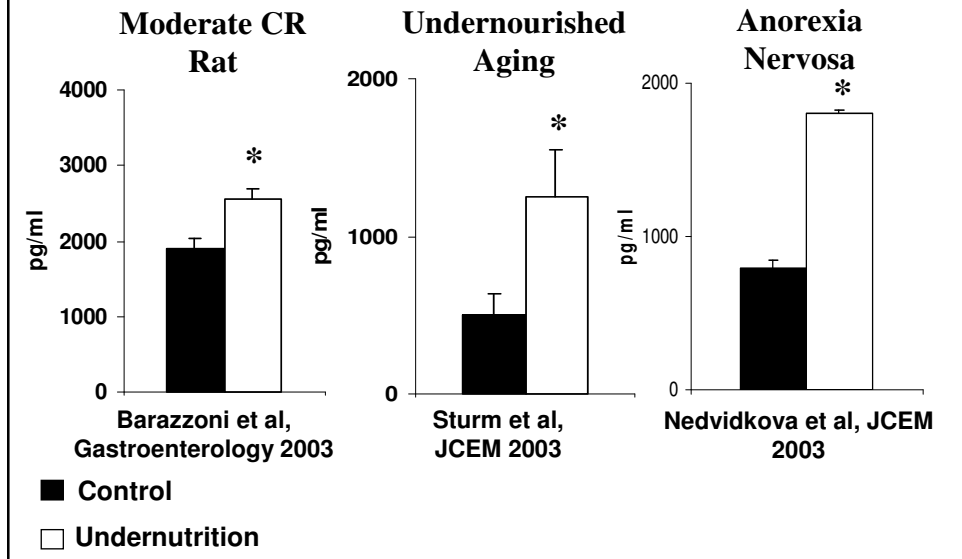
Appetito

↓ +

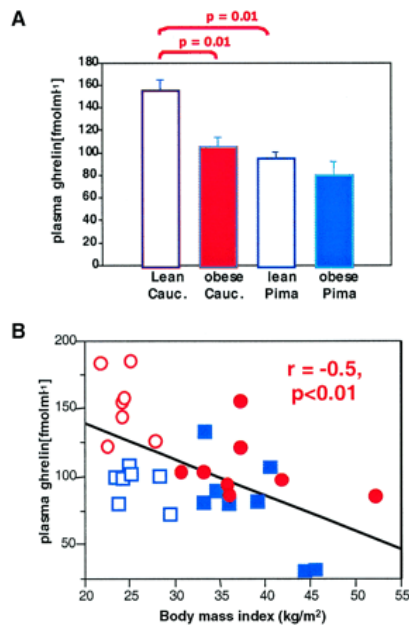
Nutrienti

..... +

Plasma ghrelin is increased in calorie-restricted states

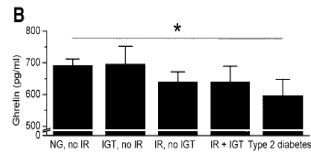
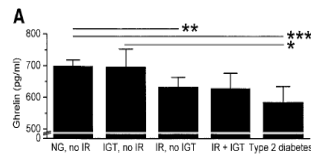


La ghrelina è ridotta nell'obesità in vivo nell'uomo

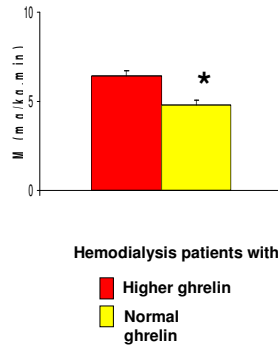


Tschop et al, Diabetes, 2001

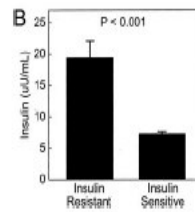
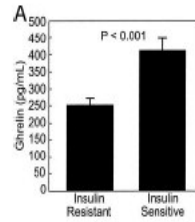
Fasting plasma ghrelin is negatively associated with insulin resistance and diabetes in population studies and in disease states



Poykko et al, Diabetes, 2003

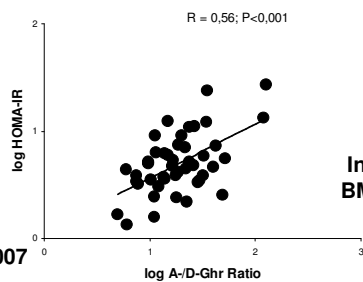
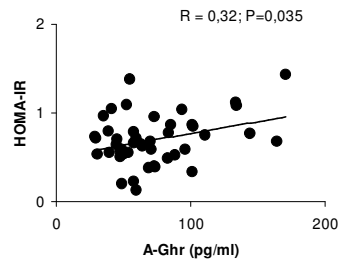
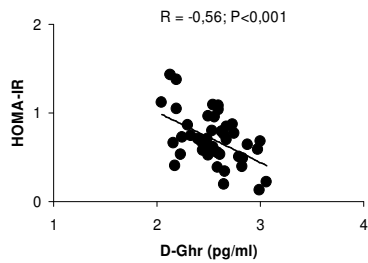


Barazzoni et al, Clin Nutr 2008



McLaughlin et al
J Clin Endocrinol Metab 2004

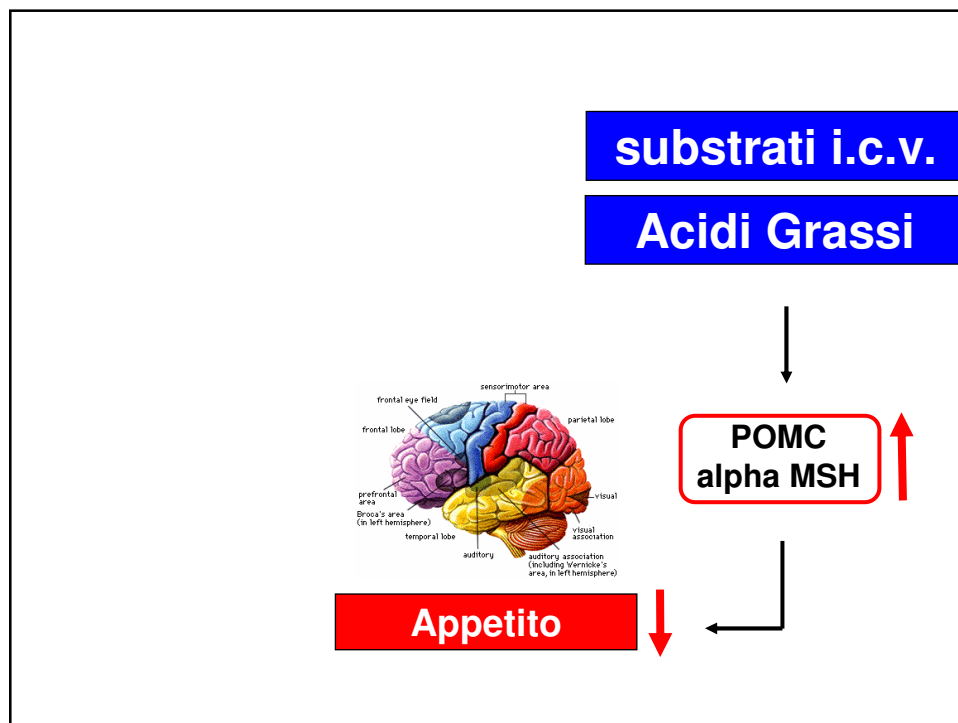
Associations between different ghrelin forms and insulin resistance (HOMA) in humans with metabolic syndrome



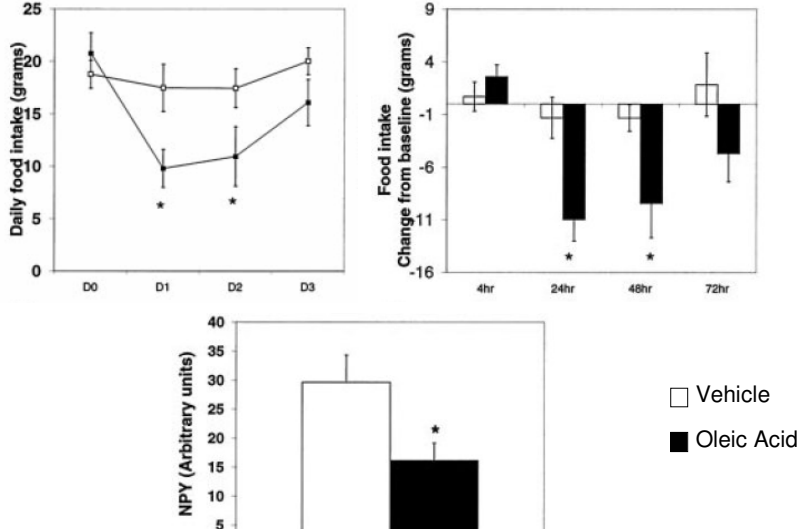
Independent of sex and BMI/waist circumference

Barazzoni et al, JCEM 2007

Regolazione nutrizionale dell'appetito



EFFECT OF ICV OLEIC ACID ON FOOD INTAKE AND NPY EXPRESSION



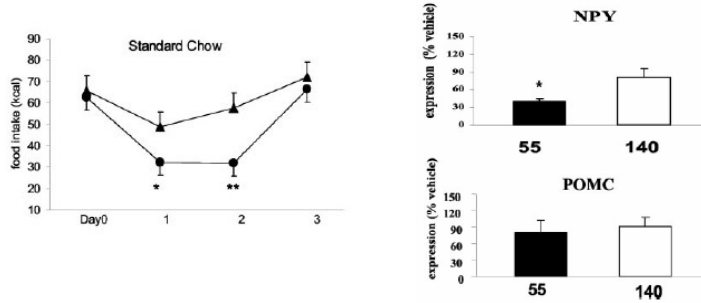
Obici S, Diabetes 2003

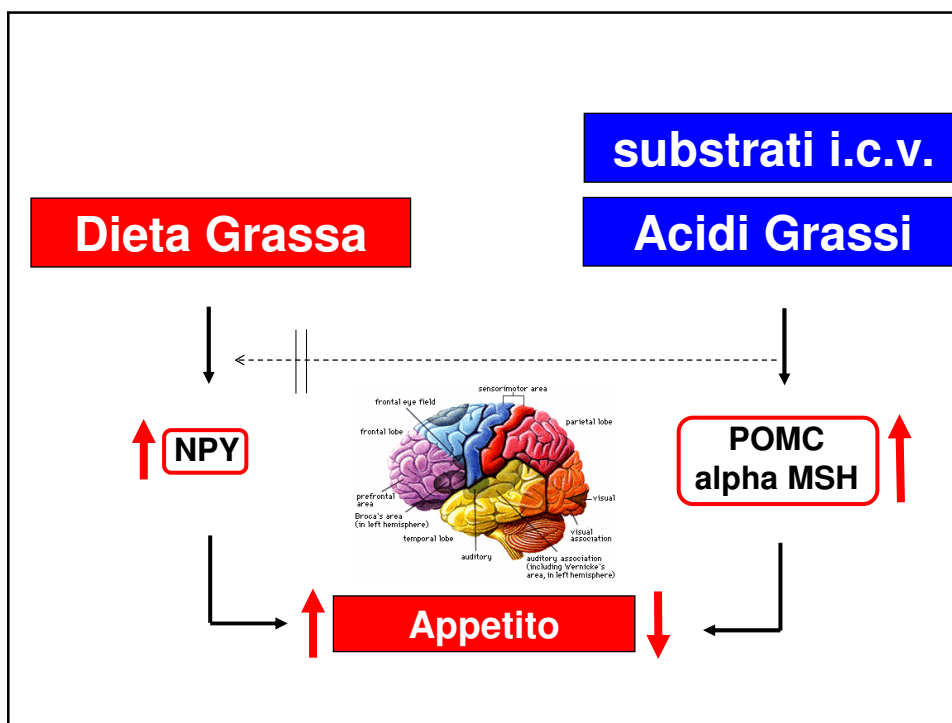
Hypothalamic Responses to Long-chain Fatty Acids Are Nutritionally Regulated*

Received for publication, January 15, 2004, and in revised form, April 15, 2004
Published, JBC Papers in Press, May 19, 2004, DOI 10.1074/jbc.M400458200

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Conclusioni

La regolazione dell'appetito a livello ipotalamico coinvolge numerosi e complessi fattori di tipo ormonale e nutrizionale.

Alterazioni della regolazione ormonale dell'appetito possono contribuire ad alterati stati nutrizionali che caratterizzano patologie degenerative e infiammatorie croniche.

I fattori coinvolti nella regolazione dell'appetito partecipano anche alla regolazione del metabolismo intermedio.

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