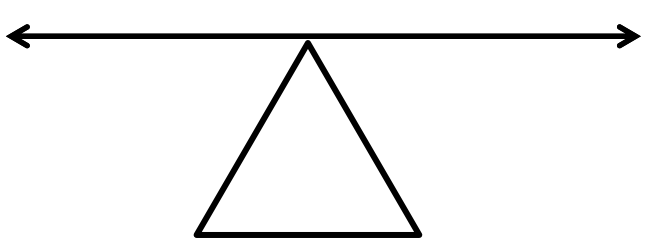
REGULACE PŘÍJMU POTRAVY

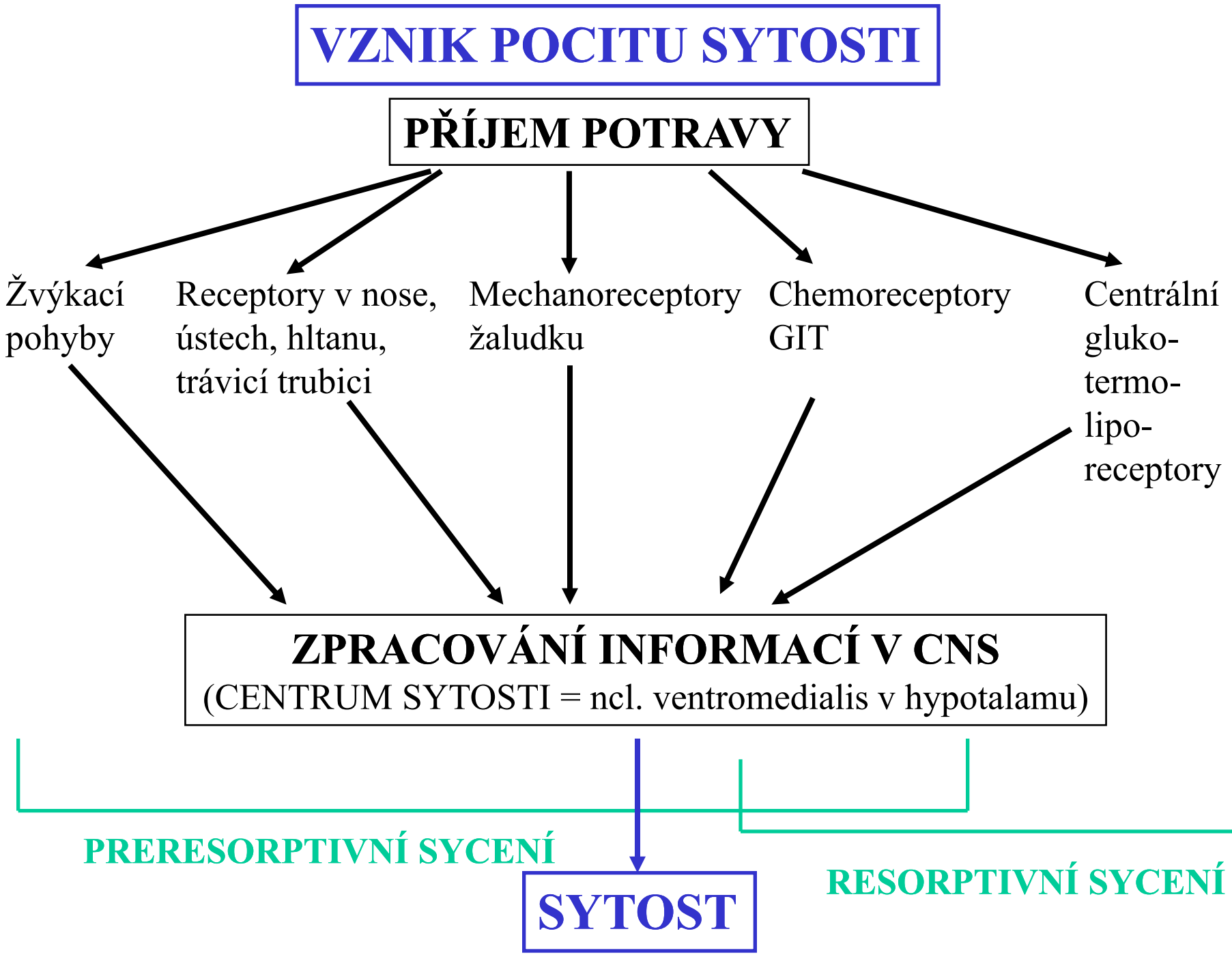
A VÝŽIVOVÉHO STAVU

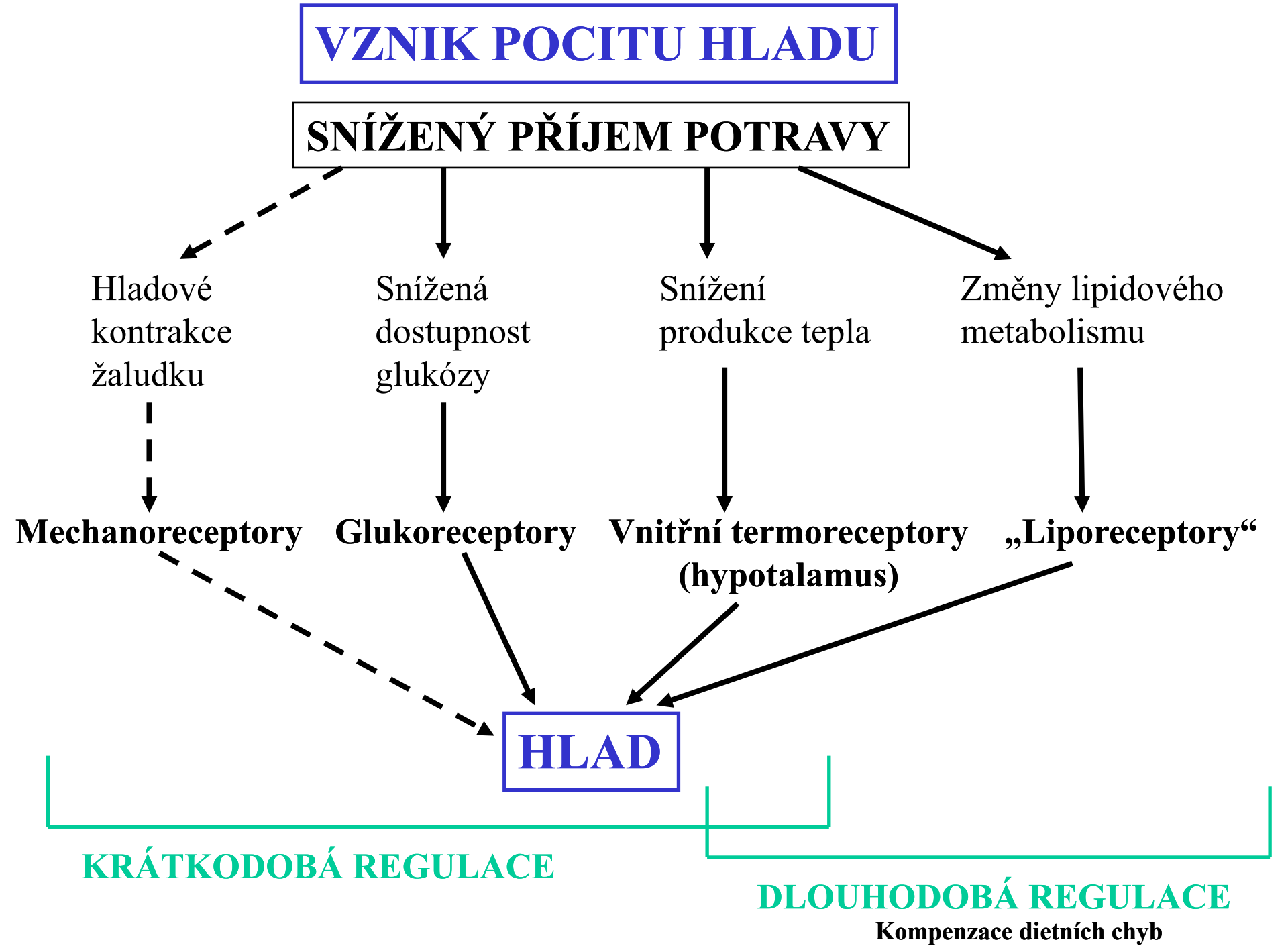
PŘÍJEM  **VÝDEJ**

CENTRUM SYTOSTI **-** → **CENTRUM HLADU**
(trvale aktivní)

ncl. ventromedialis v hypothalamu

laterální hypothalamus
(jádro pod fasciculus telencephalicus medialis)


VZNIK POCITU SYTOSTI
PŘÍJEM POTRAVY
Žvýkací pohyby
Receptory v nose, ústech, hltanu, trávicí trubici
Mechanoreceptory žaludku
Chemoreceptory GIT
Centrální gluko- termo- lipo- receptory
ZPRACOVÁNÍ INFORMACÍ V CNS
(CENTRUM SYTOSTI = ncl. ventromedialis v hypotalamu)
PRERESORPTIVNÍ SYCENÍ
RESORPTIVNÍ SYCENÍ
SYTOST


VZNIK POCITU HLADU
SNÍŽENÝ PŘÍJEM POTRAVY
Hladové kontrakce žaludku
Snížená dostupnost glukózy
Snížení produkce tepla
Změny lipidového metabolismu
Mechanoreceptory
Glukoreceptory
Vnitřní termoreceptory (hypotalamus)
„Liporeceptory“
HLAD
KRÁTKODOBÁ REGULACE
DLOUHODOBÁ REGULACE
Kompenzace dietních chyb

REGULACE PŘÍJMU POTRAVY

HYPOTÉZA:

1. Lipostatická – *množství energetických zásob (tuková tkáň)*
2. H. střevních peptidů – *význam střevních peptidů*
3. Glukostatická – *kolísání glykémie*
4. Termostatická – *vnitřní receptory, pokles produkce tělesného tepla*

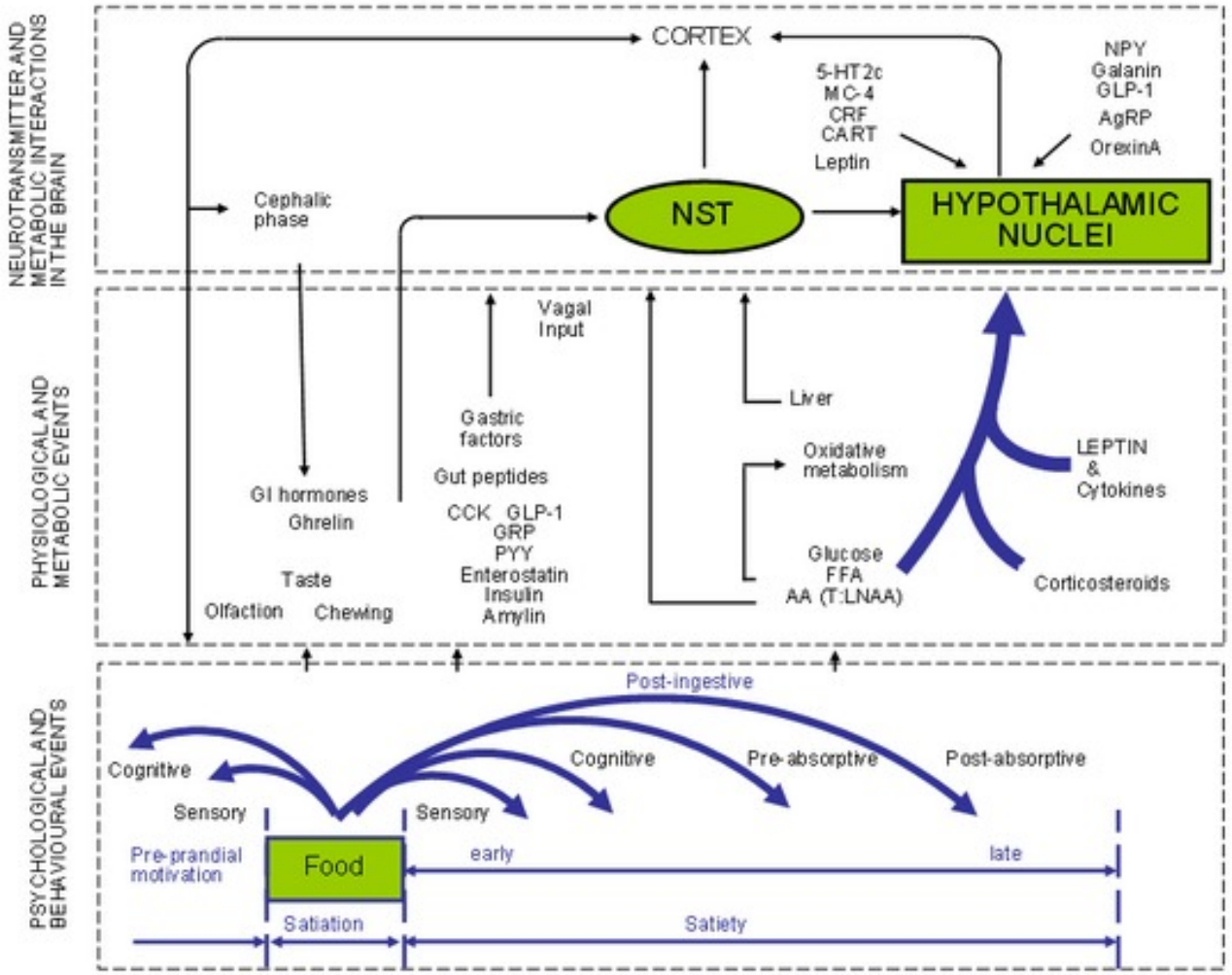


Diagram showing the expression of appetite as the relationship between three levels of operations: the behavioral pattern, peripheral physiology and metabolism, and brain activity. PVN, paraventricular nucleus; NST, nucleus of the tractus solitarius; CCK, cholecystokinin; FFA, free fatty acids; T: LNAA, tryptophan: large neutral amino acids (See (4) for detailed diagram).

OREXIGENNÍ FAKTORY

- Neuropeptid Y
- Orexin A a B (hypocretin 1 a 2)
- Hormon koncentrující melanin
- ARP (agouti-related peptide)
- Ghrelin (lenomorelin) – tzv. hormon hladu (sekrece z „prázdného“ žaludku)
- Insulin
- Cukry (fruktóza)

ANOREXIGENNÍ FAKTORY

- POMC – pouze MC4-R!
- CRH (kortikoliberin)
- CART (cocaine- and amphetamine-regulated transcript)
- Peptid YY (pankreatický peptid; L-buňky v ileum a kolon, tlumí žaludeční motilitu, zvyšuje resorpci)
- CCK (cholecystokinin)
- glukagon

LÉKY !!!

TABLE 227-4 CENTRAL NERVOUS SYSTEM MODULATORS OF ENERGY BALANCE

CENTRAL ANABOLIC (↑ INTAKE)	CENTRAL CATABOLIC (↓ INTAKE)
Neuropeptide Y	α-Melanocyte-stimulating hormone
Agouti-related protein	Corticotropin-releasing hormone
Melanin-concentrating hormone	Thyrotropin-releasing hormone
Hypocretins and orexins	Cocaine- and amphetamine-regulated transcript (CART)
Galanin	Interleukin-1β
Norepinephrine	Urocortin
Endogenous endocannabinoids (anandamide and 2-arachidonoylglycerol)	Oxytocin
	Neurotensin
	Serotonin

LEPTIN (ob-protein) – *ob* gen

Secernován adipocyty do krve
Vazebné proteiny
Účinek na CNS (regulace tělesné hmotnosti a stálosti tukové hmoty těla)

- Sérové hladiny mají pulzativní a diurnální charakter
- Forma volná a vázaná (v séru)
- HUBENÍ LIDÉ MAJÍ 2x VÍCE VÁZANÉ FORMY NEŽ OBÉZNÍ
- LEPTINOVÁ REZISTENCE: často u obézních s inzulínovou rezistencí

RECEPTORY z rodiny cytokinů (Ob)
- **Periferní** (gonády)
- **Centrální** (hypotalamus, hypofýza)

Transdukční systém není doposud plně objasněn.

ADAPTACE NA HLADOVĚNÍ

Moduluje expresi genů pro estrogeny.
Regulace obezity leptinem zprostředkována NPY a MSH.

Leptin řídí zásoby tělesného tuku koordinací příjmu potravy, metabolismu, autonomního nervstva a energetické rovnováhy.

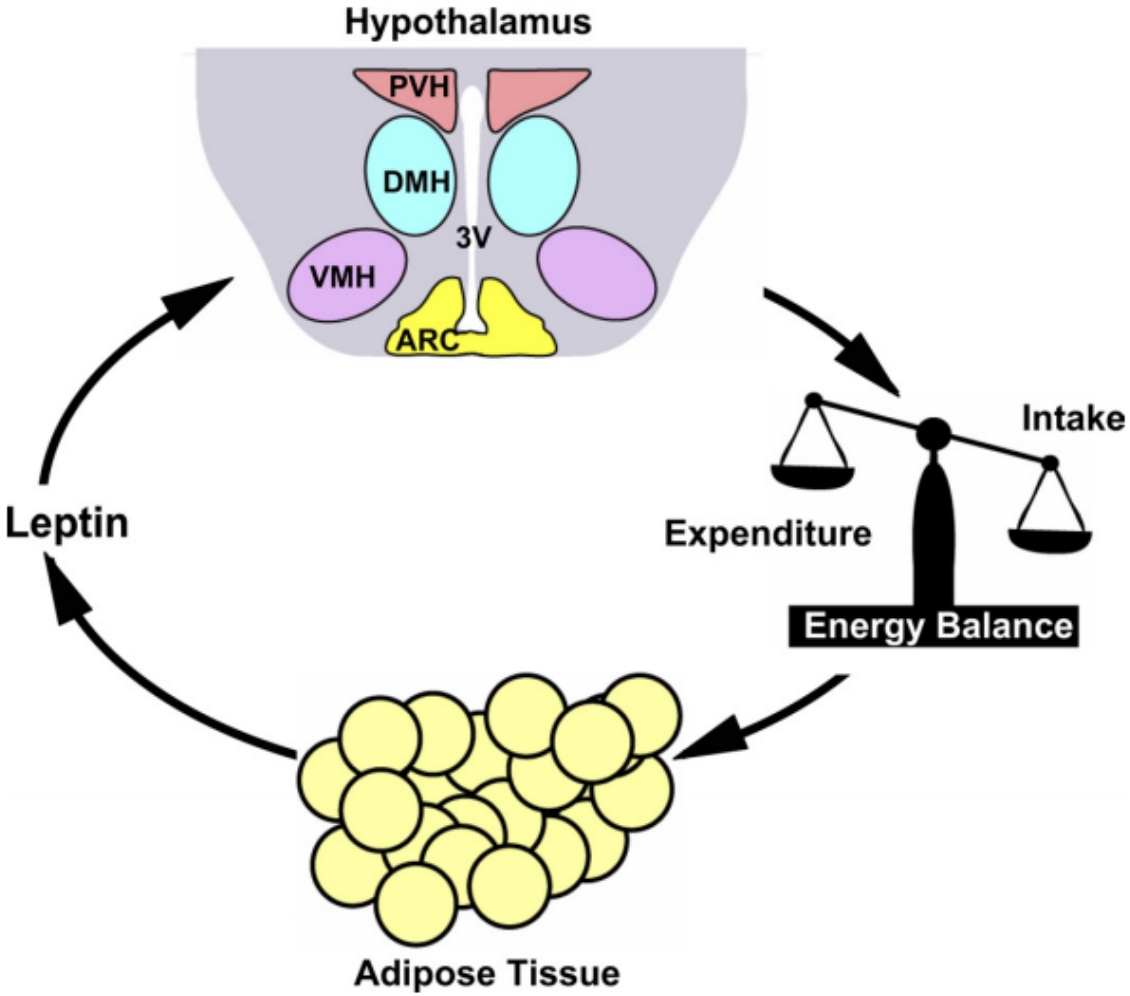


Fig. 1. A model of leptin regulation of energy balance and body weight. Leptin is secreted by adipose tissue in proportion to adipose mass and relays information about peripheral energy storage and availability to the brain. Leptin regulates neuronal activity in multiple regions of the hypothalamus, including the arcuate nucleus (ARC), ventromedial hypothalamus (VMH), and paraventricular hypothalamus (PVH). Leptin suppresses appetite (energy intake) and promotes energy expenditure primarily by regulating these neuronal activities. Leptin resistance causes an imbalance between energy intake and expenditure, resulting in obesity. 3V, 3rd ventricle.

FIGURE 1. Figure 1. An *ob/ob* mouse bearing a homozygous mutation of the Lep gene (right), and its normal sibling (left). Figure reprinted by permission from Macmillan Publishers LTD from R.L. Leibel (2008) *Int. J. Obes.* 32, S98. Copyright 2008.

TUKOVÁ TKÁŇ

LEPTINOVÁ REZISTENCE

ÚBYTEK HMOTNOSTI

↓

- LEPTIN

↓

HYPOTALAMUS

↓

NPY

↓

NPY RECEPTOR (Y1, Y2, Y5)

↓

ODPOVĚĎ NA HLADOVĚNÍ

+ Příjem potravy
- Reprodukce
- Teplota
- Výdej energie

PARASYMPATICKÁ AKTIVITA

PŘÍRŮSTEK HMOTNOSTI

↓

+ LEPTIN

↓

HYPOTALAMUS

↓

MSH

↓

MSH RECEPTOR

↓

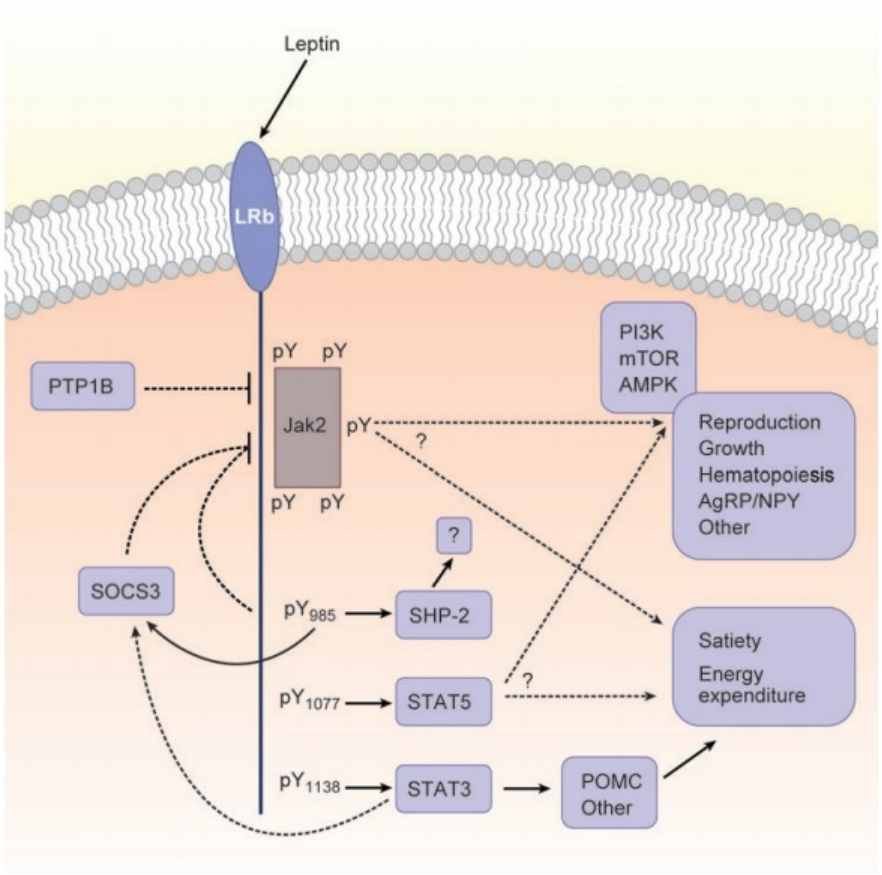
deriváty POMC (MC4-R)

↓

ODPOVĚĎ NA OBEZITU

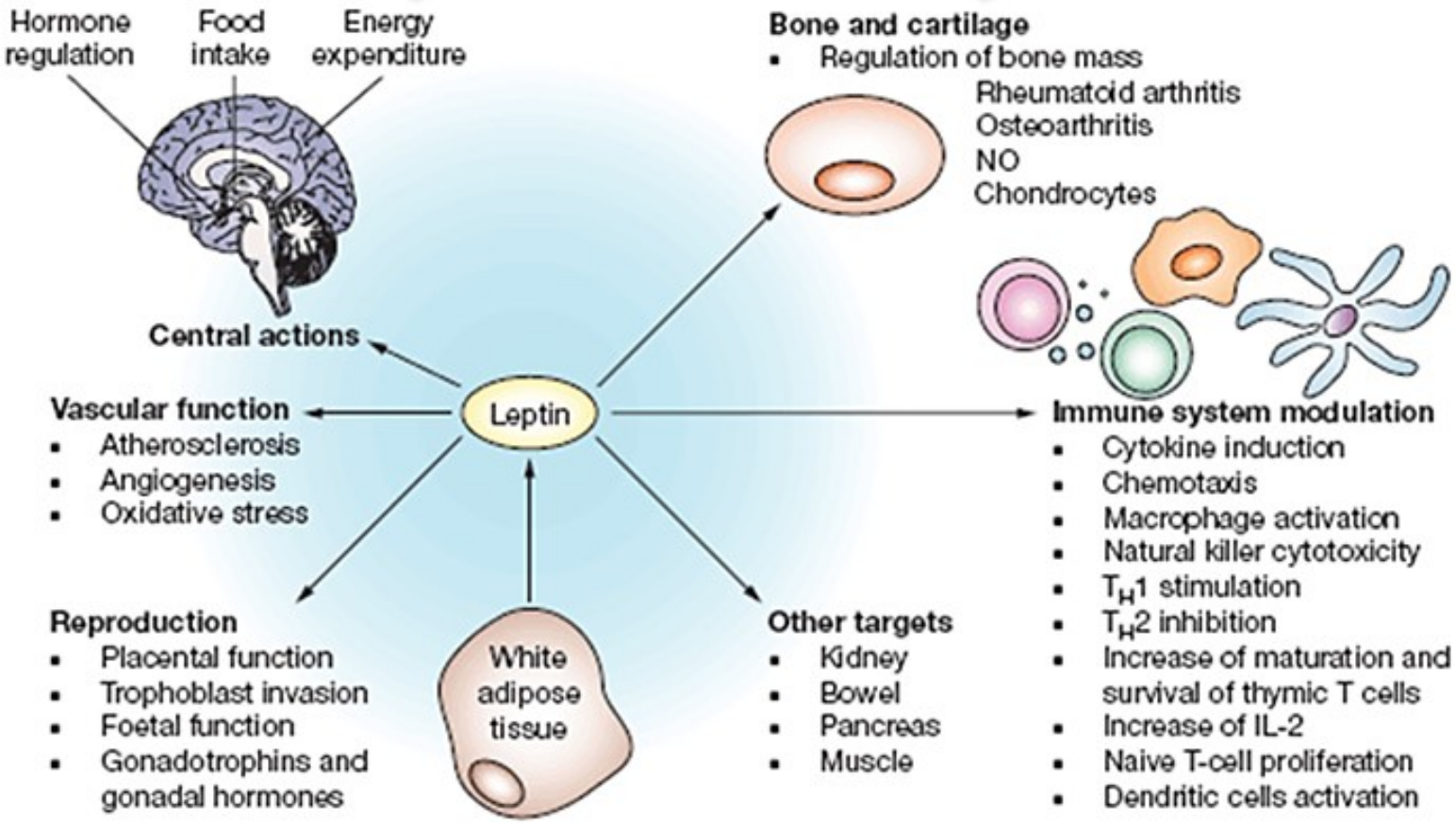
- Příjem potravy (CRH)
+ Výdej energie

SYMPATICKÁ AKTIVITA

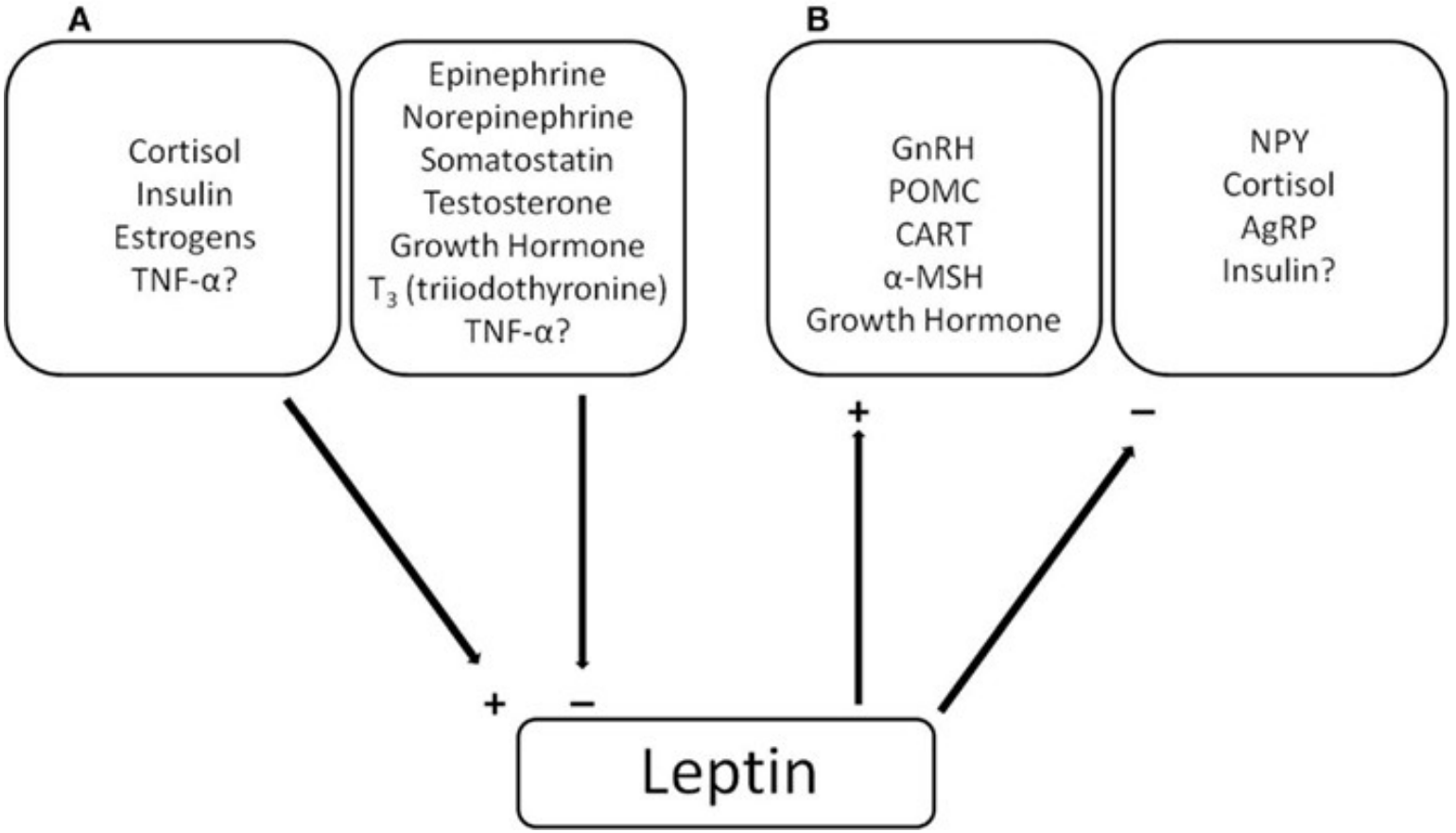


LRb signaling, feedback inhibition, and the regulation of physiology. Leptin binding to the extracellular domain of LRb, the functional leptin receptor isoform, mediates the activation of the intracellular, LRb-associated Jak2 tyrosine kinase, resulting in Jak2 autophosphorylation on tyrosine residues (pY) as well as the phosphorylation of three tyrosine residues on the intracellular tail of LRb: Y_{985}, Y_{1077}, and Y_{1138}. pY_{1138} recruits signal transducer and activator of transcription (STAT) 3, which is activated to mediate transcriptional events, including the transcription of pro-opiomelanocortin (POMC) and the inhibitory suppressor of cytokine signaling 3 (SOCS3) protein. pY_{1077} recruits and mediates the transcriptional activation of STAT5. pY_{985} recruits the tyrosine phosphatase SHP-2 and also binds to SOCS3 and mediates feedback inhibition of LRb signaling (*dotted lines*). The tyrosine phosphatase PTP1B, although not regulated by leptin in this manner, also inhibits LRb/Jak2 signaling. The cellular mechanisms by which LRb couples to the regulation of phosphatidylinositol 3-kinase (PI3K), mammalian target of rapamycin (mTOR), and AMP-activated protein kinase (AMPK) pathways remain unclear. Y_{1138}-mediated STAT3 signaling by LRb (presumably via POMC and additional mechanisms) is crucial to the regulation of anorexia and energy expenditure by leptin. Although Y_{985} clearly functions to attenuate LRb signaling in vivo, a role for Y_{985} and SHP-2 in promoting leptin action has not been defined. Leptin mediates permissive effects upon reproduction, growth, hematopoietic effects (e.g., immune and platelet function), and the inhibition of agouti-related protein (AgRP)/neuropeptide Y (NPY) neurons of Y_{1138} and Y_{985}, perhaps via pY sites on Jak2 or via pY_{1077}.

Importance Of Leptin



Source: Nat Clin Pract Rheumatol ©2007 Nature Publishing Group


A
Cortisol
Insulin
Estrogens
TNF-α?
Epinephrine
Norepinephrine
Somatostatin
Testosterone
Growth Hormone
T_3 (triiodothyronine)
TNF-α?
B
GnRH
POMC
CART
α-MSH
Growth Hormone
NPY
Cortisol
AgRP
Insulin?
+
−
+
−
Leptin

Neuropeptid Y

- Antagonistický efekt k leptinu
- - motilita + sekrece (žaludek, pankreas)
- Skupina peptidů
  - peptid YY – ileum, tlusté střevo (-)
  - pankreatický polypeptid (PP)
  - nejen příjem potravy!
    - cirkadiánní rytmy
    - kognitivní funkce
    - modulace synaptické plasticity
    - procesy stárnutí?
    - abusus alkoholu

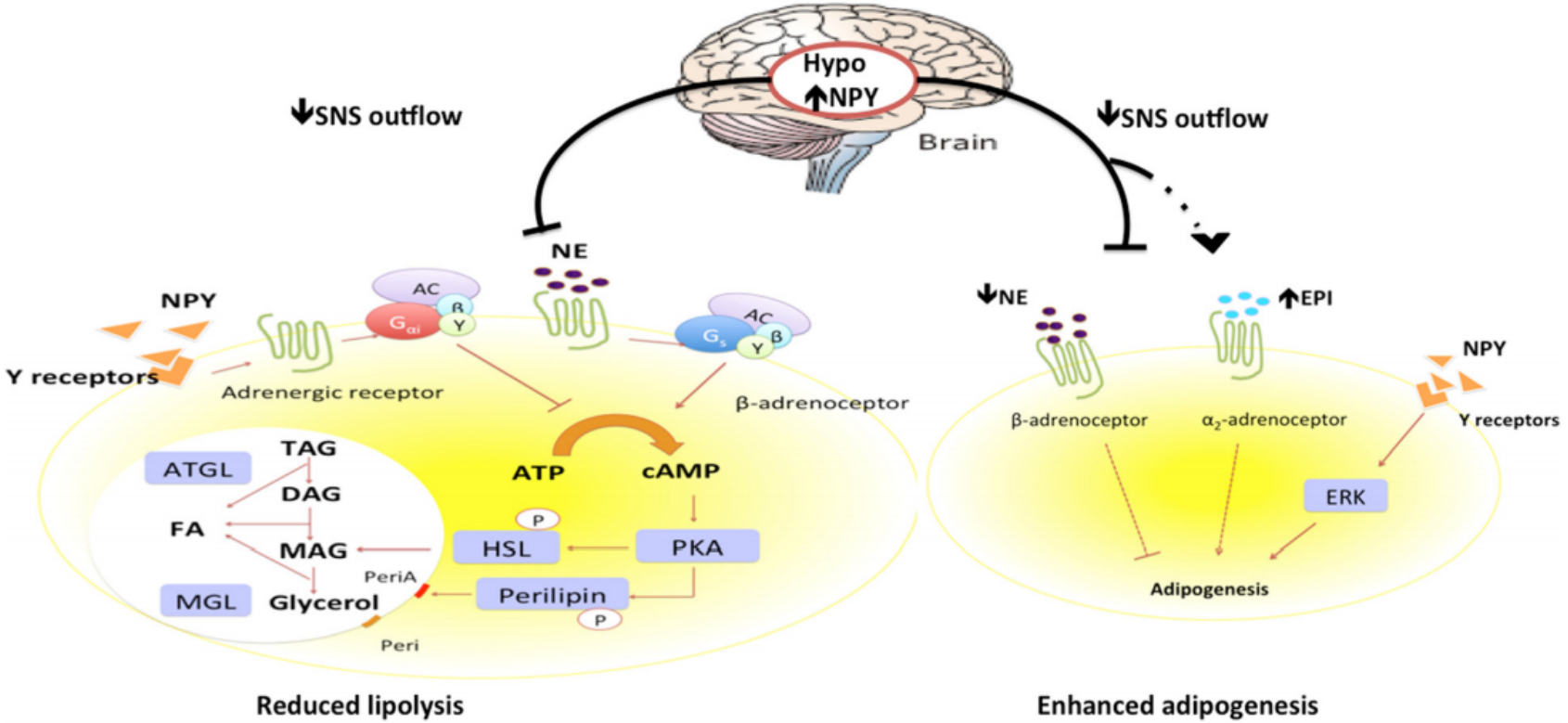


Figure 1 Antilipolytic and adipogenic effects of NPY on white adipose tissue. In the peripheral system, NPY binds to receptors 1, 2 and 5 and affects β-adrenergic receptor (β_1-AR, β_2-AR and β_3-AR; mainly through β_2-AR) configuration, the modification thereby leading to improved affinity for Gαi proteins. Subsequently, this activation of inhibitory GTP-binding protein alpha subunit (Gαi) inhibits adenylyl cyclase (AC) and cyclic AMP (cAMP) production. Decreased cellular cAMP levels inhibit protein kinase A (PKA), which phosphorylates and activates hormone-sensitive lipase (HSL). Decreased PKA activity also inhibits phosphorylation of lipid droplet-associated protein perilipin (peri) into PeriA, which controls the magnitude of lipolysis. Lipolysis is catalyzed by 3 lipases. Triacylglycerol is firstly hydrolyzed by adipocyte triglyceride lipase (ATGL) resulting in the formation of diacylglycerol (DAG) and release of a fatty acid (FA). Monoacylglycerol lipase (MGL) catalyzes hydrolysis of MAG, yielding glycerol and a FA. Increased hypothalamic (abbreviated as hypo in the figure) NPY inhibits sympathetic nerve system (SNS) outflow and suppresses catecholamine release, mainly norepinephrine (NE), and thereby their binding to β-adrenergic receptors, which in turn reduces the cAMP-PKA pathway-associated lipolysis. On the other hand, NPY itself in the peripheral system can stimulate ERK-mediated adipogenesis. Through the hypothalamus-SNS-adipose tissue axis, reduced NE enhances adipogenesis via undefined mechanisms. Reduced SNS outflow is compensated for by adrenal medullary catecholamines, primarily epinephrine (EPI), which was also known to stimulate adipogenesis, possibly through NPY regulation. Parts of the figure are adapted from references [71,72]. "→": stimulatory effect; "⊣": inhibitory effect ;"⋯→"mechanisms unknown; "—·—→" compensatory effect of EPI secretion.

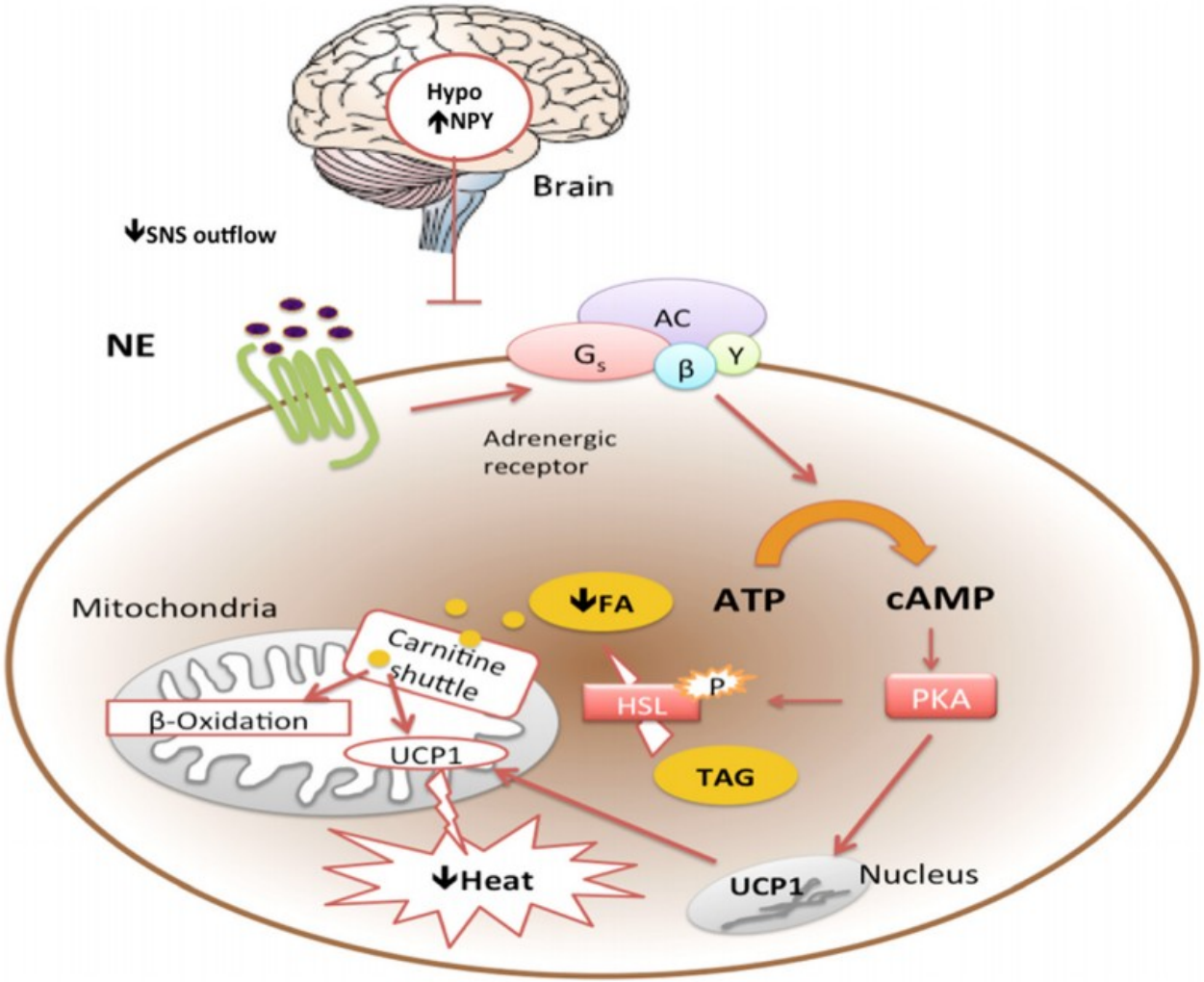


Figure 2 NPY inhibits BAT thermogenesis via reduced SNS outflow. Increased release of NPY in the hypothalamus inhibits sympathetic nerve system (SNS) outflow, particularly norepinephrine (NE) release. Consequently, it inhibits the cAMP-PKA signaling pathway via β-adrenergic receptors. Reduced lipolysis decreases the level of fatty acid storage in the brown adipose tissue, together with reduced uncoupling protin 1 (UCP1) expression and secretion, resulting in reduced thermogenic potential. Consequently, with less fatty acids being transported into the mitochondria by the carnitine palmitoyl transferase (carnitine shuttle) and also reduced UCP1 functioning to dissipate the proton-motive force across the mitochondrial membrane, there is less heat production. Part of the picture is summarized from [73].

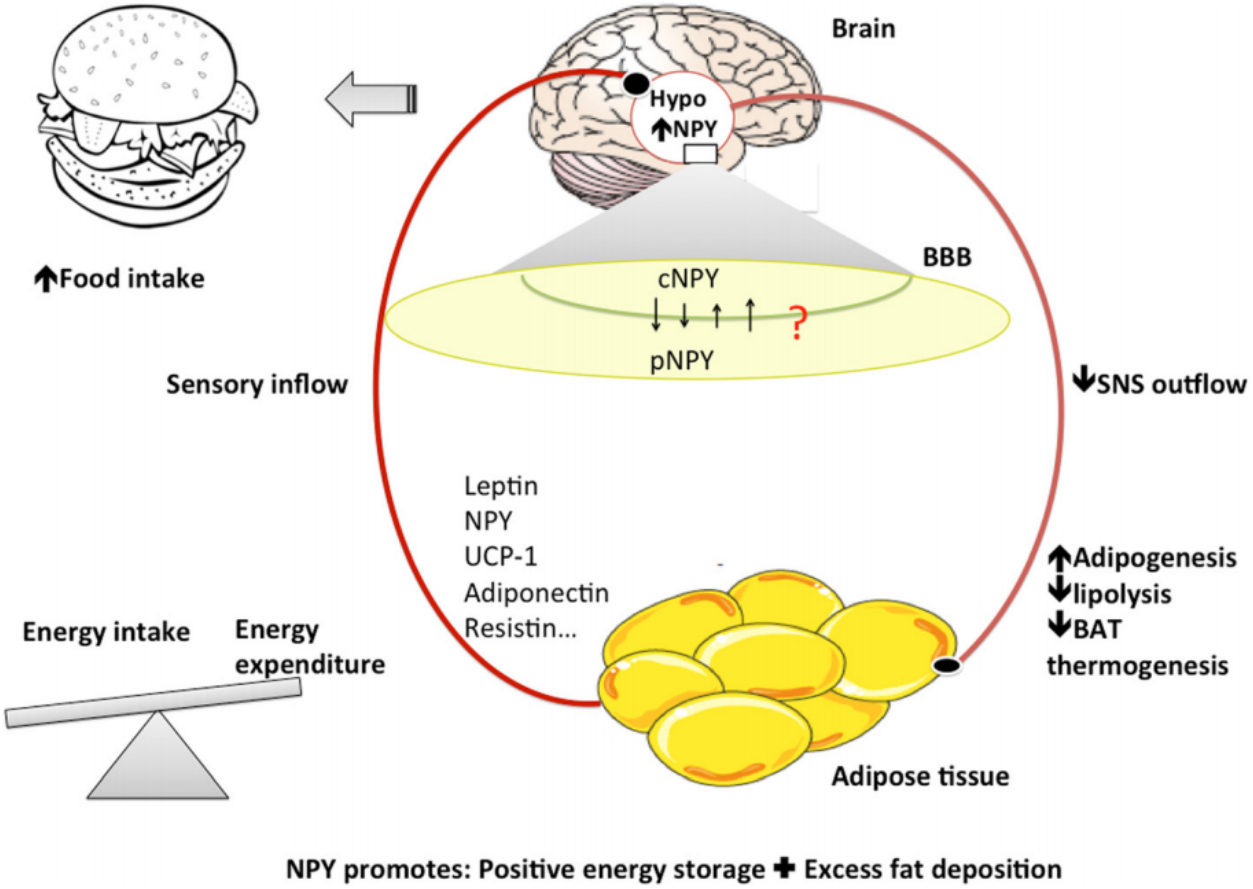


Figure 3 Role of NPY in energy intake and expenditure. cNPY: NPY in the central nervous system; pNPY: Peripheral NPY; BBB: Blood brain barrier; Hypo: hypothalamus. The cNPY stimulates food intake mainly via NPYR1 and NPYR5 to increase energy intake. Additionally, through the hypothalamus-SNS-adipose axis, NPY reduces sympathetic nervous system (SNS) outflow, which promotes white adipose tissue (WAT) deposition by enhancing adipogenesis and inhibiting lipolysis, as well as inhibiting brown adipose tissue (BAT) deposition and associated nonshivering thermogenesis. The same effects in WAT were achieved by peripheral NPY via different signaling pathways. This collectively leads to energy storage in adipose tissue. Adipose-hypothalamus crosstalk serves as a feedback loop via sensory inflow that informs the brain of the long-term peripheral energy status so that the brain can make the necessary adjustment. Numerous adipokines, hormones, and appetite regulating factors have been identified that play an important role in adjusting energy balance through the hypothalamus either by directly affecting food intake or regulating adiposity through SNS outflow, such as leptin, NPY, and UCP1. NPY is more abundant in the central nervous system as compared to the peripheral system. Whether and how it crosses the blood brain barrier is critical for understanding its role in energy regulation.

Ghrelin

- Zejména endokrinní buňky fundu žaludku (ale i jinde!) – interdigestivní fáze
- Signalizace „prázdného žaludku“ – aktivace pocitu hladu
- Změna vnímání náplně žaludku (mechanoreceptory)
- Protekce GIT (protizánětlivé účinky)
- Anabolické procesy spojené s příjmem potravy?
- Vliv na endoteliální funkce?
- Inhibice sekrece GnRH
- CNS: učení a paměť, délka spánku

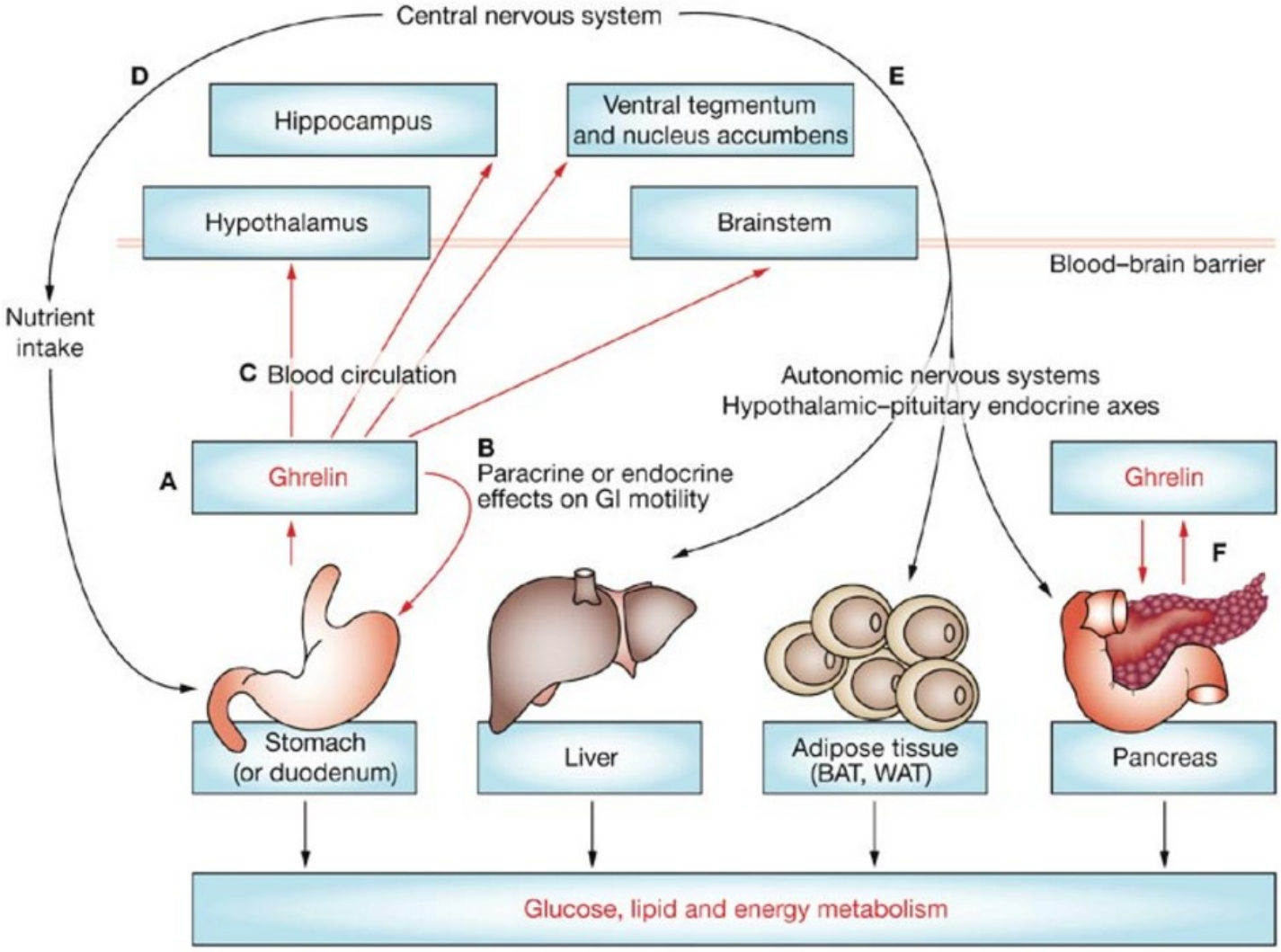
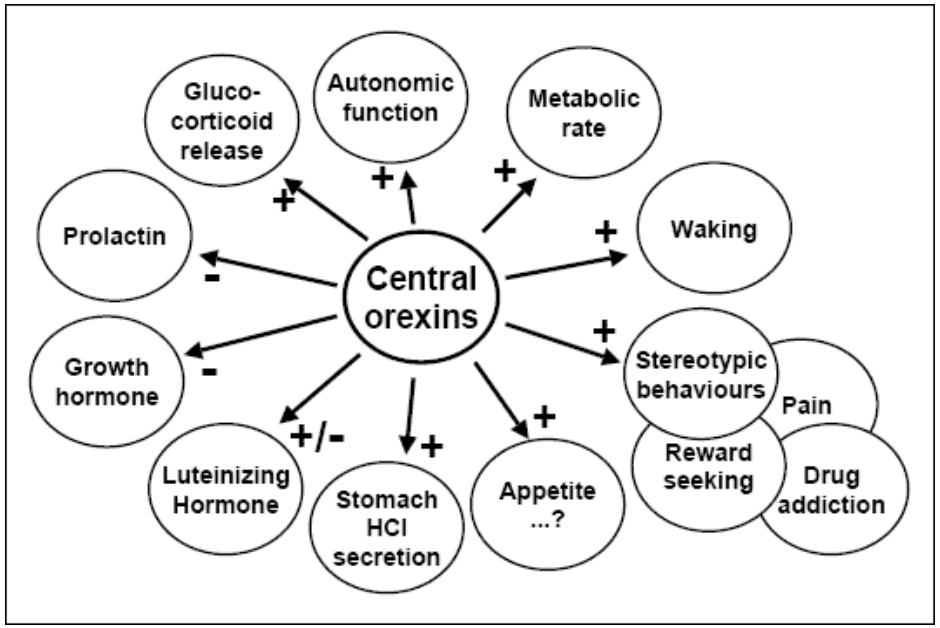
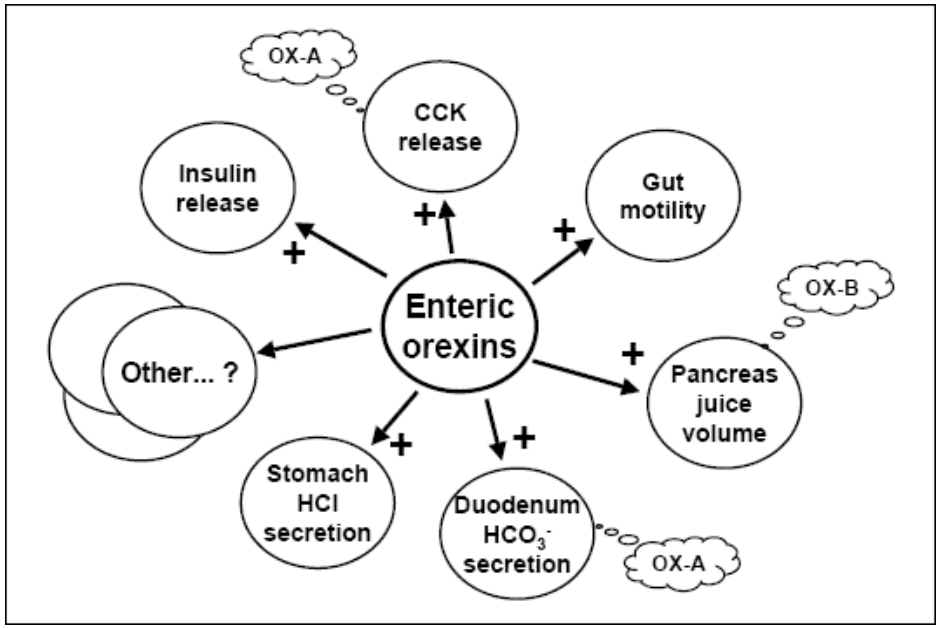


Figure 1. The effects of ghrelin on the CNS, and subsequent glucose, lipid and energy metabolism.
(**A**) Ghrelin is secreted mainly by the stomach, and can (**B**) have paracrine or endocrine effects on GI motility or (**C**) circulate in the blood and act on CNS growth hormone secretagogue receptors (GHS-Rs) inside and outside the blood–brain barrier. Known target areas in the CNS include the hypothalamus, the ventral tegmentum and nucleus accumbens, the hippocampus and GHS-R populations in the brainstem area. The actions of ghrelin in the CNS contribute (**D**) to the control of food intake and (**E**) co-regulate tissue-specific cellular pathways in the periphery, thereby governing glucose, lipid and energy metabolism. Control of peripheral metabolism by ghrelin and the CNS is mediated by the autonomic nervous system as well as the hypothalamic–pituitary endocrine axes. Apart from in the stomach, ghrelin is produced in a variety of peripheral tissues, although to a very low extent. (**F**) Paracrine ghrelin secretion from pancreatic cells might, however, be of importance for the inhibition of insulin secretion from β cells as well as for β-cell viability. Abbreviations: BAT, brown adipose tissue; CNS, central nervous system; GI, gastrointestinal; WAT, white adipose tissue.

Orexin A a B





- **Energetický metabolismus – příjem potravy**
- **také: kontrola spánku/bdění, funkce v GIT a kardiovaskulárním systému**
- **Významné modulátory endokrinních funkcí?**
- **Rytmicita některých procesů (Glu-játra)**
- **Termogeneze – hypo-/hypertermie, zejména s ohledem na spánek**
- **Narkolepsie**
- **Neuropsychiatrická onemocnění**

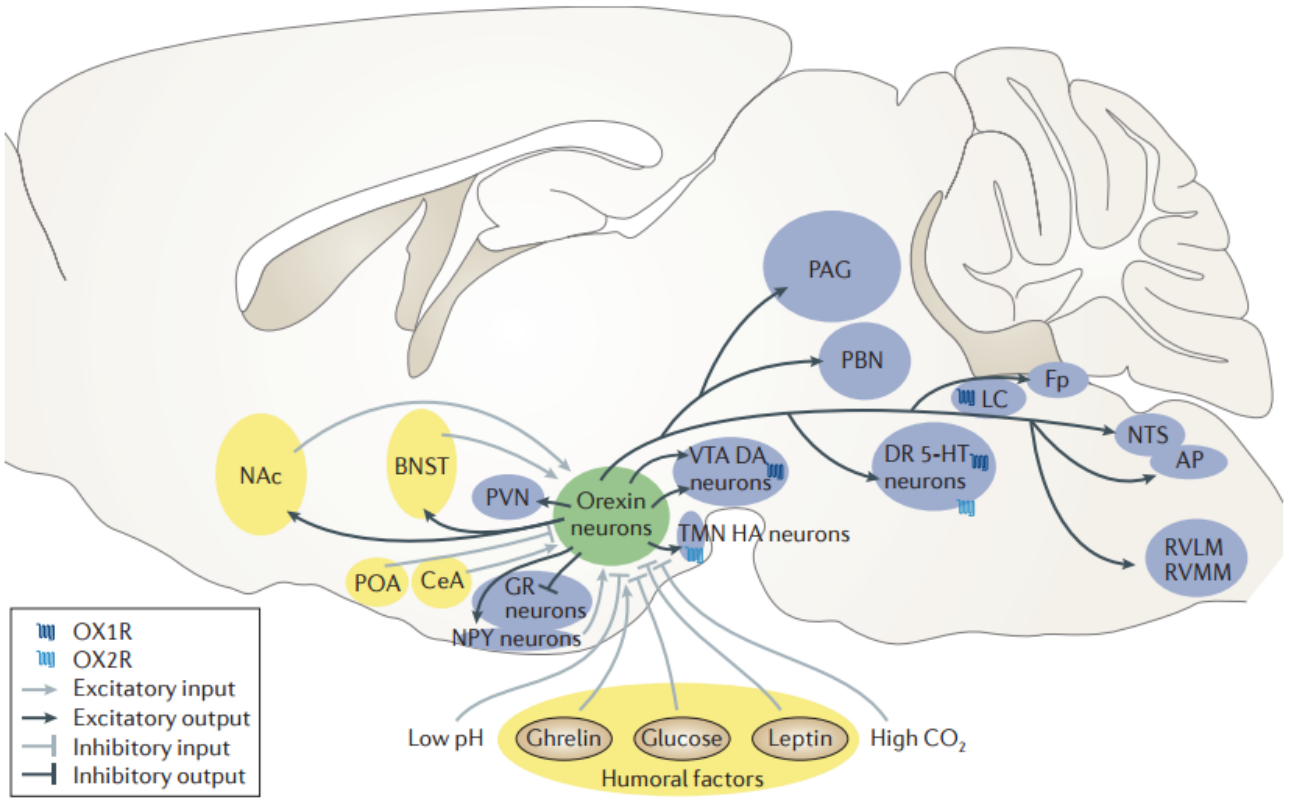


Figure 1 | **Input and output of orexin neurons.** Input areas are shown in yellow, output areas are shown in blue. Orexin neurons respond to salient cues or contexts, which are conveyed by projections from the nucleus accumbens (NAc) and limbic structures, such as the bed nucleus of the stria terminalis (BNST) and the central nucleus of the amygdala (CeA). Orexin neurons also monitor factors that reflect the metabolic state of the body, such as ghrelin, glucose and leptin, and their activity is further affected by CO_2 and pH levels. Orexin neurons send excitatory projections to various regions that are implicated in the regulation of feeding, including the NAc, nucleus of the solitary tract (NTS), paraventricular nucleus of the hypothalamus (PVN), neuropeptide Y (NPY) neurons in the arcuate nucleus and glucoreceptor (GR) neurons in the ventromedial hypothalamus. Orexin neurons also connect with autonomic regulatory regions to increase sympathetic outflow in response to salient cues or contexts. Connections between the NAc, orexin neurons and the ventral tegmental area (VTA) might have a role in the reward system. Perception of cues that predict reward might be conveyed by the connection between the NAc and orexin neurons, which send excitatory signals to dopamine (DA) neurons in the VTA. Orexin neurons also increase arousal to support motivated behaviour through connections between these cells and monoaminergic centres, including the dorsal raphe nuclei (DR), locus coeruleus (LC) and tuberomamillary nucleus (TMN). Note that 'excitatory' and 'inhibitory' do not necessarily indicate direct excitatory and inhibitory connections. 5-HT, 5-hydroxytryptamine (also known as serotonin); AP, area postrema; Fp, folium-p; HA, histamine; OX1R, orexin receptor type 1; OX2R, orexin receptor type 2; PAG, periaqueductal grey; PBN, parabrachial nucleus; POA, preoptic area; RVLM, rostral ventrolateral medulla; RVMM, rostral ventromedial medulla.

Melanin-concentrating hormone - MCH

- Laterální hypothalamus + zona incerta
- Příjem potravy – spánek/bdění – nálada

Table 1 Summary of results of key mammalian energy balance MCH studies.

Availability of MCH	Experimental intervention	Effect on food intake	Effect on locomotor activity and energy expenditure (EE)/metabolic rate (MR)	Effect on body weight (BW), % fat mass and % lean mass
Increased	Pharmacological/dietary	Hyperphagia/no effect	↓ Locomotor activity	↑ BW; ↑ fat
	Genetic manipulation	Hyperphagia	Not reported	↑ BW; ↑ fat
Decreased	Pharmacological/dietary	Hypophagia/no effect	Not reported	↓ BW; ↓ fat mass
	Genetic manipulation	Hypophagia/no effect/hyperphagia	↑ Locomotor activity; [a]no effect/↑ EE/MR	↓ BW; ↓ fat; no effect/↑ lean mass

Whilst manipulation of the availability of MCH has variable effects on food intake, the effects on locomotor activity/EE/MR and BW/% fat mass/% lean mass are consistent.
[a]Some effects were observed in males but not in females.

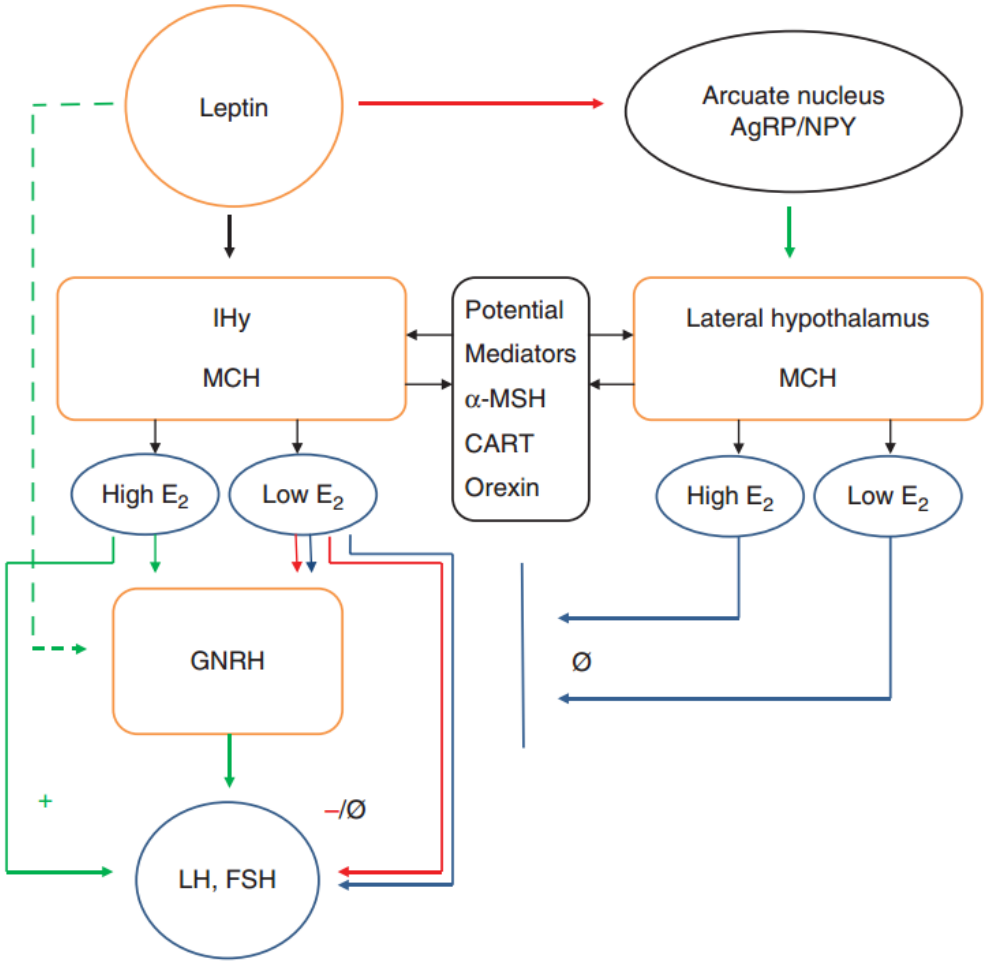
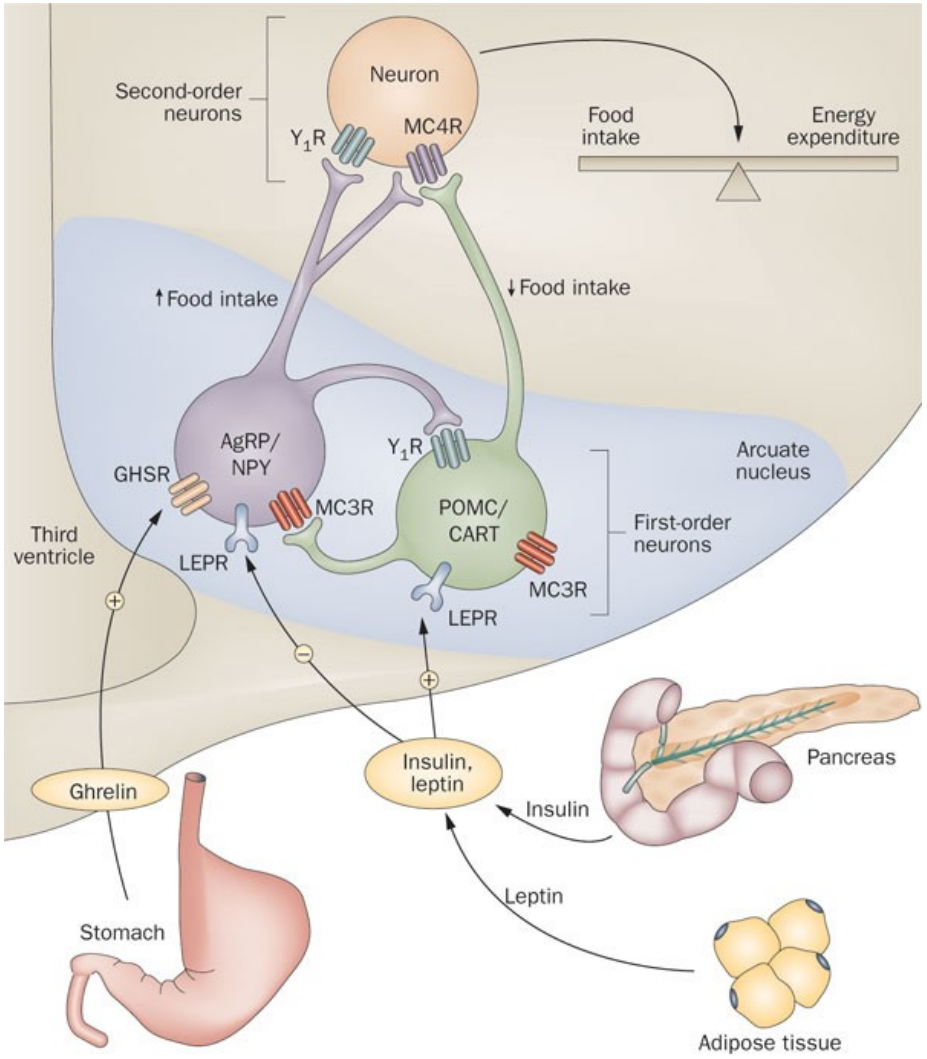


Figure 1 Distinct MCH neuronal populations in the LHA receive peripheral input from leptin via orexigenic AgRP/NPY neurones in the arcuate nucleus. LHA MCH neurones communicate with MCH neurones in the IHy directly or indirectly via inter-neurones (examples of potential mediators are given). The IHy MCH neurones exert stimulatory or inhibitory effects on GNRH, LH and FSH depending on the presence or absence of oestrogen. There is no evidence to date that the MCH neuronal populations of the LHA have a direct role in the reproductive axis, while there is evidence that the MCH cell bodies of the IHy may modulate reproductive function (e.g. electrolytic and chemical lesioning of the IHy disrupts the oestrous cycle: MacKenzie *et al.* (1988)). Red arrows, inhibitory; green arrows, stimulatory; blue arrows, no effect; Ø, no effect; α-MSH, α-melanocyte-stimulating hormone; CART, cocaine-and-amphetamine-related transcript. IHy, rostral zona incerta/incertohypothalamic area.

ARP - agouti-related peptide

- Ventromediální část nucleus arcuatus - koexprese s NPY
- I jiné tkáně (nadledviny, plíce, ledviny, varlata, atd.)
- Receptory pro melanokortin (3, 4)
- Výrazně orexigenní + snížení metabolismu a výdeje energie
- ! Jeden z nejsilnějších *dlouhodobých* orexigenních faktorů

- + ACTH
- - tyreoliberin



Galanin

- Orexigenní – CNS + GIT (duodenum, žaludek, ileum, colon)
- Nocicepce, regulace spánku/bdění, regulace příjmu potravy a některých kognitivních funkcí
- Význam u některých chorob (neurodegenerativní) a u poškozen nervové tkáně
- Diabetes typu 2 (inzulínová rezistence)

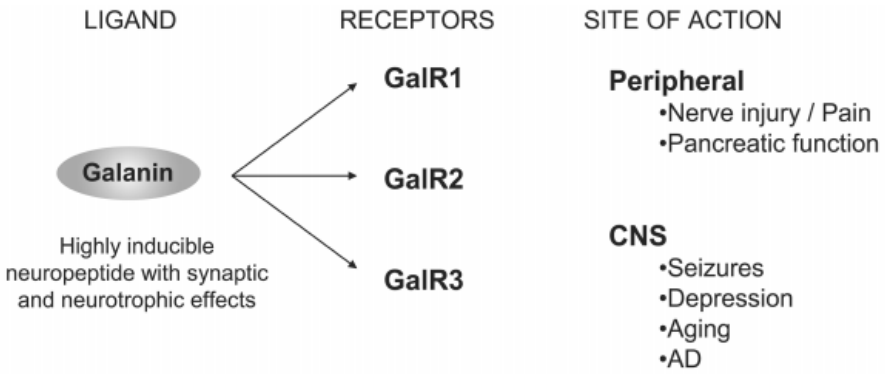
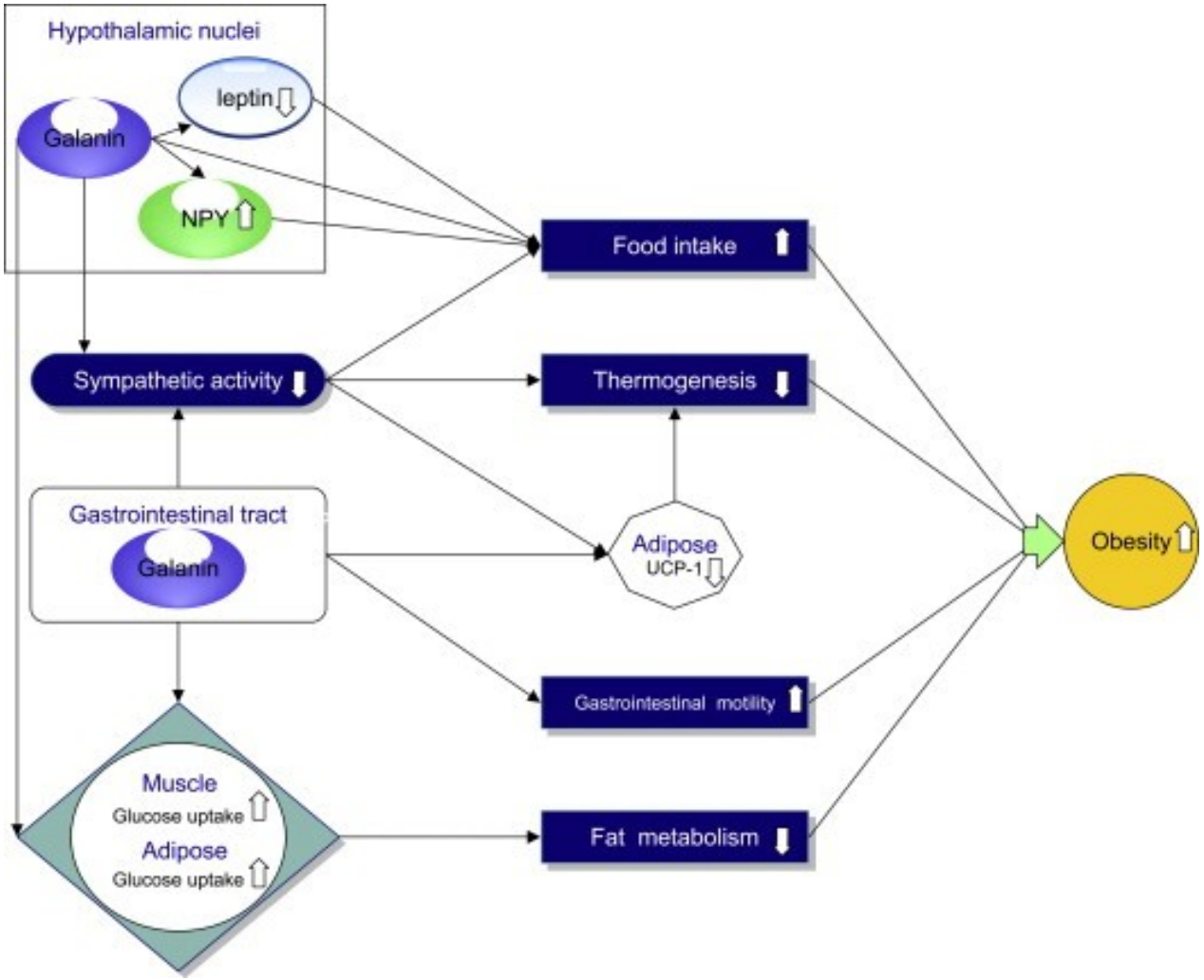


Fig. 1. Galanin is a highly inducible neuropeptide, mediating its synaptic and neurotrophic effects via three G-protein coupled receptors, GalR1-3. Galanin and its receptors show a widespread distribution, both in the central and the peripheral nervous system and galanin has shown to play a role in several physiological functions such as nerve injury, nociception, pancreatic functions, cognition, mood regulation, aging, AD and seizures. Regionally specific expression of the galanin receptors are suggesting different physiological roles.


Hypothalamic nuclei
leptin
Galanin
NPY
Food intake
Sympathetic activity
Thermogenesis
Gastrointestinal tract
Galanin
Adipose
UCP-1
Obesity
Gastrointestinal motility
Muscle
Glucose uptake
Adipose
Glucose uptake
Fat metabolism

Cukry – fruktóza

- Mechanismus závislý na dostupnosti ATP

PNAS

Differential effects of central fructose and glucose on hypothalamic malonyl–CoA and food intake

Seung Hun Cha[a], Michael Wolfgang[a], Yuka Tokutake[b], Shigeru Chohnan[b], and M. Daniel Lane[a,1]

[a]Department of Biological Chemistry, The Johns Hopkins University School of Medicine, Baltimore, MD 21205; and [b]Department of Bioresource Science, College of Agriculture, Ibaraki University, Ibaraki 300-0393, Japan

Contributed by M. Daniel Lane, September 18, 2008 (sent for review September 2, 2008)

The American diet, especially that of adolescents, contains highly palatable foods of high-energy content and large amounts of

AMP ⇆ ADP + ADP) (13, 14). Because AMP is an activator of AMP kinase (AMPK), a drop in AMP level causes the dephos-

$$\text{Glucose} \rightarrow \Uparrow[\text{ATP}] \rightarrow \Downarrow[\text{AMP}] \rightarrow \underset{(inactive)}{\text{dephospho-AMPK}} \rightarrow$$

$$\underset{(active)}{\text{dephospho-ACC}} \rightarrow \Uparrow[\text{malonyl-CoA}] \rightarrow \Downarrow \text{food intake.}$$

In contrast to the anorexigenic effect of centrally administered glucose, fructose exerts an orexigenic effect (ref. 8 and Fig. 7).

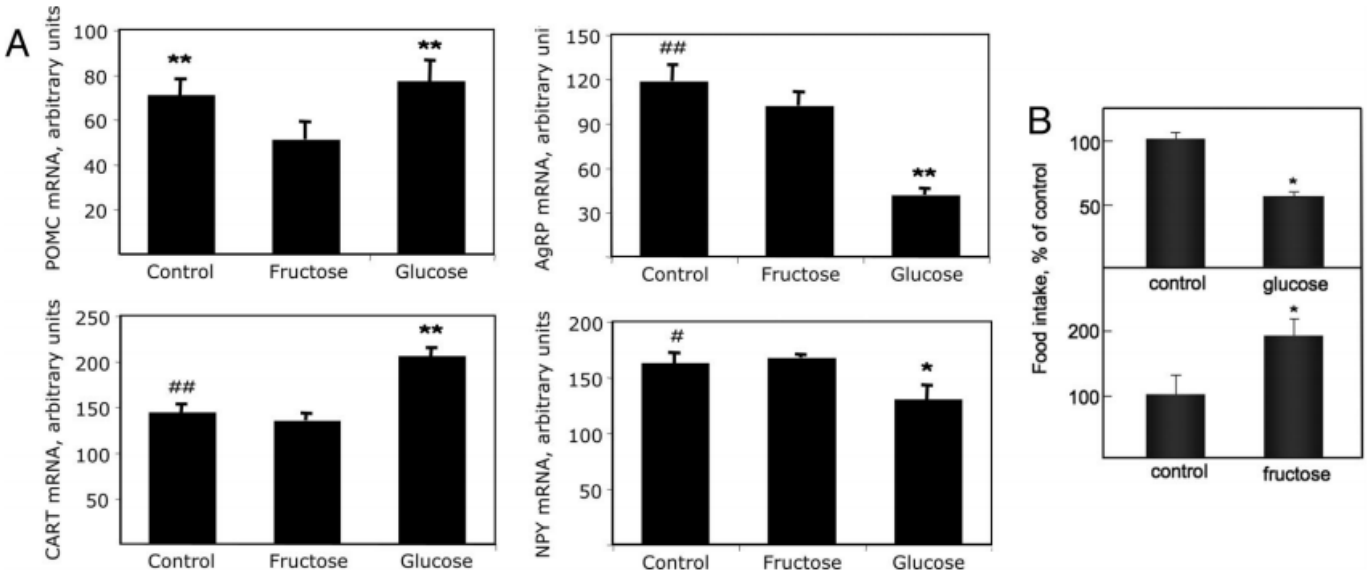


Fig. 7. Effect of i.c.v. injection of fructose and glucose on neuropeptide mRNA expression and food intake. Food-deprived mice were given i.c.v. injections (400 μg/2 μl) of fructose or glucose ($n = 4$ mice per group). (*A*) After 10 min hypothalami were removed, RNA was isolated, and mRNA content was determined as described (9, 16). **, $P < 0.01$; *, $P < 0.05$ versus fructose; ##, $P < 0.01$; #, $P < 0.05$ versus glucose. (*B*) Mice were given access to food and food intake measured over the next 30 min ($n = 4$ mice per group). *, $P < 0.01$ versus control.

CART - Cocaine- and amphetamine-regulated transcript

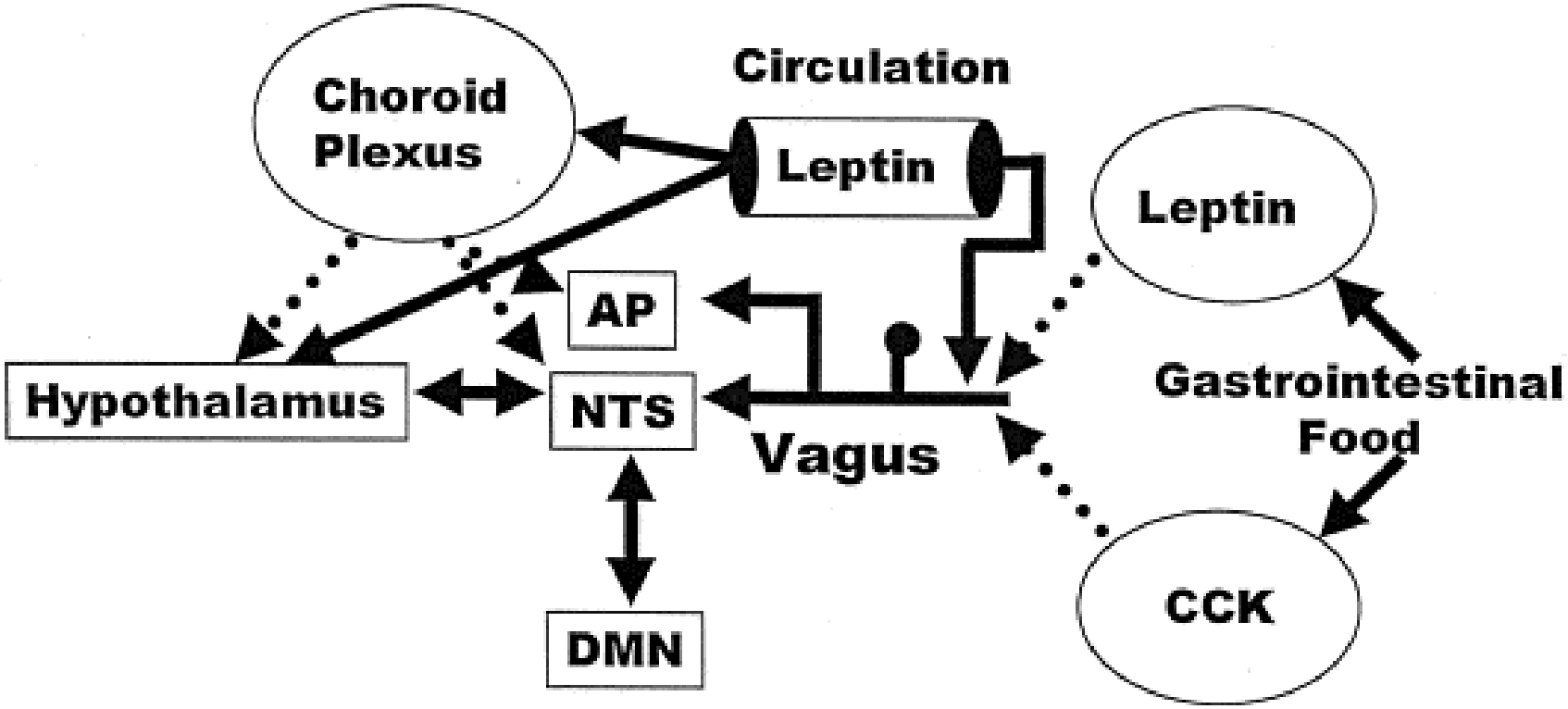
- Název?
- Nejen hypothalamus (také např. GIT)
- Systém odměny, nálada, stress, endogenní psychostimulant
- Pocity úzkosti ve vztahu k návykovým látkám?

- Stimulace metabolismu tuků směrem k mobilizaci tuků
  - mRNA signifikantně zvýšena u jedinců s vysokým obsahem tuků v potravě
  - Zvýšení rovněž i u obézních jedinců
  - Úzký vztah k leptinu (pozitivní korelace)

CCK

- Zpětnovazebná kontrola GIT
  - Krátkodobá inhibice vyprazdňování žaludku a sekrece HCl
  - Stimulace sekrece pankreatické šťávy a žluče
  - Anorexigenní efekt – efektivní trávení?

- CCK receptory v mozku (CCK-A/B) – area postrema
- Periferní CCK receptory (CCK-A)
- CCK-B antagonisté a potlačení pocitu sytosti
- Další specifické funkce, např. ve vztahu k inzulínu (transport přes HEB)



Leptin a CCK – integrace krátko- a střednědobých signálů do dlouhodobé kontroly energetické bilance organismu

STAV VÝŽIVY - VYŠETŘOVACÍ METODY

METODY ANTROPOMETRICKÉ

Inspekce
Tělesná hmotnost (kg)
BMI
Obvod pasu, poměr pas-boky
Určení procenta tělesného tuku (kaliper, impedanční metoda, densitometrie, CT)
Určení ATH (aktivní tělesná hmotnost, %, vážení pod vodou)
Měření objemu velkých svalových skupin

METODY BIOCHEMICKÉ

Celková dusíková bilance
Odpad dusíku močí
Stanovení plazmatických hladin bílkovin
Inkorporace AMK
Určení prealbuminů, transferinu
Vylučování vitamínů nebo jejich metabolitů

METODY IMUNOLOGICKÉ

VÝŽIVA

RACIONÁLNÍ

ZVLÁŠTNÍ VÝŽIVOVÉ SMĚRY

HLEDISKO: evoluční
náboženské
historické

POŽADAVKY RACIONÁLNÍ VÝŽIVY

- Kvantitativní
- Kvalitativní
- Nadstavbový
- Estetický
- Ekonomický

Esenciální složky potravy:
AMK, MK, stopové prvky

Aspekt výživových zvyklostí: kulturně-historický
sociálně-ekonomický

OBEZITA (OTYLOST)

Patologické zvýšení tělesné hmotnosti podmíněné nadměrným hromaděním tělesného tuku a doprovázené řadou závažných komplikací.

INCIDENCE

2008 v ČR: **52%** populace s vyšší hmotností těla (35% nadváha, 17% obezita), nad 45 let – jen 30% populace s normální hmotností (muži – 72% vs. ženy – 60%)

Narůstá procento obézních dětí!!! (**2014**: 24% hoši, 23% dívky)

TYPY OBEZITY:

ALIMENTÁRNÍ (EXOGENNÍ)
SEKUNDÁRNÍ, SYMPTOMATICKÁ

DŮVODY PŘEJÍDÁNÍ

Rodinné zvyklosti vs. GENETIKA???
Jídlo zdarma
Psychické poruchy (deprese, poruchy příjmu potravy)
Náboženské důvody
Frekvence obezity přímo úměrná stupni vzdělání

TABLE 227-1 CLASSIFICATION OF OVERWEIGHT AND OBESITY BY BODY MASS INDEX

	OBESITY CLASS	BMI KG/M^2
Underweight		<18.5
Normal		18.5-24.9
Overweight		25.0-29.9
Obesity	I	30.0-34.9
Obesity	II	35.0-39.9
Extreme obesity	III	≥40

- **Genetické příčiny obezity:**
  - ***LEP* gen, příslušný receptor!**
  - ***FTO* gen (*fused toes and other abnormalities*, diabetes 2. typu, obezita)**
  - **melanocortin-4 receptor *(MC4R)***
  - ***TMEM18, KCTD15, GNPDA2, SH2B1, MTCH2, NEGR1***

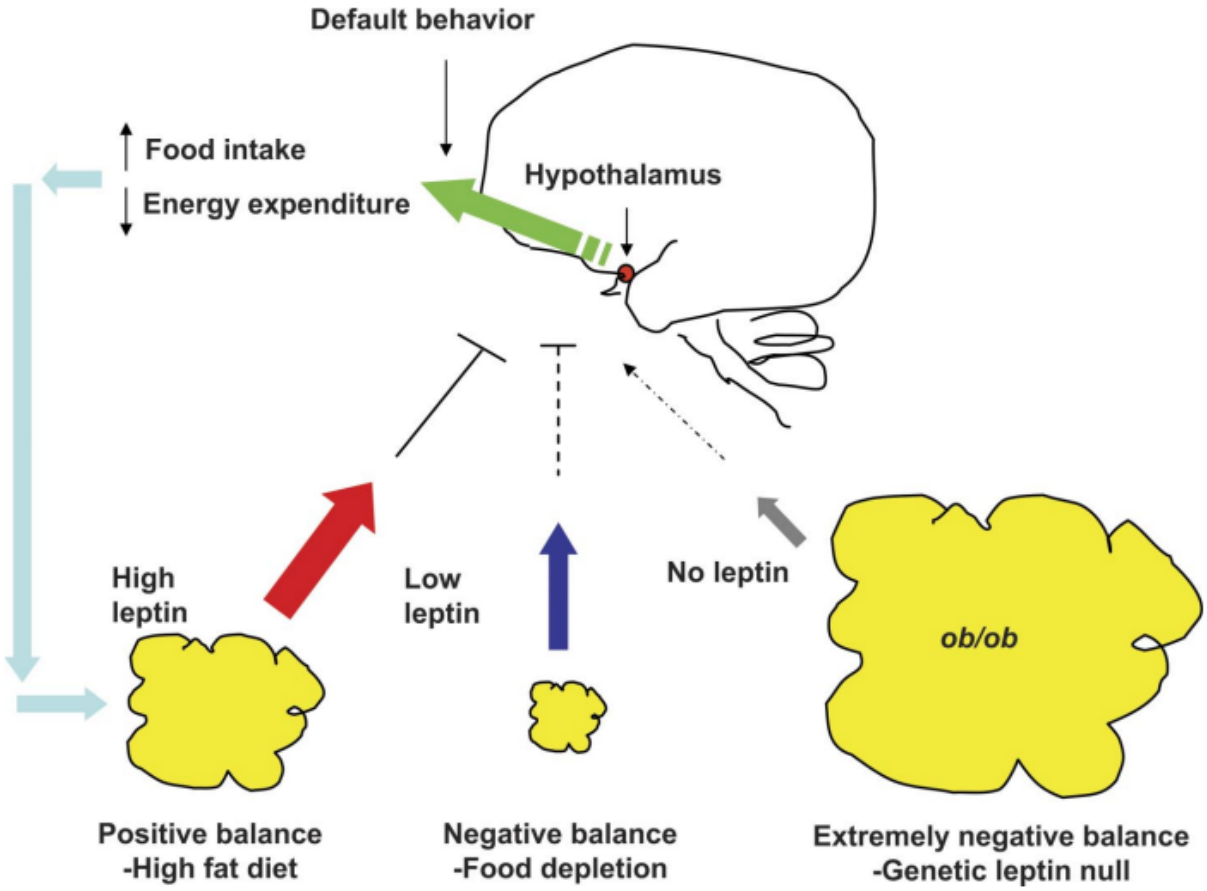


Fig. 1. Obesity is a state of negative energy balance. Body energy levels are detected by hypothalamic neurons through measuring of leptin levels in circulation. When leptin levels are low, due to either food depletion or leptin signaling deficiency (*ob/ob*), the inhibition of leptin to hypothalamic feeding and metabolic circuits is released, and the default activity of these systems promotes feeding and restricts energy expenditure.

TABLE 227-5 PHARMACOLOGIC INFLUENCES IN WEIGHT GAIN AND ALTERNATIVE THERAPIES

DRUGS THAT MAY PROMOTE WEIGHT GAIN	ALTERNATIVE TREATMENTS—WEIGHT NEUTRAL OR WEIGHT LOSS
PSYCHIATRIC AND NEUROLOGIC MEDICATIONS	**ALTERNATIVE PSYCHIATRIC AND NEUROLOGIC MEDICATIONS**
Antipsychotics: olanzapine, clozapine, respiridone, quetiapine, aripiprazole	Ziprasidone
Antidepressants	Nortriptyline, bupropion, nefazodone, fluvoxamine, sertraline, duloxetine
Tricyclics: imipramine, amitriptyline	Topiramate, zonisamide (weight loss), lamotrigine (less weight gain)
Triazolopyridines: trazodone	
Serotonin reuptake inhibitors: paroxetine, fluoxetine, citalopram	
Tetracyclics: mirtazapine	
Monamine oxidase inhibitors	
Antiepileptic drugs: gabapentin (higher doses), valproic acid, carbamazepine, divalproex	
Mood stabilizers: lithium, carbamazepine, lamotrigine, gabapentin (higher doses)	
STEROID HORMONES	**ALTERNATIVES TO STEROID HORMONES**
Progestational steroids	Barrier methods, IUD
Corticosteroids	Nonsteroidal anti-inflammatory drugs
Hormonal contraceptives	
ANTIDIABETES AGENTS	**ALTERNATIVE ANTIDIABETES AGENTS**
Insulin (most forms)	Metformin
Sulfonylureas	Acarbose, miglitol
Thiazolidinediones	Exenatide
	DPP-4 inhibitors
ANTIHISTAMINES	**DECONGESTANTS, MAST CELL STABILIZERS, ANTAGONISTS OF ENDOGENOUS MEDIATORS OF INFLAMMATION**
Commonly reported with older agents; also oxatomide, loratadine and azelastine	
ANTIHYPERTENSIVE AGENTS	**ALTERNATIVE ANTIHYPERTENSIVE AGENTS**
α-Adrenergic and β-adrenergic receptor blockers	Angiotensin-converting enzyme inhibitors,
Calcium channel blockers: nisoldipine	Calcium channel blockers—most other agents
	Angiotensin receptor blockers
	Diuretics
HIGHLY ACTIVE ANTIRETROVIRAL THERAPY	

PROBLÉMY SPOJENÉ S OBEZITOU

1. Nepřitažlivý vzhled (společenská izolace, problémy v partnerství, problémy s vyhledáním zaměstnání)
2. Ekonomická zátěž (jedince - zvýšené výdaje za potraviny, společnosti – výdaje zdravotních pojišťoven)
3. Předčasné opotřebení kloubů (kolena, kyčle, páteř)
4. Varixy, trombózy, embolizace
5. Diabetes mellitus
6. Poruchy lipidového metabolismu
7. Hypertenze
8. Srdeční infarkt
9. Mozková mrtvice
10. Zhoubné nádory !!!!!
11. Poruchy fertility (potence, cyklu)

+ RIZIKOVÉ CHOVÁNÍ

Tlustí lidé umírají dříve, mají těžší život a trpí množstvím nepříjemných chorob

Metabolický syndrom

Metabolický syndrom

- jedna z nejčastějších příčin morbidity a mortality populace
- Definice
  - obvod pasu nad 102/88 cm
  - TG v plazmě na 1,7 mmol/l
  - HDL v plazmě pod 1 mmol/l
  - TK 130/85 a vyšší
  - Gly nalačno nad 6,1 mmol/l

INZULINOVÁ REZISTENCE

- NAFLD (steatóza jater) je považován za jaterní manifestaci metabolického syndromu

METABOLIC SYNDROME

nature medicine

Definition (IDF):
Central obesity
(usually BMI > 30 kg/m2),
plus 2 of the following:
- TGs > 150 mg/dL
- HDL < 40-50 mg/dL
- ↑ blood pressure
- hyperglycemia

Food intake >>
energy needs

Abnormal hedonic response

Abnormal homeostatic response

Abnormal satiety

Abnormal nutrient sensing

Abnormal central regulation of systemic metabolism:
- Disrupted endocrine hormone axis (HPT)
- Dysregulated efferent autonomic nervous system

Dysregulated afferent autonomic nervous system

Abnormal liver function:
- Hepatic glucose output ↑
- Glucose uptake ↑↑ (& conversion into lipids)
- Fatty acid uptake ↑↑ (& ↑ conversion into TGs and VLDL and their release into the blood stream)

Systemic glucotoxicity

Fatty liver disease

Heart disease

Pancreatic hormones:
Glucagon ↑
Insulin ↑ (but with resistance)

Pre-diabetes, followed by overt diabetes

Pancreatic islet mass ↑, followed by exhaustion

Dietary nutrients ↑↑

Abnormal gastrointestinal activity:
- Dietary fats & sugar absorption ↑
- Gut motility ↑
- Alterations in gut microflora, contributing to metabolic disease

Gut hormones:
CCK
Ghrelin
PYY
ECs ↑
GLP-1 ↓
GIP

Incretin action ↓:
- stimulates insulin release
- inhibits glucagon release
- increases insulin sensitivity
- effects on gut motility

Systemic low-grade inflammation

Abnormal visceral adipose tissue function:
- Glucose uptake ↓ (& conversion into lipids & stored as fat)
- Lipid uptake ↑↑ (& stored as fat)
- Lipolysis ↑ (release of fatty acids into the blood stream)

Net result:
Increased fat storage & fat tissue hypertrophy

↓ Anti-inflammatory &
↑↑ pro-inflammatory cytokines

Adipose tissue hormones:
- Leptin ↑ (but with resistance)
  satiety ↓
  energy expenditure ↓
  immune dysregulation
  angiogenesis dysregulation
  subfertility
  bone dysfunction
- Adiponectin ↓
  gluconeogenesis ↑
  glucose uptake ↓
  insulin sensitivity ↓
  body weight ↑
  endothelial function ↓

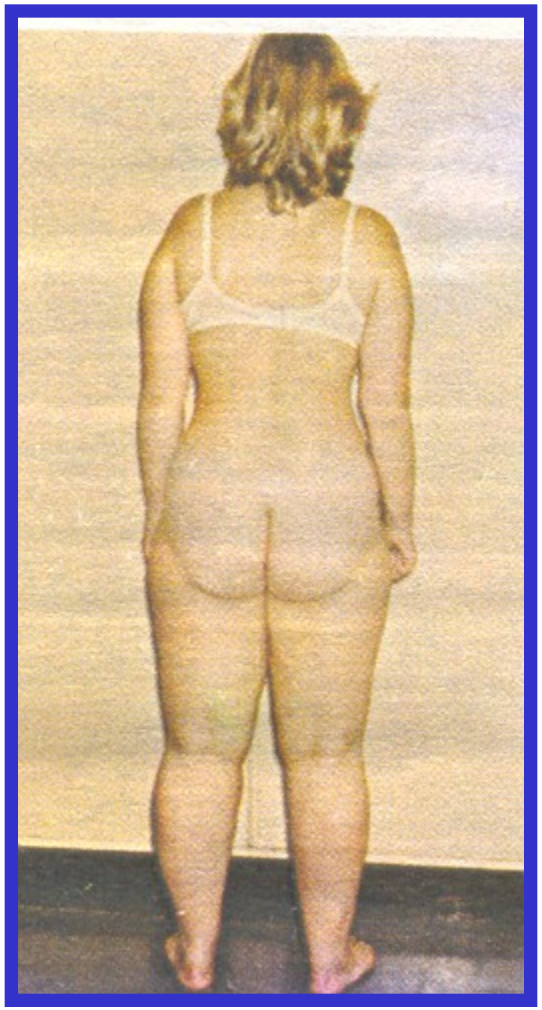
Systemic lipotoxicity

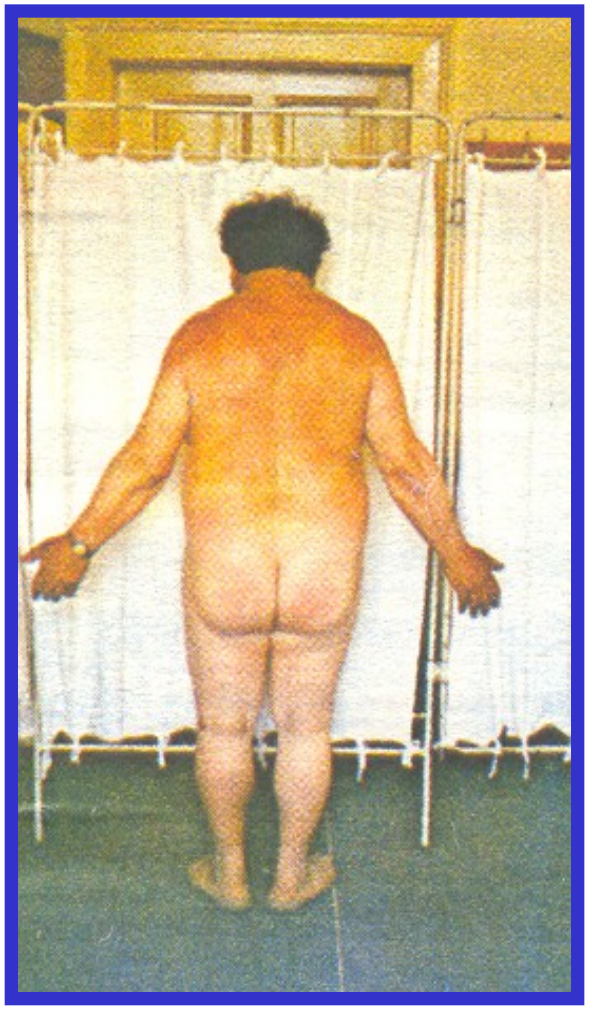
Abnormal muscle function:
- Glucose uptake ↓
- Fatty acid uptake ↑↑

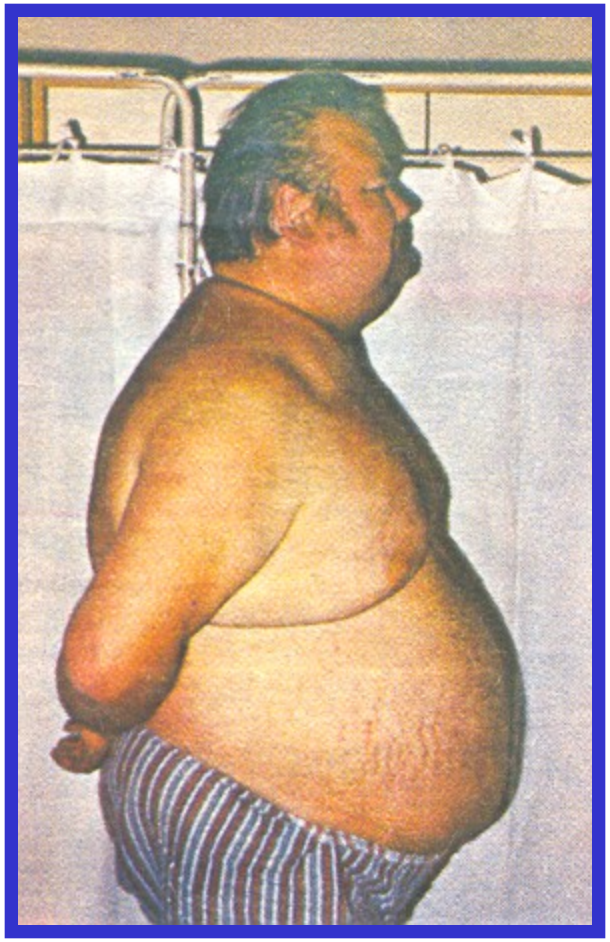
Complications of Chronic Diabetes:
- chronic kidney disease
- cardiovascular disease
- peripheral nerve damage
- eye disease & blindness
- non-healing skin ulcers, usually leading to amputations
- non-alcoholic fatty liver disease, which can lead to cirrhosis

ROZLOŽENÍ TUKU

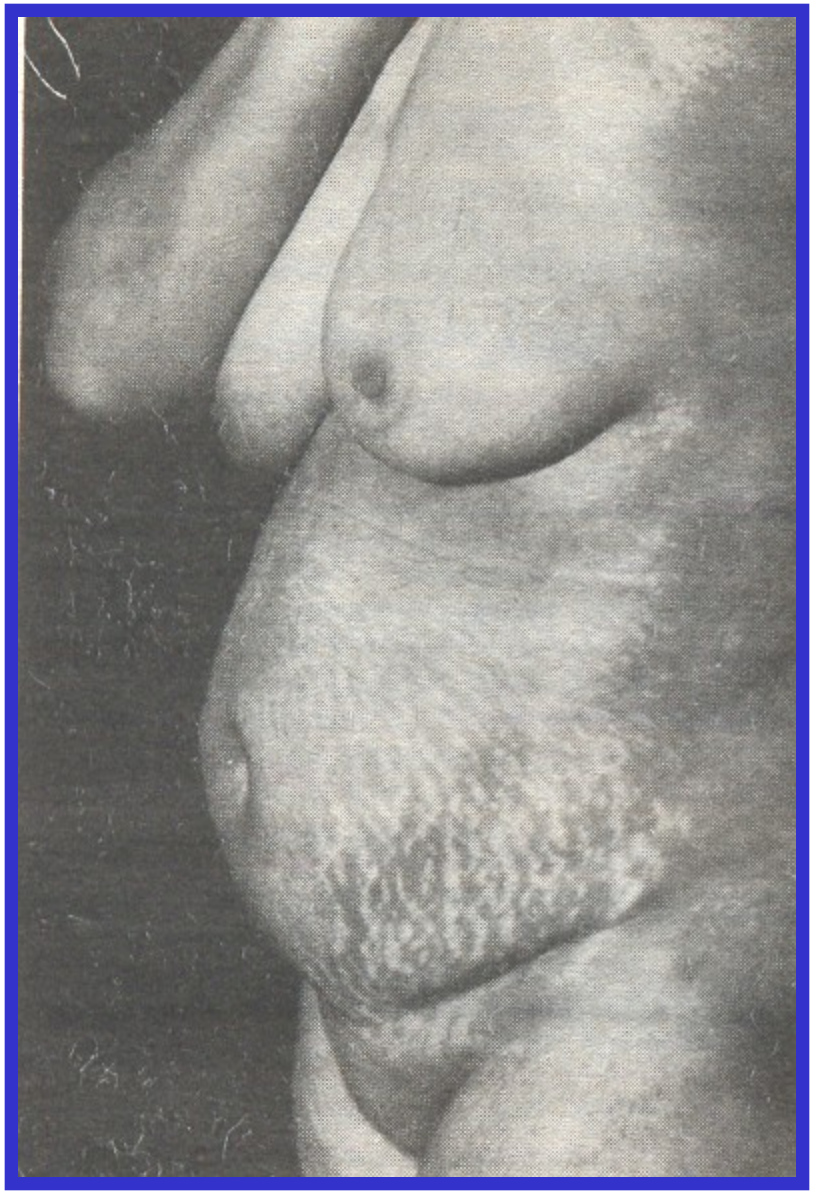
- Difuzní (plíživý nástup obezity)
- Androidní (vysoká frekvence DM – typ „jablko“)
- Gynoidní (typ „hruška“), zvláštní typ - steatopygie







Madelungův límec



Strie

SEKUNDÁRNÍ OBEZITA

Nejčastější příčiny:

- **Hyperkotizolismus**
- **Mužský hypogonadismus**
- **Prolaktinom**
- **Hypotalamická obezita**

TERAPIE OBEZITY

PREVENCE

1. Omezení příjmu energie potravou

U mužů pod 11 tis.kJ/den, u žen – pod 8 tis.kJ/den
Omezit sacharidy (INZ – antilipofilický hormon), omezit lipidy (občas tukový den).
Vynechat: sůl, koření, kávu, alkohol.

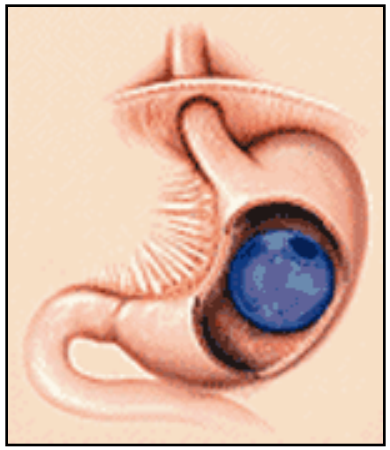
2. Zvýšení výdeje energie pohybem

Aktivita vyvolávající zvýšení TF na 140-150/min.
Cyklické, švihové pohyby (základní gymnastika).
Omezeně plavání.

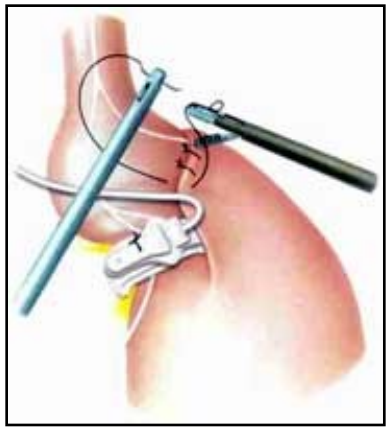
3. Doplňkové metody

Anorektika - farmakoterapie
Hormony štítné žlázy
Lázně
Psychoterapie
Chirurgické zásahy – BARIATRICKÁ CHIRURGIE

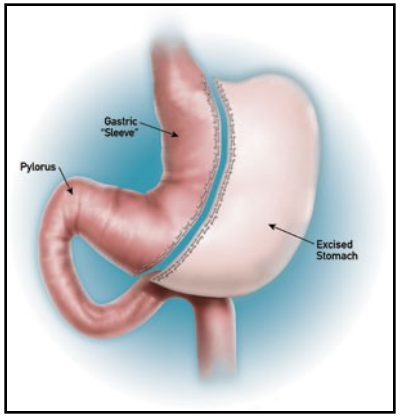
„METABOLICKÁ CHIRURGIE“



INTRAGASTRICKÝ BALONEK



BANDÁŽ ŽALUDKU



SLEEVE-RESEKCE ŽALUDKU