msu
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Physiological Basis of Control of Appetite and Body Weight

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- Regulation of food intake
- Regulation of energy balance
- Clinical importance

WHY DO WE EAT

- **Hunger**
  - Physiological (internal) drive to eat
  - The feeling that prompts thought of food and motivates food consumption
  - Influenced by nutrients in the bloodstream, eating patterns, climate, etc
  - Controlled internally

WHY DO WE EAT

Appetite

- Psychological (external) drive to eat
- Often in the absence of hunger
- Often of particular type of food
- Combination of internal and external signals drive us to eat
- Appetite is affected by a variety of external forces
- Not a perfect system; desire to eat can be overwhelming

WHY WE EAT

SATIETY

If the quest for food is successful the brain signals the body to stop eating (hunger is suppressed).

Sustaining Hunger and Satiety

- Protein --- most satiating
- Complex carbohydrates --- satiating
- Fat --- stimulate and entice people to eat more

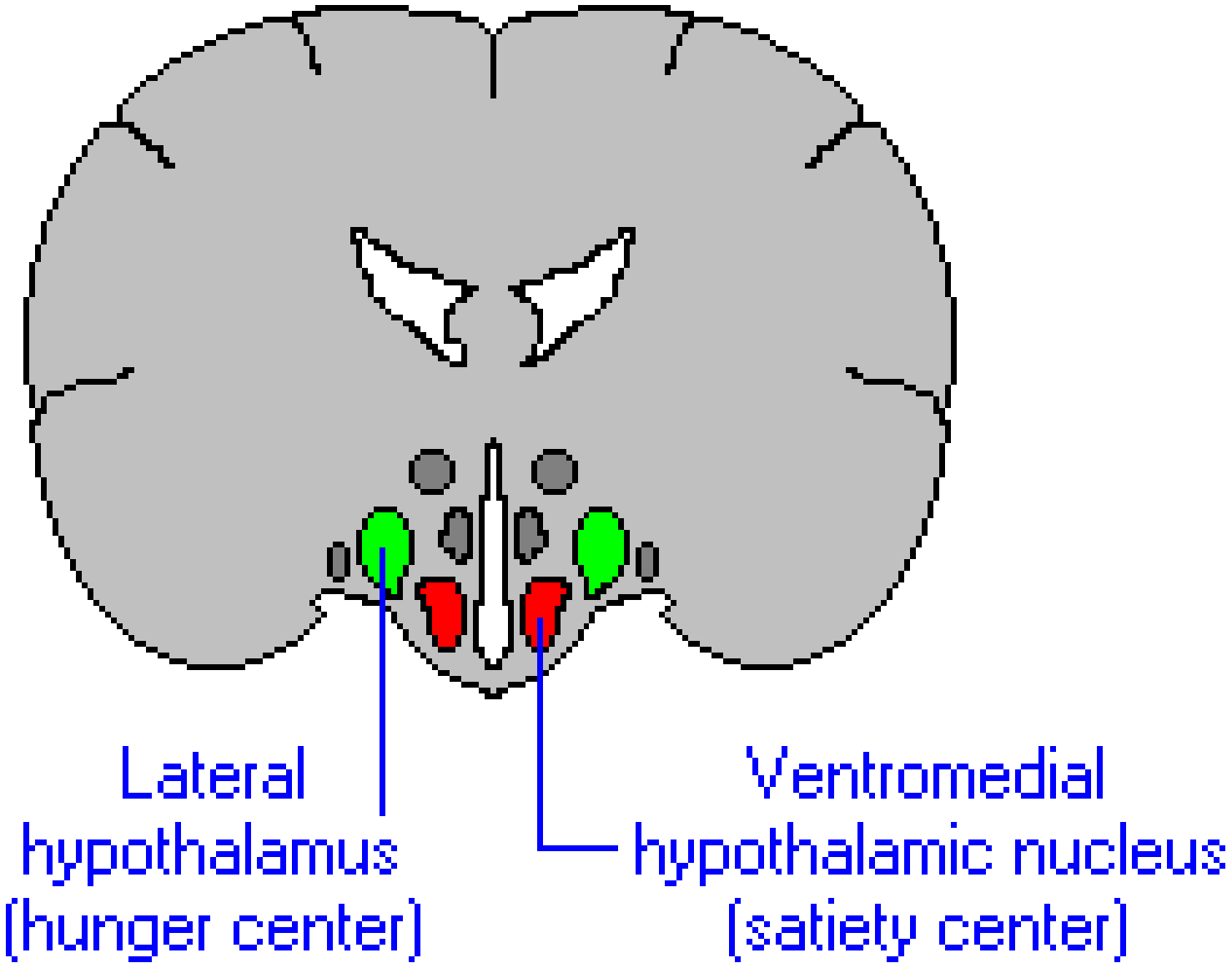
Four Types of Input to the Hypothalamus

Hypothalamus contains **HUNGER** and **SATIETY** centre

Paraventricular, Dorsomedial, and Arcuate nuclei of the

Hypothalamus also play a major role

- Neural input from the cerebral cortex
- Neural input from the limbic system
- Peptide hormones from the GI tract
- Adipocytokines from adipose tissue


Lateral
hypothalamus
(hunger center)
Ventromedial
hypothalamic nucleus
(satiety center)

HUNGER AND SATIETY CENTRE

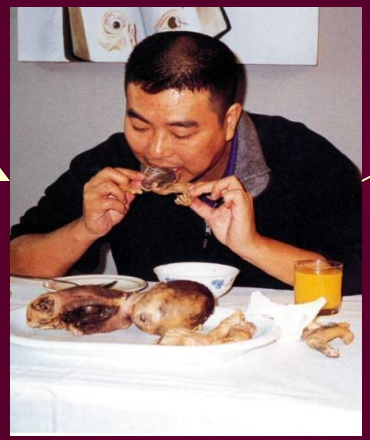
FEEDING CENTRE

SATIETY CENTRE

LATERAL NUCLEI OF HYPOTHALAMUS

INHIBITION

VENTROMEDIAL NUCLEI OF HYOTHALAMUS



FOOD INTAKE

Control of Food Intake and Energy Balance

- Food intake
  - Primarily controlled by hypothalamus
    - Appetite center
      - Signals give rise to hunger and promote eating
    - Satiety center
      - Signals lead to sensation of fullness and suppress eating
- Arcuate nucleus of hypothalamus
  - Contains two clusters of appetite regulating neurons
    - Neurons that secrete **neuropeptide Y (NPY)**
      - Increases appetite and food intake
    - Neurons that secrete **melanocortins**
      - Suppress appetite and food intake

Control of Food Intake and Energy Balance

- **Adipocytes**
  - Secrete hormone leptin
    - One of the most important adipokines
    - Reduces appetite and decreases food consumption

- **Insulin**
  - Hormone secreted by pancreas in response to rise in glucose concentration
- **Ghrelin**
  - Hunger hormone
  - Appetite stimulator produced by stomach and regulated by feeding status
  - Stimulates the hypothalamic NPY-secreting neurons

Control of Food Intake and Energy Balance

- PYY_{3-36}
  - Produced by small and large intestines
  - At lowest level before meal
  - Rises during meals and signals satiety
  - Believer to be an important mealtime terminator
- Lateral hypothalamus area (LHA)
  - Secretes orexins
    - Strong stimulators of food intake
- Paraventricular nucleus (PVN)
  - Releases neuropeptides that decrease food intake

Control of Food Intake and Energy Balance

- Nucleus tractus solitarius (NTS)
  - In brain stem
  - Serves as satiety center
  - Plays key role in short-term control of meals
- Psychological and environmental factors can also influence food intake above and beyond internal signals that control feeding behavior

Many Peptides Alter Food Intake

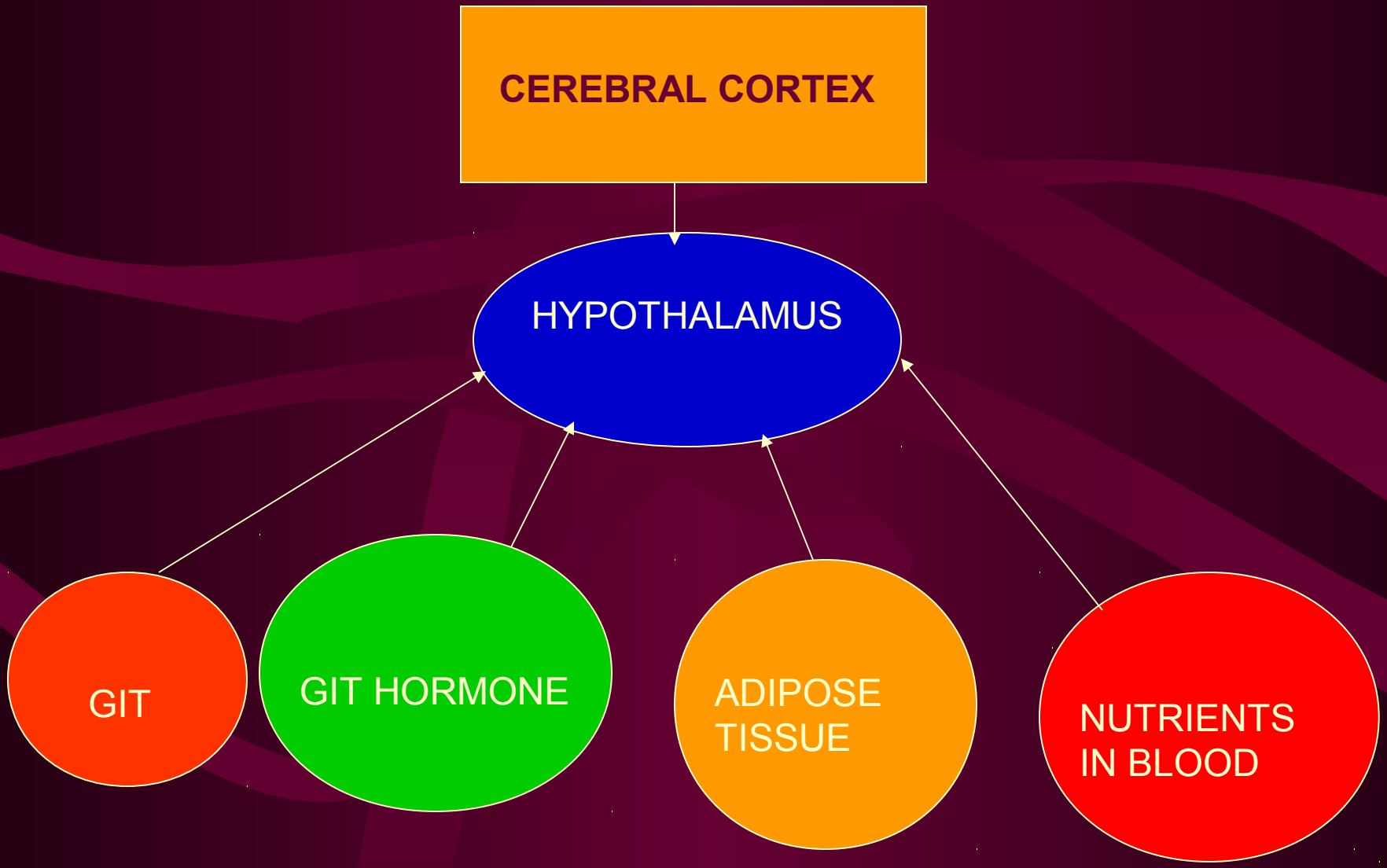
TABLE 22-1 Some Peptides That Modulate Food Intake

PEPTIDE	SOURCE
Increase food intake	
Ghrelin	Stomach
Neuropeptide Y (NPY)	Hypothalamus
Orexins (also called hypocretins)	Hypothalamus
Decrease food intake	
CCK	Small intestine; neurons
Leptin	Adipose tissue
Obestatin	Stomach
Corticotropin-releasing hormone (CRH)	Hypothalamus
α-Melanocyte-stimulating hormone (α-MSH)	Hypothalamus
CART (cocaine- and amphetamine-regulated transcript)	Hypothalamus
Glucagon-like peptide-1 (GLP-1)	Intestines
PYY_{3-36}	Intestines

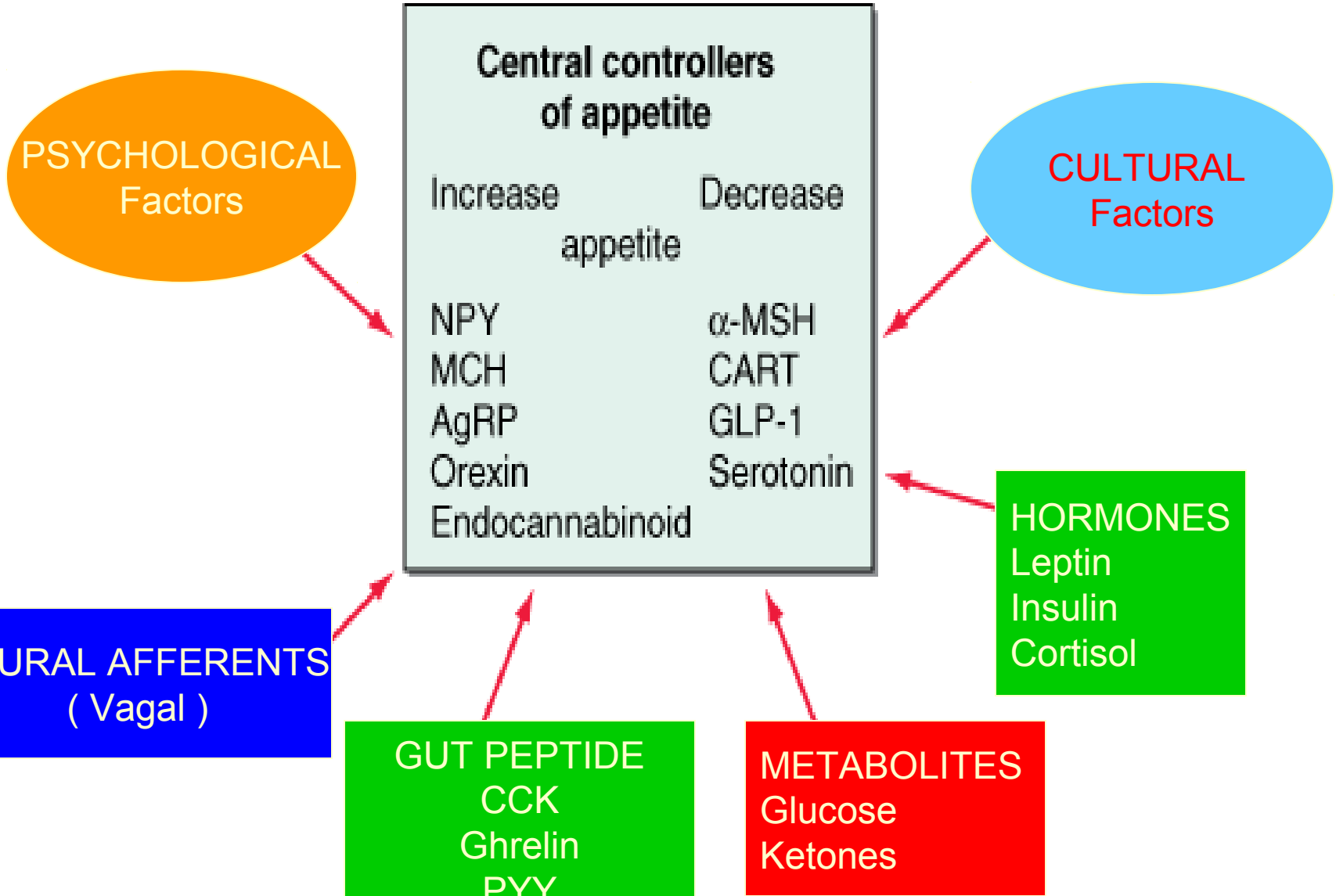
Control of Food Intake and Energy Balance

- **Sympathetic nervous system**
  - When activity increases, it signals to stop eating
  - When activity decreases, it signals to eat

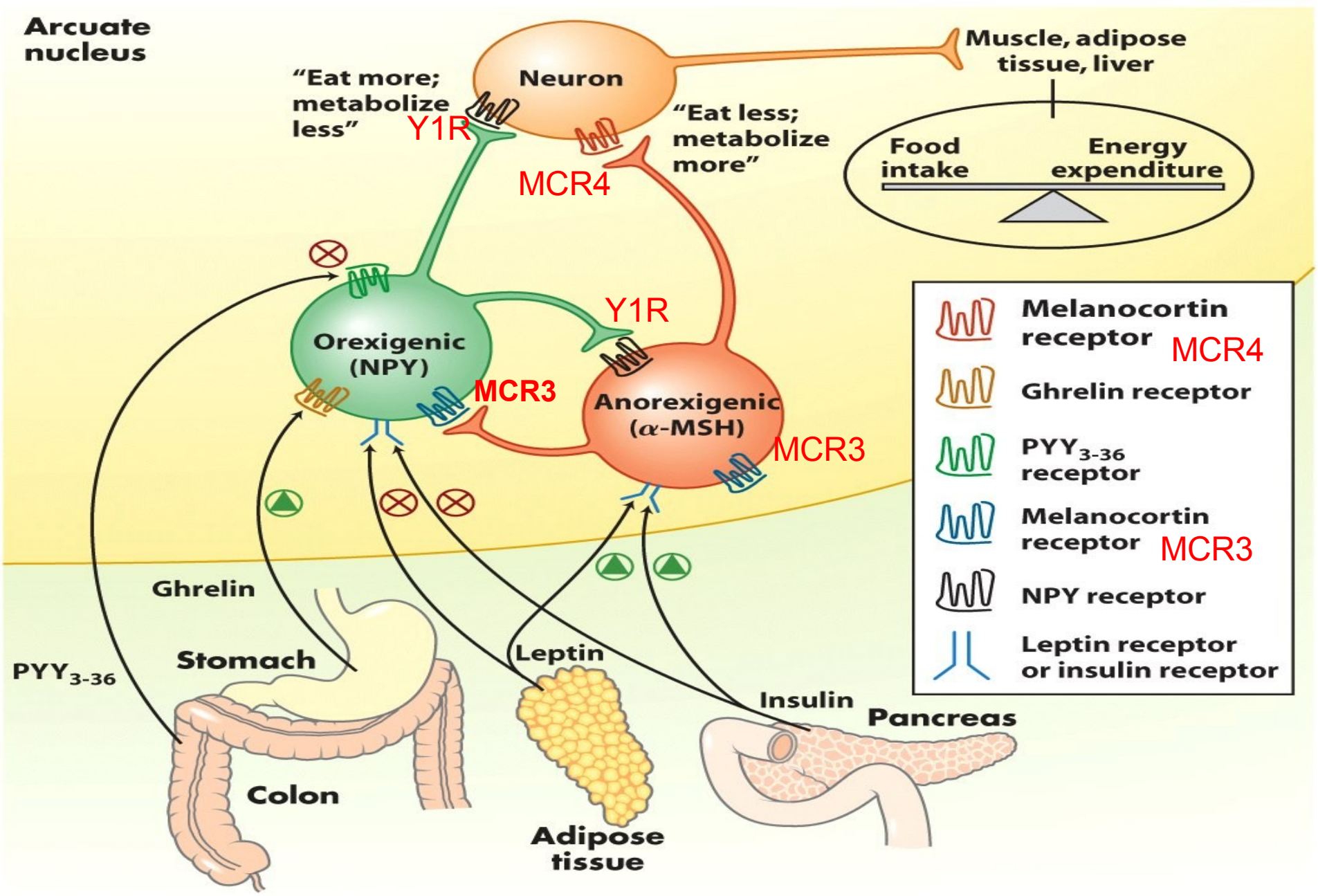
Hypothalamus Receives Signals



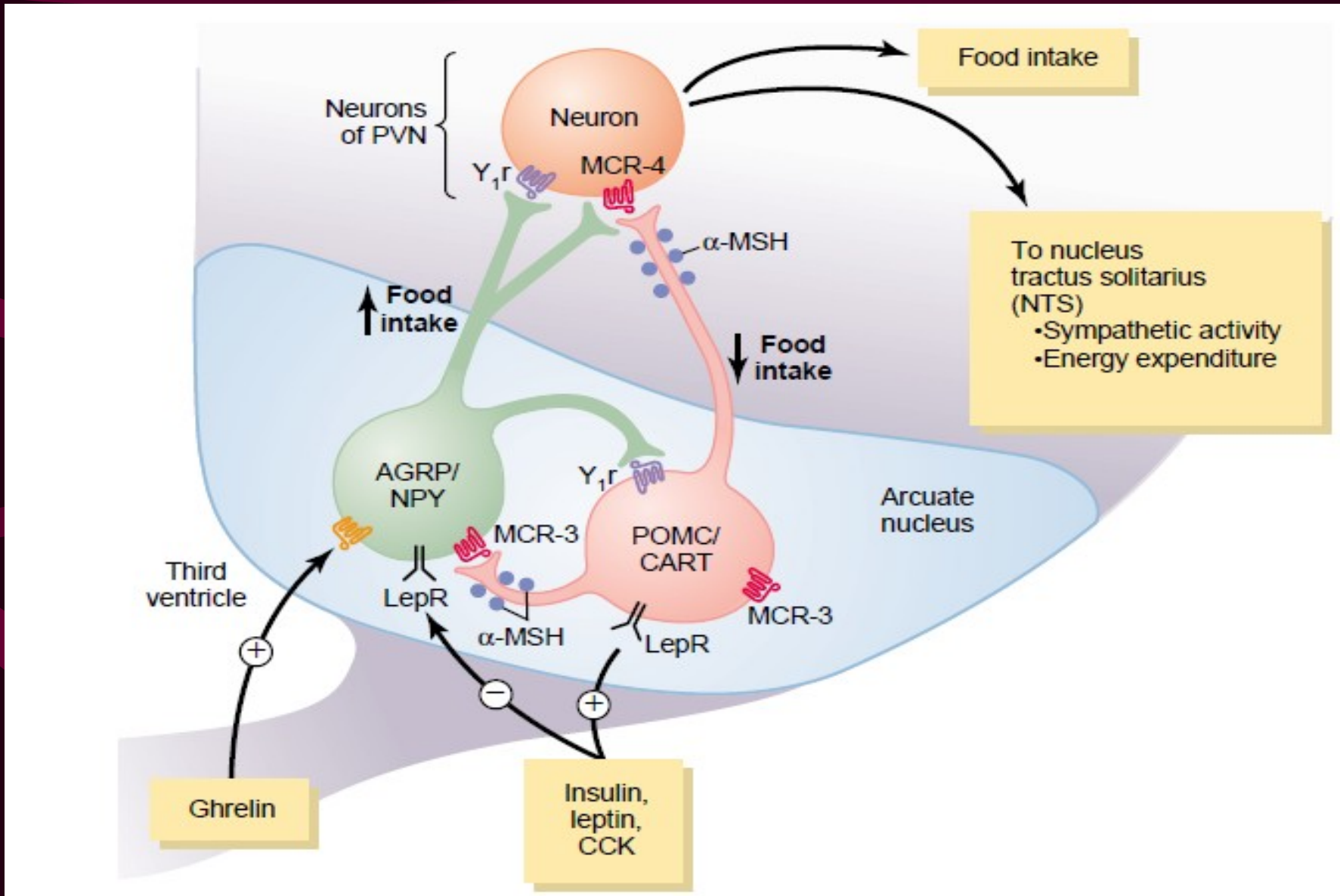
The Factors That Regulate Appetite Through Effects On Central Neural Circuit

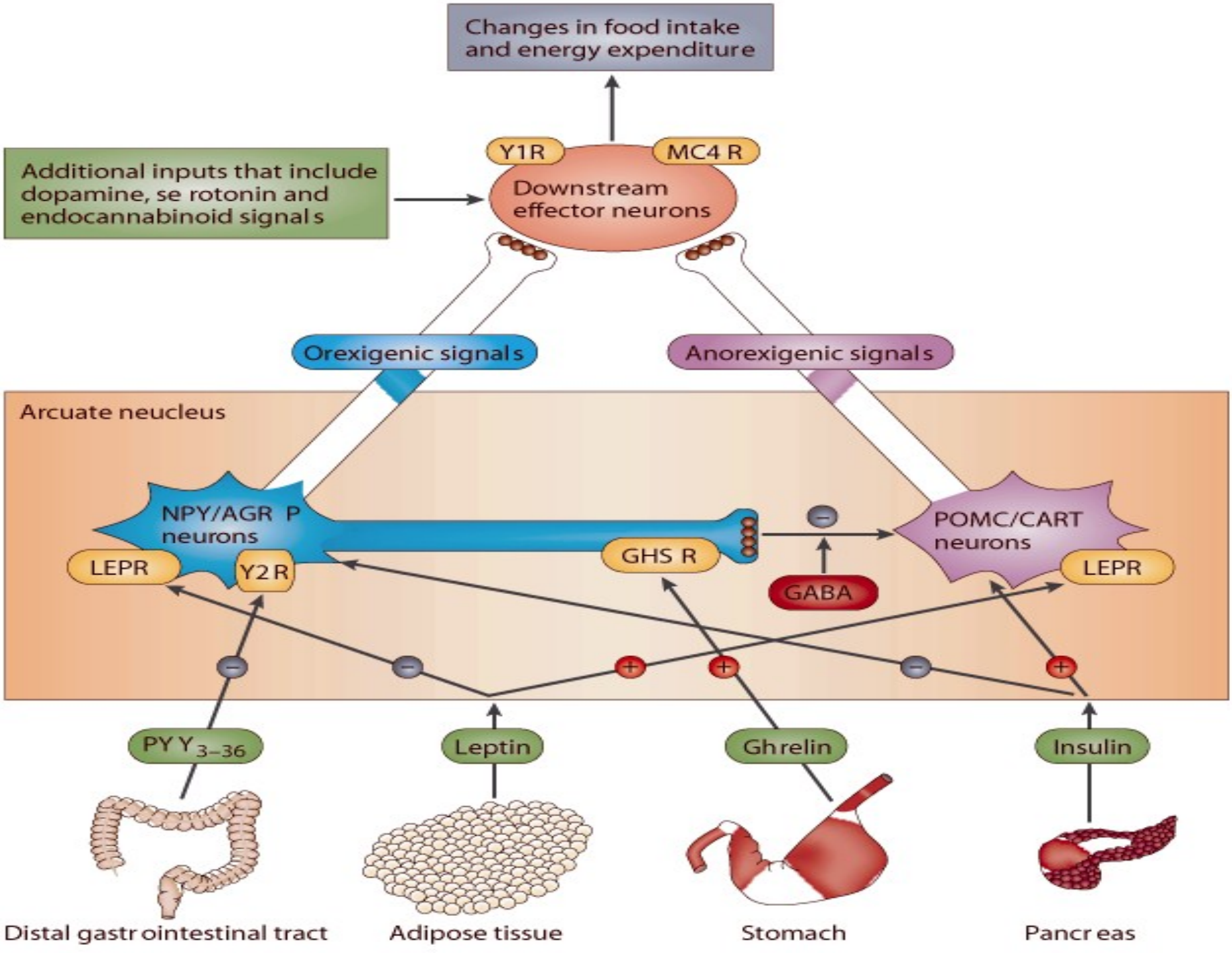


HORMONAL CONTROL



Neuron And Neurotransmitters In The Hypothalamus That Stimulate Or Inhibit Feeding




Changes in food intake and energy expenditure
Additional inputs that include dopamine, se rotonin and endocannabinoid signal s
Y1R
MC4 R
Downstream effector neurons
Orexigenic signal s
Anorexigenic signal s
Arcuate neucleus
NPY/AGR P neurons
LEPR
Y2 R
GHS R
GABA
POMC/CART neurons
LEPR
PY Y3–36
Leptin
Gh relin
Insulin
Distal gastr ointestinal tract
Adipose tissue
Stomach
Pancr eas

Two Theories for Regulation of Food Intake

- **Glucostatic** theory
  - Theory proposes that blood glucose levels ultimately control the feeding and satiety centers
- **Lipostatic** theory
  - Theory proposes that the level of body fat regulates the feeding and satiety centers
  - Recent discovery of several peptides (especially **leptin** and neuropeptide Y) seems to support this theory

FACTORS THAT REGULATE QUANTITY OF FOOD INTAKE

- Short term regulation

  Concerned primarily with preventing over eating at each meal

- Long term regulation

  Concerned primarily with maintenance of normal quantities of energy stores in the body

Short Term Regulation Of Food Intake

1. Gastrointestinal filling inhibits feeding
2. GI hormones

   CCK (Cholecystokinin)

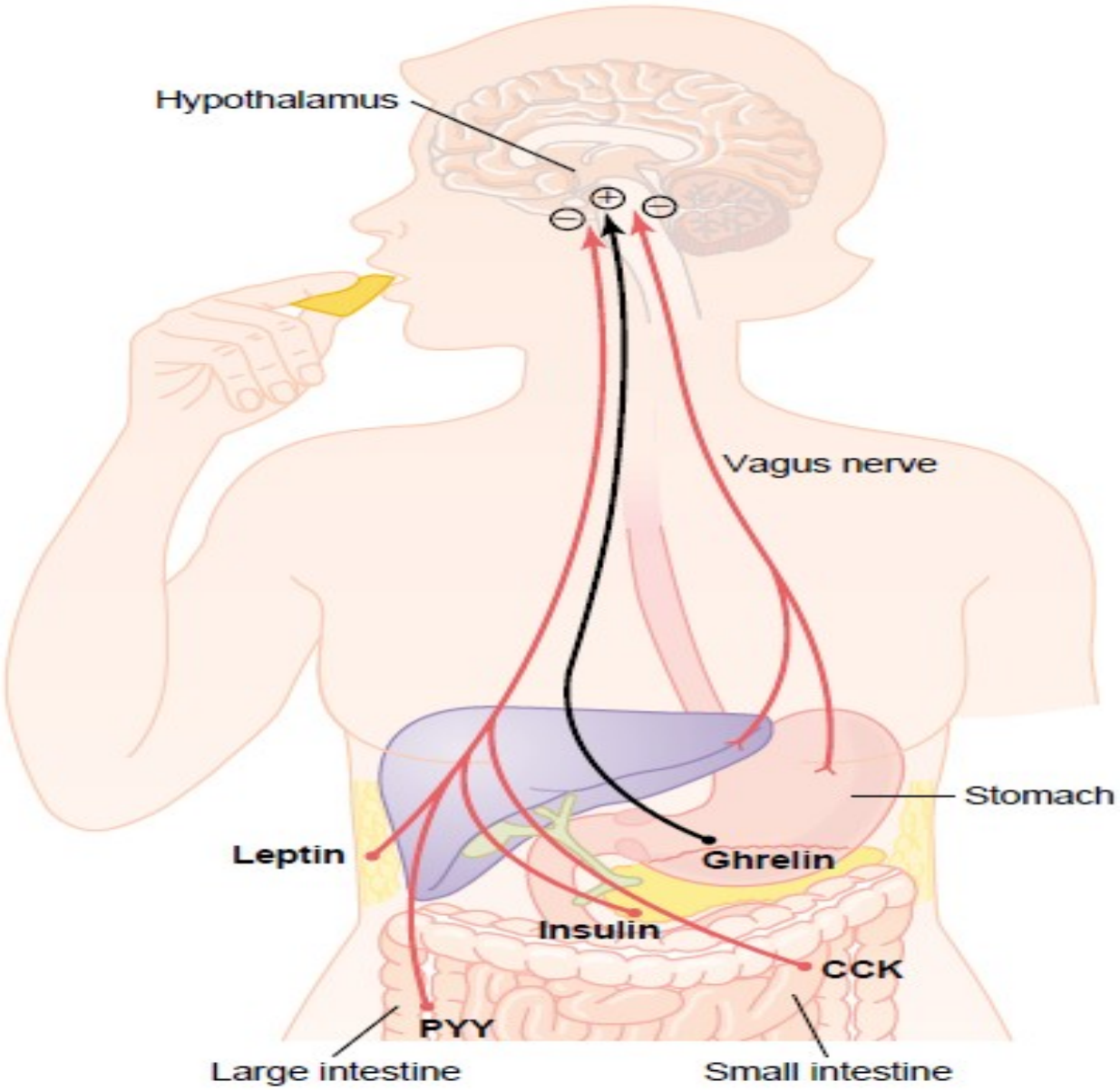
   PEPTIDE YY

   GLP

   INSULIN

   GHRELIN
3. Oral receptors meter food intake

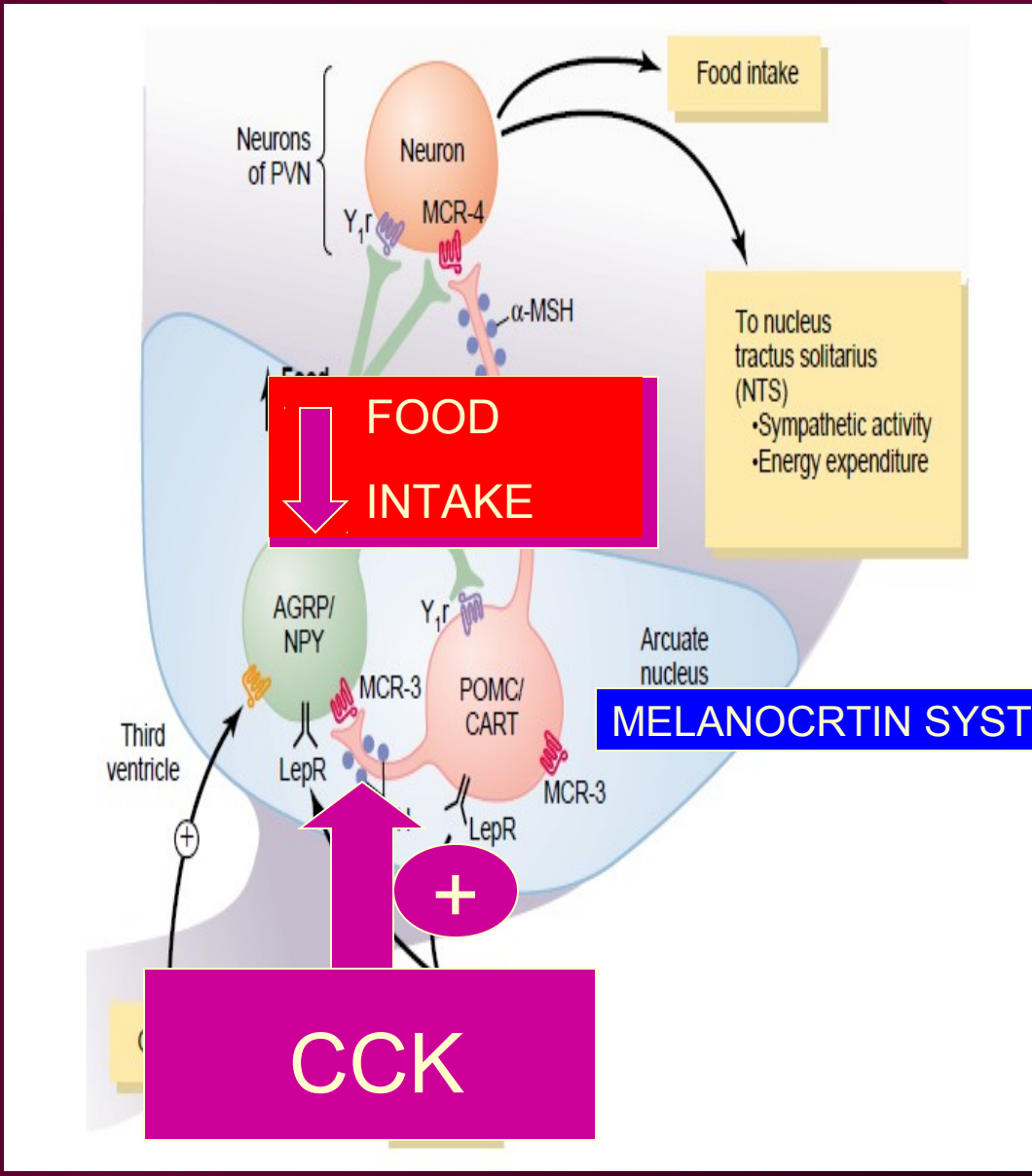
Feedback Mechanisms For Control Of Food Intake



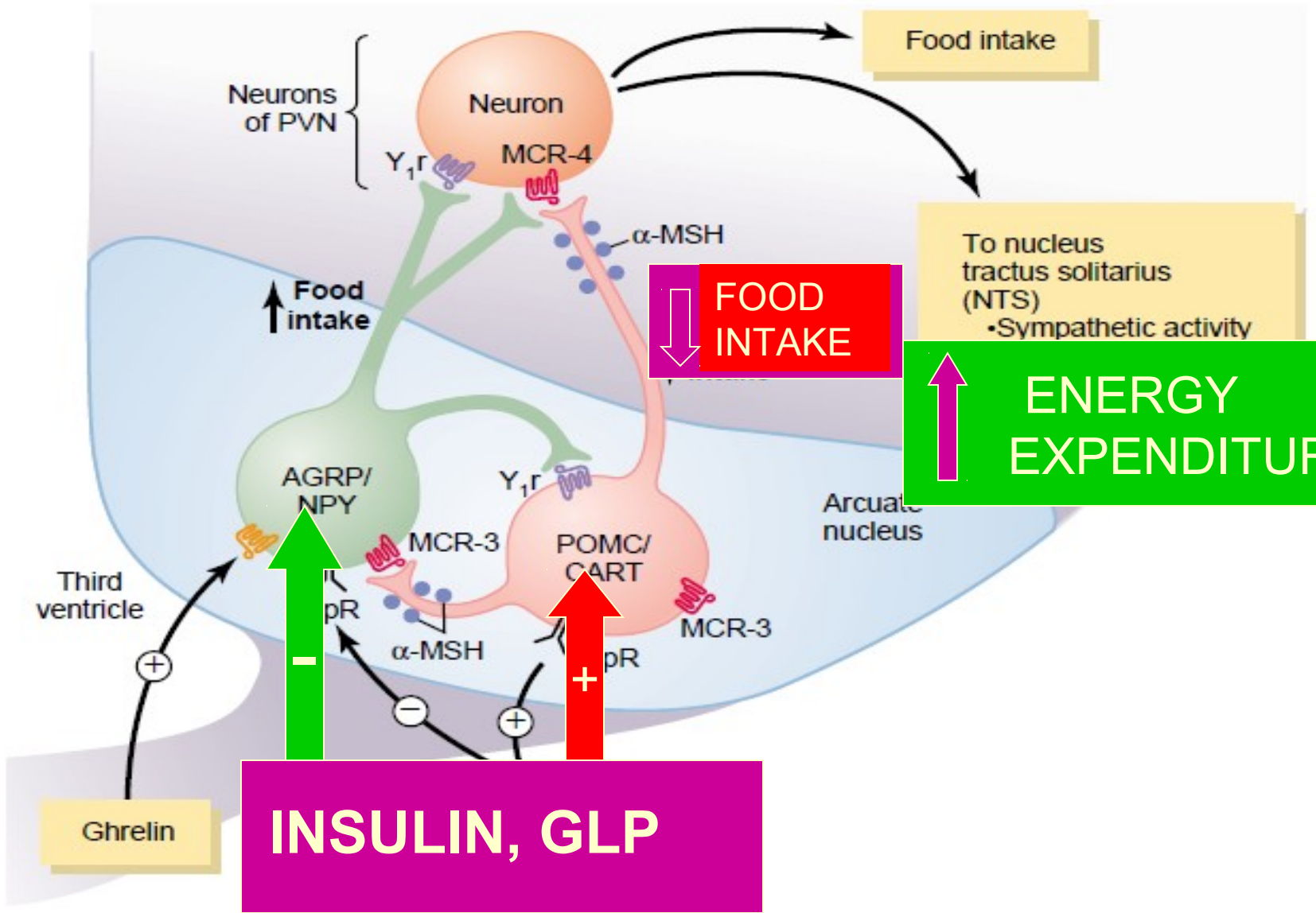
C C K

- **Cholecystokinin** released from duodenum in response to fat entry

- Direct effect on feeding centre to reduce subsequent feeding by activation of the MELANOCORTIN pathway in the hypothalamus



INSULIN

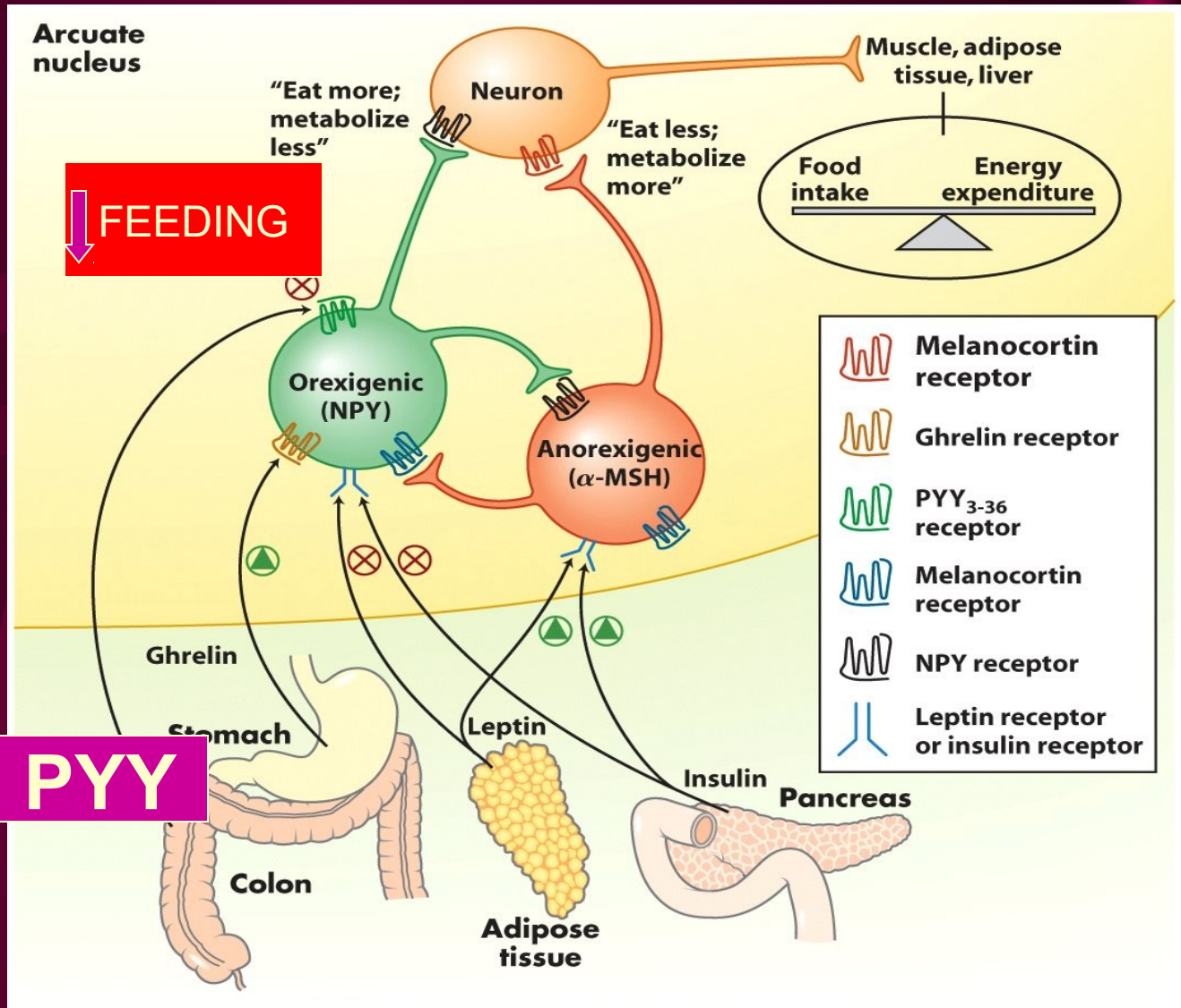

Food intake
Neurons of PVN
Neuron
MCR-4
Y_1r
α-MSH
To nucleus tractus solitarius (NTS)
•Sympathetic activity
Food intake
FOOD INTAKE
ENERGY EXPENDITURE
AGRP/ NPY
Y_1r
MCR-3
POMC/ CART
Arcuate nucleus
Third ventricle
pR
α-MSH
MCR-3
pR
−
+
Ghrelin
INSULIN, GLP

PEPTIDE YY

PYY:

1. made in response to food entering the GIT especially from ILEUM and COLON

2. Binds to an inhIbitory receptor on NPY/AgRP → ↓ secretion of NPY and AgRP → ↓ APPETITE



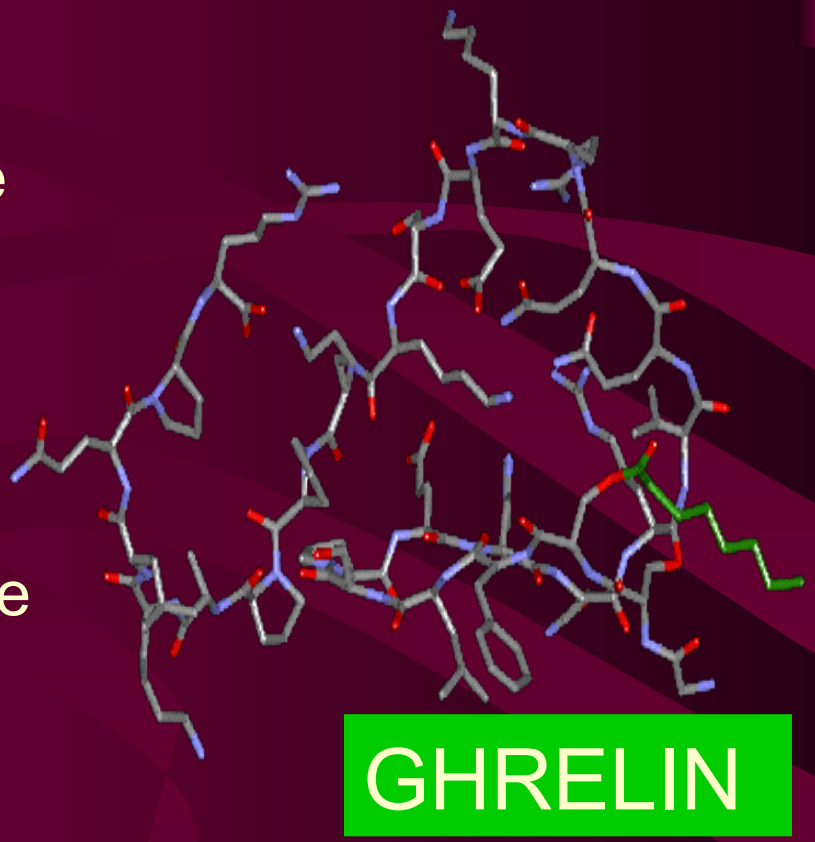
GHRELIN - THE HUNGER HORMONE

Identified in 1999 by Kojima and Kangawa

28 amino-acid, orexigenic peptide hormone

- Secreted by gastric mucosa (oxyntic cells) on an empty stomach

↑ during fasting, peak level before meal, fall rapidly after meal

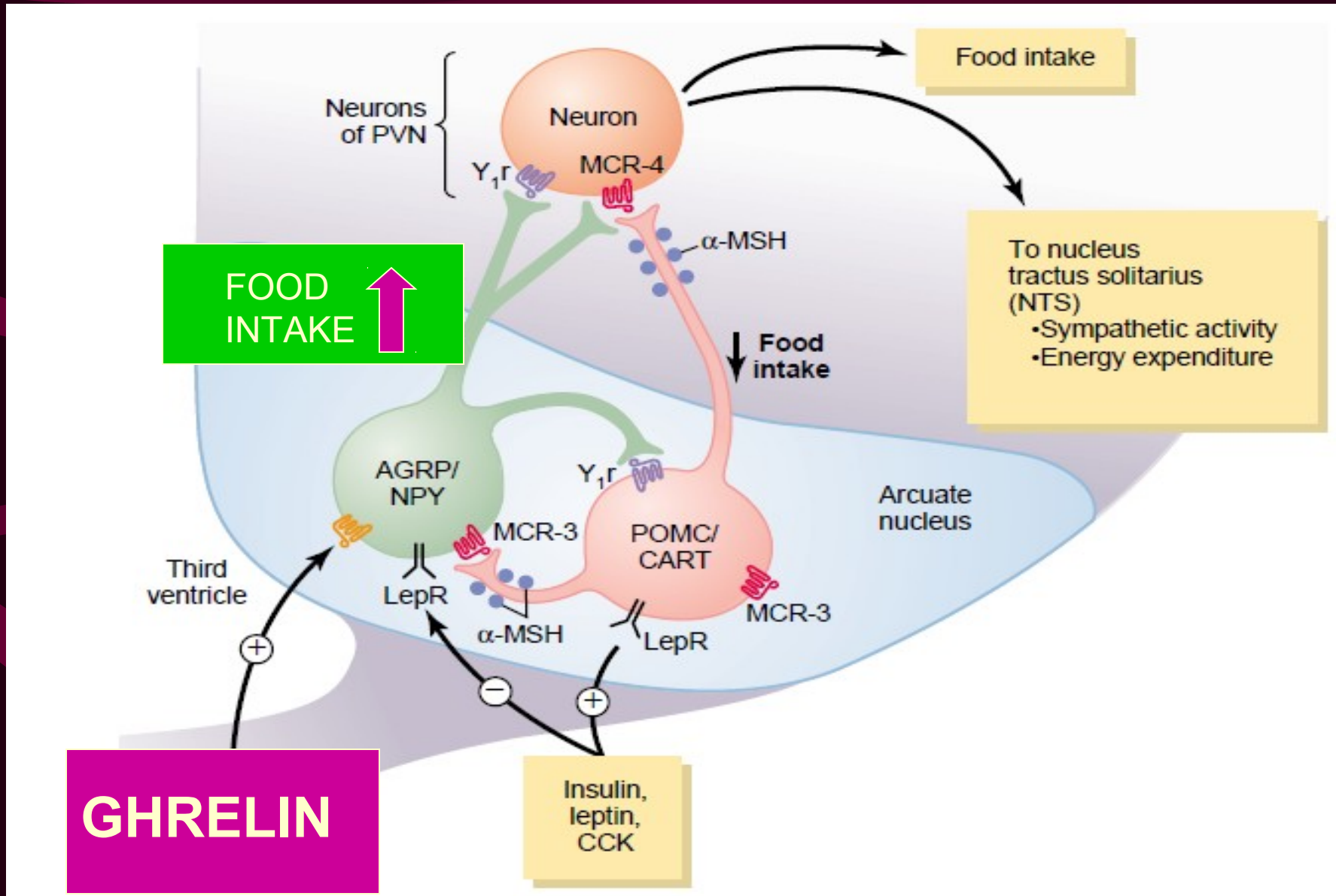


Two major roles

GH regulation

Energy balance

GHRELIN TO INCREASE APPETITE



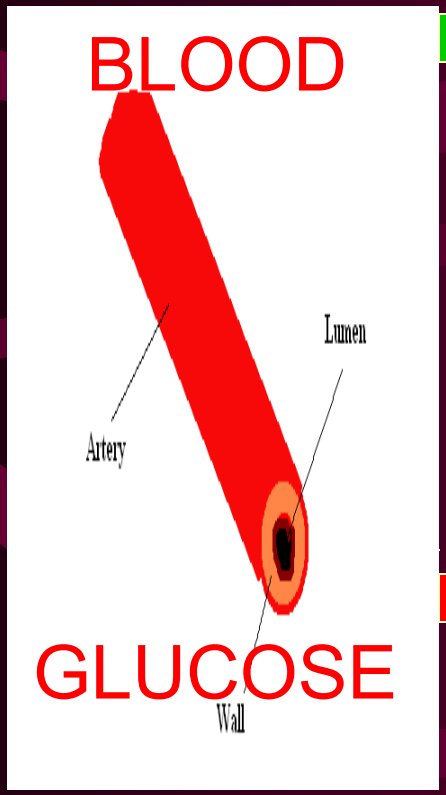
Intermediate And Long Term Regulation Of Food Intake

1. Nutrients in blood
2. Environmental temperature
3. Feed back signals from adipose tissue

Effect Of Nutrients In Blood

- Theories – Glucostatic
  Lipostatic
  Aminostatic

GLUCOSTAT



INCREASE

SATIETY CENTRE

SATIATED

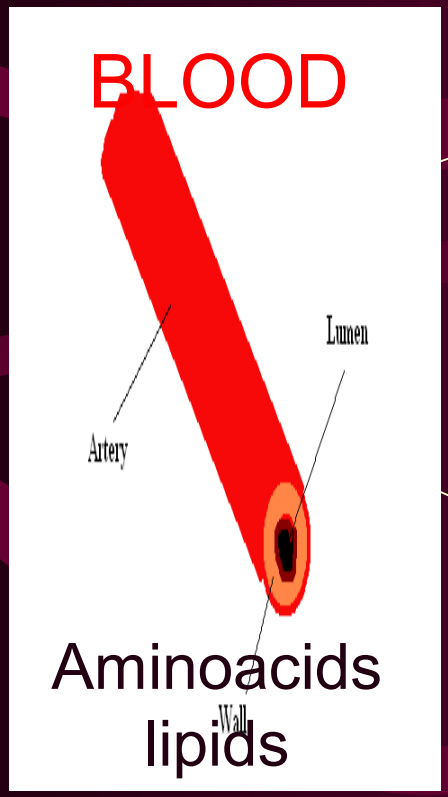
INHIBITION

DECREASE

HUNGER CENTRE

HUNGRY

AMINOSTAT, LIPOSTAT



INCREASE

SATIETY CENTRE

SATIATED

INHIBITION

DECREASE

HUNGER CENTRE

HUNGRY

CLINICAL IMPORTANCE

PRADER-WILLI SYDROME

- In Prader-Willi syndrome over production of GHRELIN (highest level ever measured in human) -- hyperphagia →OBESITY
- Other obesity syndromes
  - Laurence-Moon-Biedl
  - Ahlstrom
  - Cohen
  - Carpenter

HYPERPHAGIA

- **Diabetes** –Polyphagia; though blood glucose is high but cellular utilization is low in the satiety centre because of the insulin deficiency
- **Hyperthyroidism** – NPY activated by concurrent hypermetabolism induced starvation
- **GI disorder-** malabsorption (coeliac sprue, short bowel syndrome) adaptive hyperphagia
- **Kluver Bucy syndrome-** bilateral medial temporal lobe lesion

HYPERPHAGIA

- **Tumors** – direct invasion of the hypothalamus with axial tumors or extrinsic compression and displacement of hypothalamic structure by suprasellar masses or third ventricular lesion

EATING DISORDERS

- Anorexia nervosa
  - Refuses to attain or maintain a minimal healthy body weight (BMI $\leq$ 17.5 kg/m^2)
  - Excessive concern with weight or weight gain
  - Distorted perception of weight or body shape and /or related medical dangers
  - Amenorrhea

EATING DISORDERS

- Bulimia nervosa
  - Recurrent binge-eating
  - Recurrent behavior to purge or neutralize excessive intake or to control weight
  - Excessive concern with weight or body shape

These are multifactorial, with psychodevelopmental, sociocultural, and genetic contribution to risk

REDUCE YOUR EXTRA WEIGHT