

Determinants affecting the cognitive or emotional brain

Biological influences:

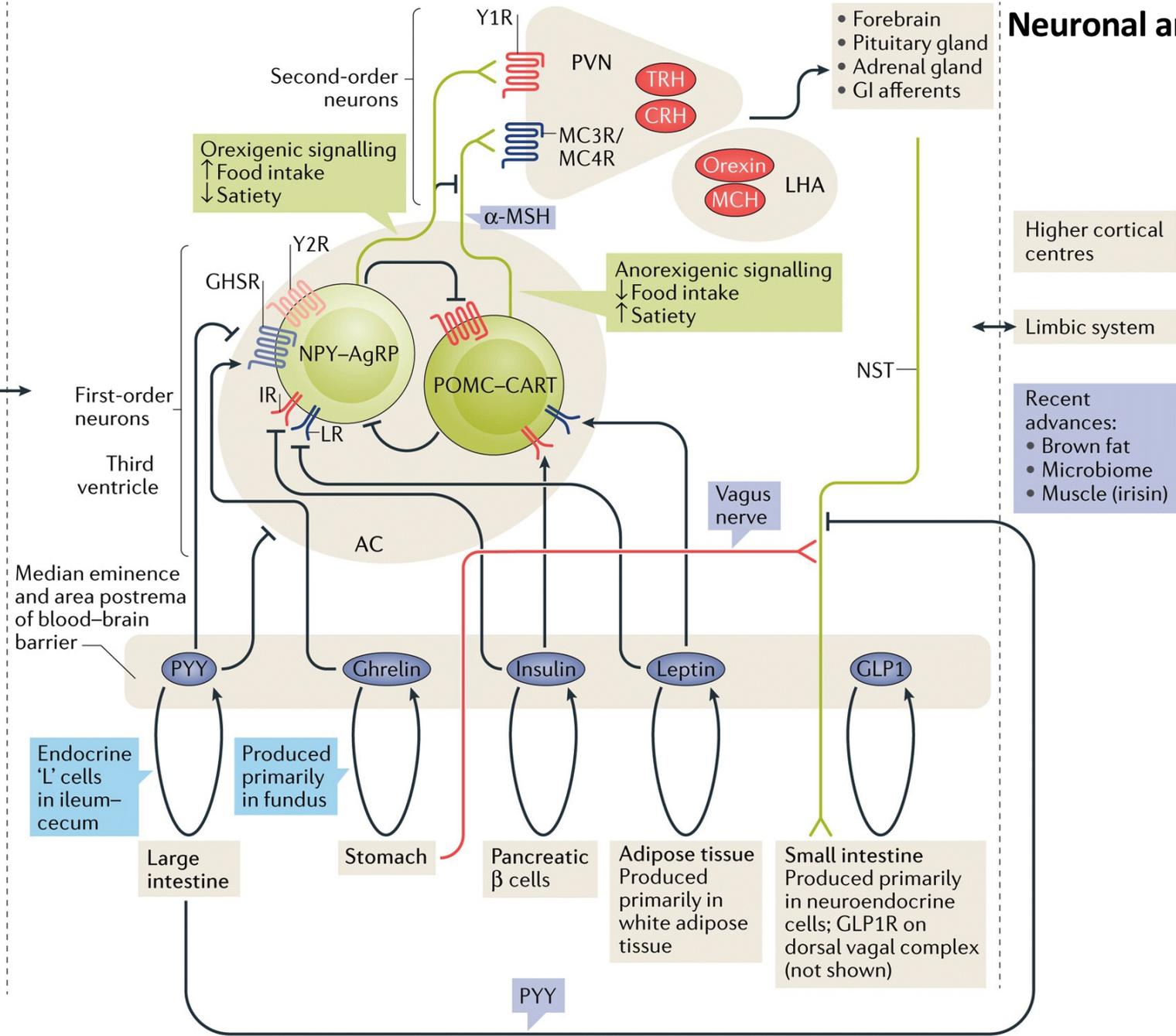
- Early-life events
- Imprinting
- Epigenetics
- Genetics

Modern macroenvironment:

- Food production, consumption and availability
- Social structure and cues
- Weather or outdoor temperatures influencing physical activity
- Television and technology
- Cultural norms
- Endocrine disruptors

Modern microenvironment:

- Nutrition
- Exercise
- Sleep
- Stressors
- Circadian rhythm



Neuronal and hormonal pathways influencing food intake and satiety in the brain

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- Forebrain
 - Pituitary gland
 - Adrenal gland
 - GI afferents
- α -MSH, α -melanocyte-stimulating hormone
 CRH, corticotropin-releasing hormone
 GHSR, growth hormone secretagogue receptor
 GI, gastrointestinal
 GLP1, glucagon-like peptide 1
 GLP1R, GLP1 receptor
 IR, insulin receptor
 LHA, lateral hypothalamic area
 LR, leptin receptor
 MCH, melanin-concentrating hormone
 MC3R, melanocortin receptor 3
 NST, nucleus of the solitary tract
 PYY, peptide YY
 TRH, thyrotropin-releasing hormone
 Y1R, Y1 receptor; Y2R, Y2 receptor

- Higher cortical centres
- ↔
- Limbic system

- Recent advances:
- Brown fat
 - Microbiome
 - Muscle (irisin)

Complex neuro-hormonal pathways, gut hormones and adiposity signals reciprocally interact between the hypothalamus, brain-stem, higher cortical areas and limbic system to control appetite regulation. Peripheral signals can also interact via neural pathways directly.

Neuropeptide Y-agouti-related protein (NPY-AgRP; orexigenic) and pro-opiomelanocortin-cocaine-and amphetamine-related transcript (POMC-CART; anorexigenic) neurons reside within the arcuate nucleus (AC) of the hypothalamus. The cumulative effect of either inhibition or activation of these orexigenic and anorexigenic neurons from various signals in the bloodstream through the incomplete blood-brain barriers (median eminence and area postrema) or neural pathways influences food intake and satiety.

In addition, biological and modern microenvironmental and macroenvironmental determinants affect the cognitive or emotional brain with an impact on energy regulatory pathways that gives rise to clinical heterogeneity (variation) in individuals with obesity.