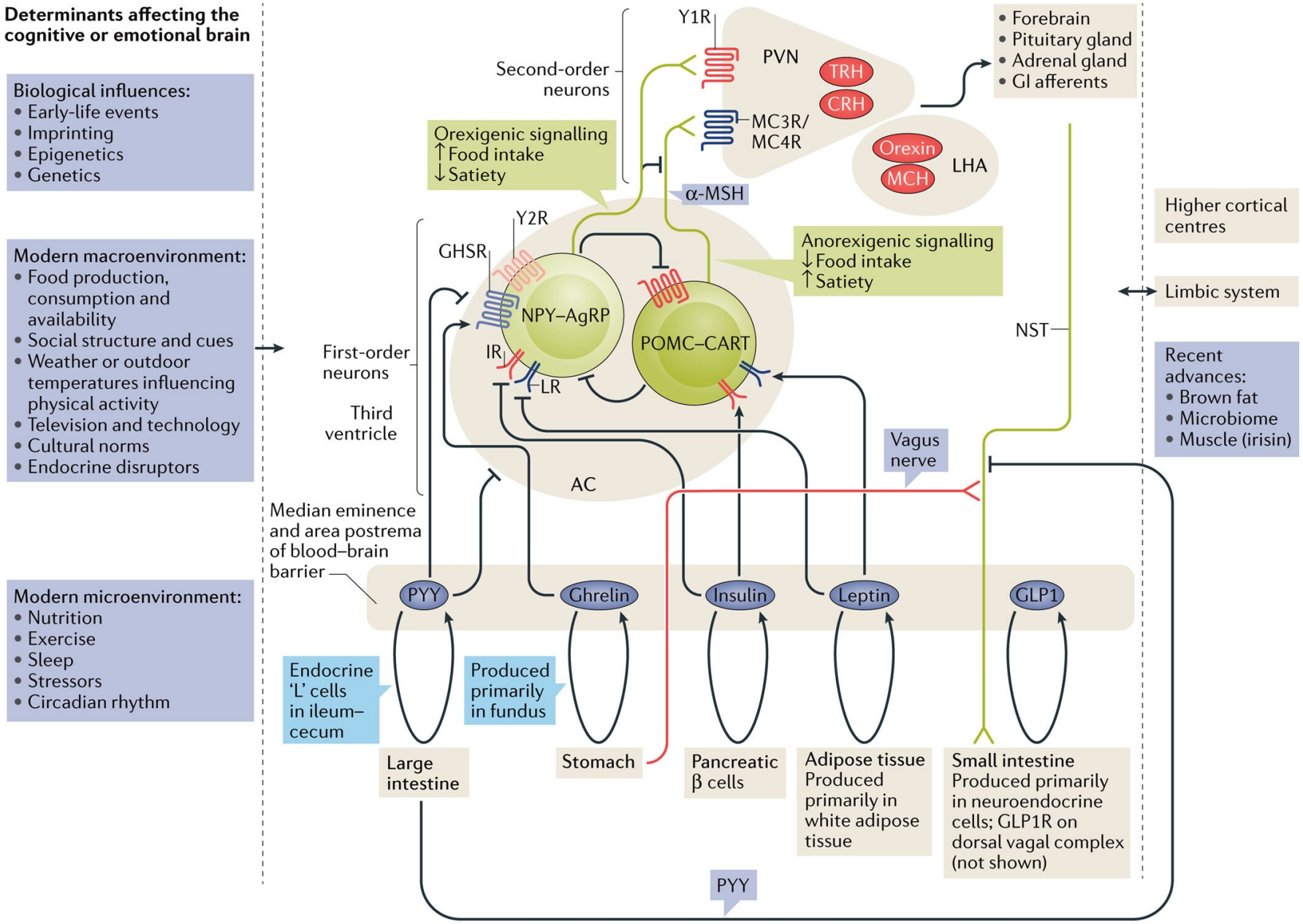
Determinants affecting the cognitive or emotional brain
Biological influences:
• Early-life events
• Imprinting
• Epigenetics
• Genetics
Modern macroenvironment:
• Food production, consumption and availability
• Social structure and cues
• Weather or outdoor temperatures influencing physical activity
• Television and technology
• Cultural norms
• Endocrine disruptors
Modern microenvironment:
• Nutrition
• Exercise
• Sleep
• Stressors
• Circadian rhythm
Y1R
Second-order neurons
PVN
TRH
CRH
MC3R/ MC4R
Orexigenic signalling
↑Food intake
↓Satiety
α-MSH
Orexin
MCH
LHA
• Forebrain
• Pituitary gland
• Adrenal gland
• GI afferents
Higher cortical centres
Limbic system
Y2R
GHSR
NPY–AgRP
POMC–CART
IR
LR
Anorexigenic signalling
↓Food intake
↑Satiety
NST
First-order neurons
Third ventricle
AC
Vagus nerve
Recent advances:
• Brown fat
• Microbiome
• Muscle (irisin)
Median eminence and area postrema of blood–brain barrier
PYY
Ghrelin
Insulin
Leptin
GLP1
Endocrine 'L' cells in ileum–cecum
Produced primarily in fundus
Large intestine
Stomach
Pancreatic β cells
Adipose tissue
Produced primarily in white adipose tissue
Small intestine
Produced primarily in neuroendocrine cells; GLP1R on dorsal vagal complex (not shown)
PYY

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

Complex neuro–hormonal pathways, gut hormones and adiposity signals reciprocally interact between the hypothalamus, brainstem, 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.

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
PVN, paraventricular nucleus
PYY, peptide YY
TRH, thyrotropin-releasing hormone
Y1R, Y1 receptor; Y2R, Y2 receptor