

Endogenous morphine signalling and sympathetic drive pull the cyclic adenosine monophosphate-protein kinase A axis, abbreviated cAMP-PKA, in opposite directions, yet over time they converge on the same transcription factor, the cAMP response-element binding protein (CREB). Activation of μ -opioid receptors engages the inhibitory G-protein family (Gi), suppresses adenyl cyclase, lowers basal cAMP and reduces PKA activity. In compensation, neurons and hepatocytes increase expression of certain cyclase isoforms, of the catalytic sub-unit of PKA and of CREB itself, gradually restoring throughput despite continuing receptor inhibition. Sympathetic tone, arriving through β -adrenergic stimulatory G-proteins (Gs), pushes cAMP the other way; each burst of epinephrine now strikes tissue that has already amplified its signalling sensitivity.

5-HT₁ - Serotonin 1 Receptor Family
A₁ - Adenosine A1 Receptor
α₂-AR - Alpha-2 Adrenergic Receptor
AC - Adenylyl Cyclase
Akt - Protein Kinase B
AR - Androgen Receptor
β-AR - Beta-Adrenergic Receptor
BHB - Beta-hydroxybutyrate
Ca²⁺/CaM - Calcium/Calmodulin Complex
cAMP - Cyclic Adenosine Monophosphate
CB₁ - Cannabinoid CB1 Receptor
cGMP - Cyclic Guanosine Monophosphate
CREB - cAMP Response Element-Binding Protein
D₂-like - Dopamine D2-like Receptor Family
DHEA - Dehydroepiandrosterone
ERK - Extracellular Signal-Regulated Kinase
GABA - Gamma-Aminobutyric Acid
Gi - Inhibitory G-alpha Sub-unit
GPR109A - Nicotinic Acid Receptor
GP1R1 - G protein-Coupled Oestradiol Receptor 1 (GPR30)
GRK3 - G Protein-Coupled Receptor Kinase 3
Gs - Stimulatory G-alpha Sub-unit
GSK3β - Glycogen-Synthase-Kinase-3β
HCAR2 - Hydroxycarboxylic Acid Receptor 2
ICER - Inducible cAMP Early Repressor
IR - Insulin Receptor
mGluR - Metabotropic Glutamate Receptor
MOR - Mu-Opioid Receptor
mPR - Membrane Progesterone Receptor
MT1 - Melatonin Receptor 1
NAD⁺ - Nicotinamide Adenine Dinucleotide
NO - Nitric Oxide
NOS - Nitric Oxide Synthase (coupled)
NMNAT - Nicotinamide Mononucleotide Adenylyltransferase
PDE - Phosphodiesterase
PEM - Post Exertional Malaise
PEPCK - Phosphoenolpyruvate Carboxykinase
PFK2 - 6-Phosphofructo-2-Kinase
PI3K - Phosphoinositide 3-Kinase
PKA - Protein Kinase A
PKG - cGMP-dependent Protein Kinase
POTS - Postural Orthostatic Tachycardia Syndrome
R - Receptor
ROS - Reactive Oxygen Species
RSK - Ribosomal S6 Kinase
RTK - Receptor Tyrosine Kinase
sGC - Soluble Guanylyl Cyclase
THDOC - Tetrahydrodeoxycorticosterone

