

	Source	Receptors expressed	Relevant Target brain region	Influence Reward associated behaviors via
Anorexogenic Signals, Peripheral + Central				
Leptin	adipocytes	VTA/SN ¹	Hyp (arcuate) >VTA ¹ .	GABA ² , glutamate ³ , DA ⁴ and 5HT ⁵ transmission.
Insulin⁶	pancreatic Langerhans cells	In humans, highest density in Hypothalamus (arcuate), cerebral cortex, and cerebellum	SN/VTA DA neurons ⁷	Increased DAT expression ^{8,9} /activity ¹⁰ . Insulin dependent LTD induction in VTA requires EC-dependent presynaptic inhibition of glutamate release ¹¹
Cholesystokinin	Duodenum/ jejunum	CCK1R in VT ¹² A, SN, NAc and dorsal striatum (NAc) ¹³ .	VTA	Anti-opioid action ¹⁴ . CCK decreased in sated, pleasure eating ¹⁵ .
Amylin	Pancreatic β-cell	Multiple sites, including NAc. Olfactory tubercle, amygdalostriatal transition zone, amygdaloid nuclei, various hypothalamic nuclei, DR, LC, and NTS ¹⁶ .	VTA DA neurons	-
GLP-1	Intestine mucosa NTS ¹⁷	Dorsal raphe ¹⁸	PVH, DNH, Arc ¹⁷ VTA, NAc ¹⁹	Systemic administration reduces rewarding effects of nicotine, alcohol, and stimulants in rodents ²⁰
PYY	Intestinal L-cell ileum/colon	To inhibits gastric motility and pancreatic secretion	Modulates cortical and hypothalamic areas that predict feeding behavior in humans ²¹	-
CART	ARC hypothalamus		Limbic and sensory related brain regions ²²	Central administration of CART attenuates behavioral effects of cocaine ²³
Orexigenic Signals, Peripheral + Central				
Ghrelin	Stomach, hypothalamus ²⁴	Arc and VMN, cortex, hippocampus, thalamus, SN, VTA, raphe ²⁴	Hyp arc. Via the vagus and NTS	Increased in sated, pleasure eating ¹⁵ . Intraventricular injection increases impulsive behavior ²⁵
Orexin	LH, Arc	Arc, PVN, DMH, VMH ^{26,27}	VTA, NAc	+ morphine relapse ²⁸
NPY	ARC	High density NPY ¹³⁻³⁶ sensitive binding in hippocampus, striatum and nucleus accumbens ²⁹	VTA, NAc	Inhibits VTA GABA> NAC DA boost ³⁰ . Anxiolytic, stress-reducing, and fear extinction properties ³¹

MCH ³²	LH	Wide distribution Including LH, VMH, OFC CG, amygdala, LC, meso-corticolimbic structures.	enriched in the striatum, with high expression in the NAc shell ³³	Implicated in the regulation of mood/emotional states. Modulates cocaine reward ³⁴
CRF	cAmy	Broad but distinct distribution of CRF-R1 and R2. Sites include cortex, cerebellum, BNST, NTS, VMH, hippocampus, SN/VTA ³⁵ .	CRF1: anterior pituitary, cerebral cortex, cerebellum, amygdala, hippocampus, and striatum ³⁶	Mediates stress induced reinstatement of drug (alcohol, cocaine, nicotine) seeking behavior ^{36,37}

Supplemental Table: Influence of selected food-related signals on reward associated areas and behaviors

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