

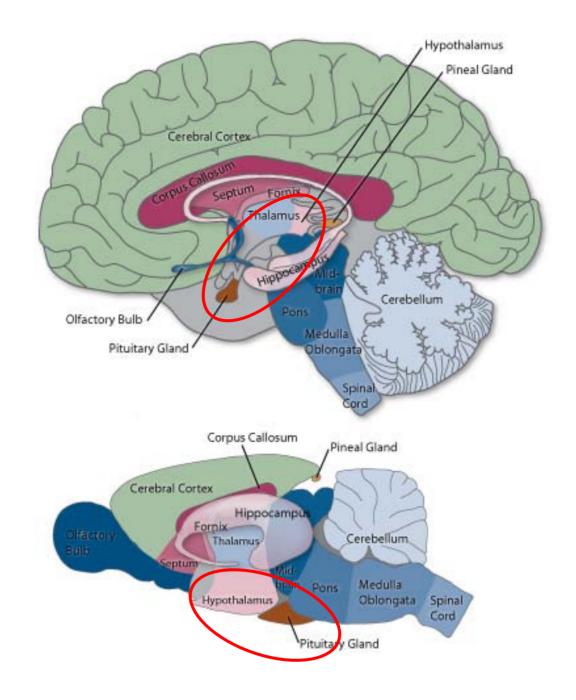
Neuroendocrine system – HPA axis

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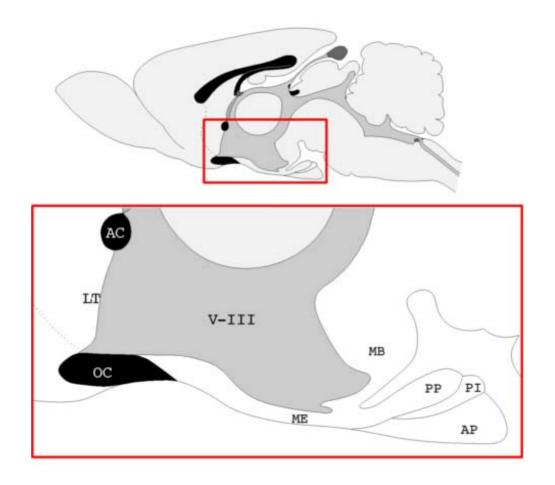
(christopher.pryce@bli.uzh.ch)



Relative situation of the hypothalamus and pituitary in human and rat brains



Boundaries of the hypothalamus of the rat (midsagittal section)



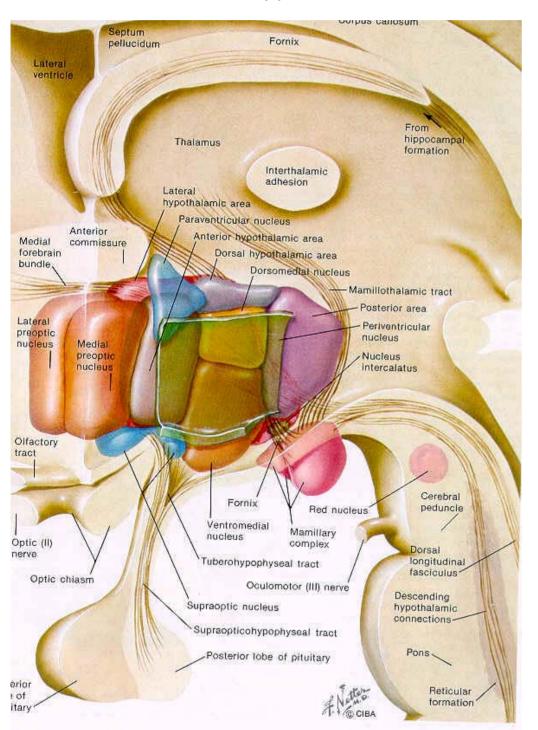
OC, Optic chiasm
ME, Median eminence
MB, Mamillary body
LT, Lamina terminalis
AC, Anterior commissure

IS, Infundibular stalk

PP, posterior Pituitary
AP, anterior Pituitary
PI, pars intermedia of Pituitary

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Hypothalamic Subdivisions and their Nuclei



Preoptic Vascular organ of the lamina terminalis

Median preoptic nucleus

Preoptic periventricular nucleus

Anteroventral periventricular nucleus

Medial preoptic nucleus Lateral preoptic area

Anterior Suprachiasmatic nucleus

Anterior periventricular nucleus Anterior hypothalamic nucleus

Paraventricular nucleus Subparaventricular zone

Supraoptic nucleus Retrochiasmatic area

Lateral hypothalamic area

Tuberal Intermediate periventricular nucleus

Arcuate nucleus

Ventromedial nucleus Dorsomedial nucleus

Lateral hypothalamic area
Ventral premamillary nucleus

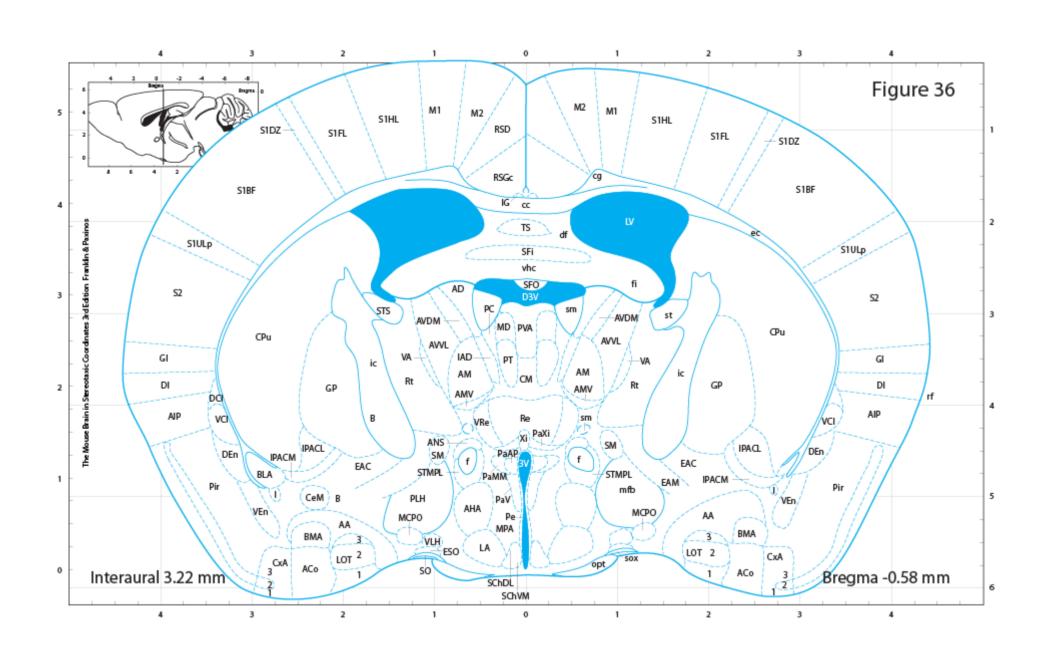
Mammillary Posterior periventric

Posterior periventricular nucleus Posterior hypothalamic nucleus Dorsal premammillary nucleus

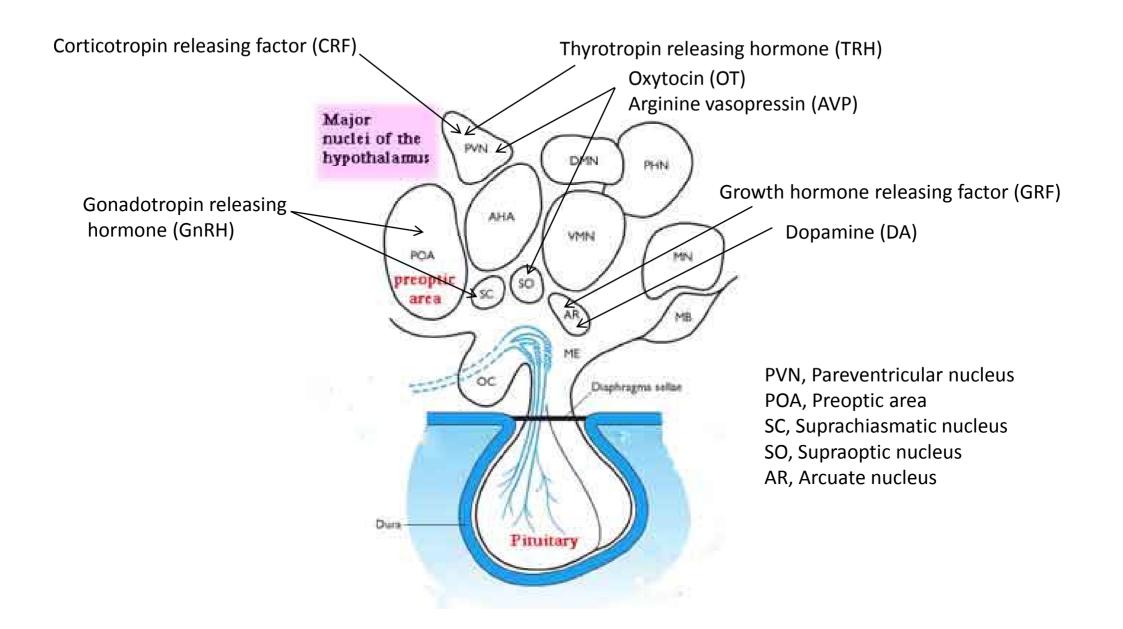
Mammillary nuclei

Supramammillary nuclei Tuberomammillary nuclei Lateral hypothalamic area

Coronal representation of the mouse brain at level of preoptic-anterior hypothamaus



Hypothalamic nuclei with neurosecretory cells for | Neuro-Hormones



Neuroendocrine system as an Effector - End organ Motor system

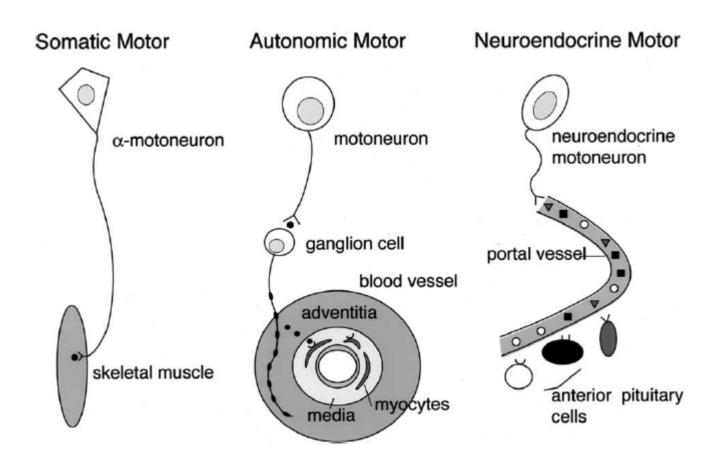
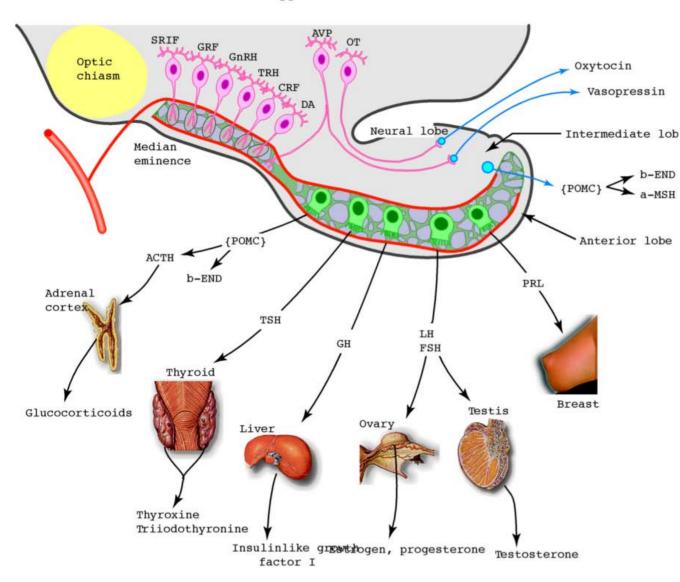


Fig. 2. Motor systems. The three types of motor systems compared. The fixed wiring of the skeletal motor system allows for one universal neurotransmitter in that system. The less fixed autonomic motor system uses a two neuron chain and several neurtransmitters. The neuroendocrine motor system represents the next step in the liberation of effector from end organ using a blood delivery system and showing specificity between neurotransmitter and receptor type.

General organization of the hypothalamus-pituitary-organ axes

Hypothalamus



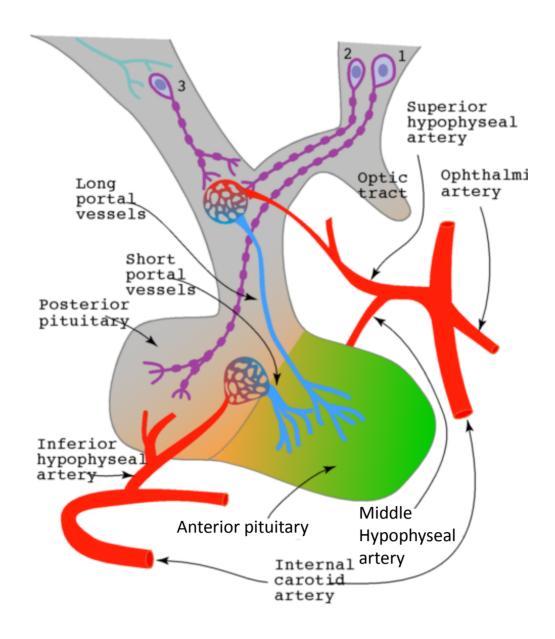
SRIF, Somatostatin GRF, Growth hormone releasing factor GnRH, Gonadotropin releasing hormone TRH, Thyrotropin releasing hormone CRF, Corticotropin releasing factor DA, Dopamine

AVP, Arginine vasopressin OT, Oxytocin

POMC, Proopiomelanocortin
ACTH, Adrenocorticotropic hormone
B-END, B-endorphin
TSH, Thyroid stimulating hormone
GH, Growth hormone
LH, Luteinising hormone
FSH, Follicle stimulating hormone
PRL, prolactin

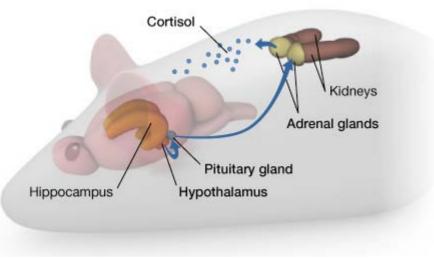
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Neurovascular communication between hypothalamus and pituitary

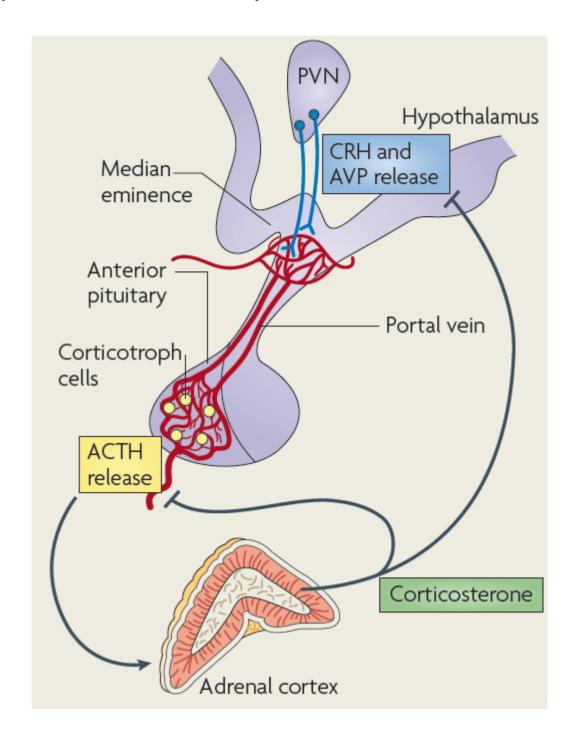


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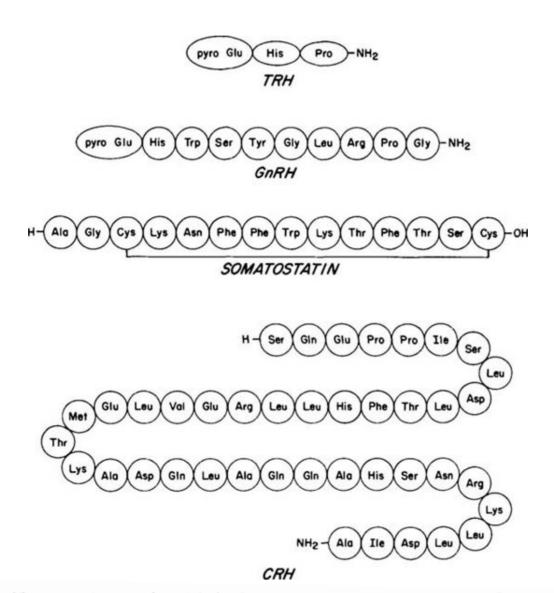
Neuroendocrine system: Hypothalamic-Pituitary-Adrenal Axis



Paraventricular Nucleus Corticotropin Releasing Factor/Hormone Neurohormone Pituitary Gland Adrenocorticotropic Hormone Hormone Adrenal Gland Corticosterone/Cortisol Hormone

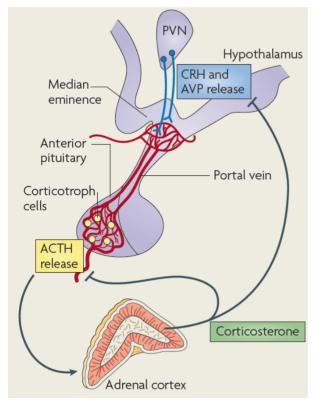


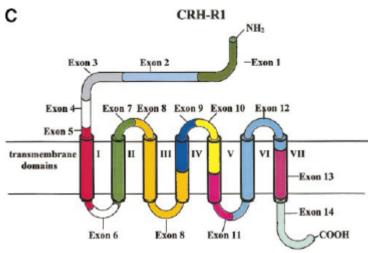
41-amino acid sequence of corticotropin releasing factor/hormone

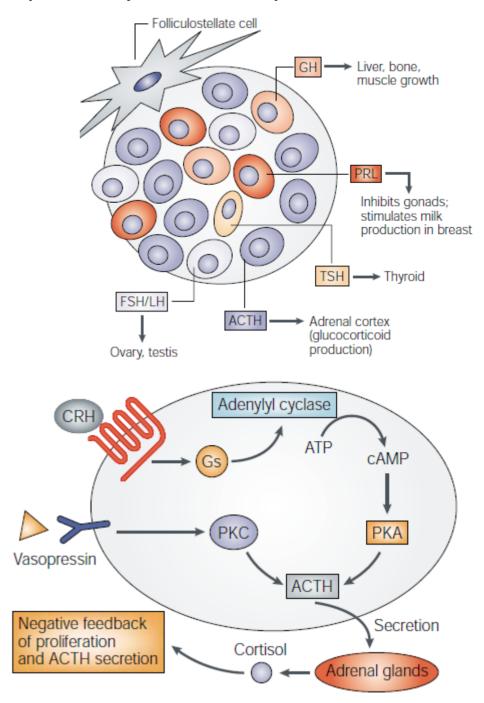


Abstract. A peptide with high potency and intrinsic activity for stimulating the secretion of corticotropin-like and β -endorphin-like immunoactivities by cultured anterior pituitary cells has been purified from ovine hypothalamic extracts. The primary structure of this 41-residue corticotropin- and β -endorphin-releasing factor has been determined to be:

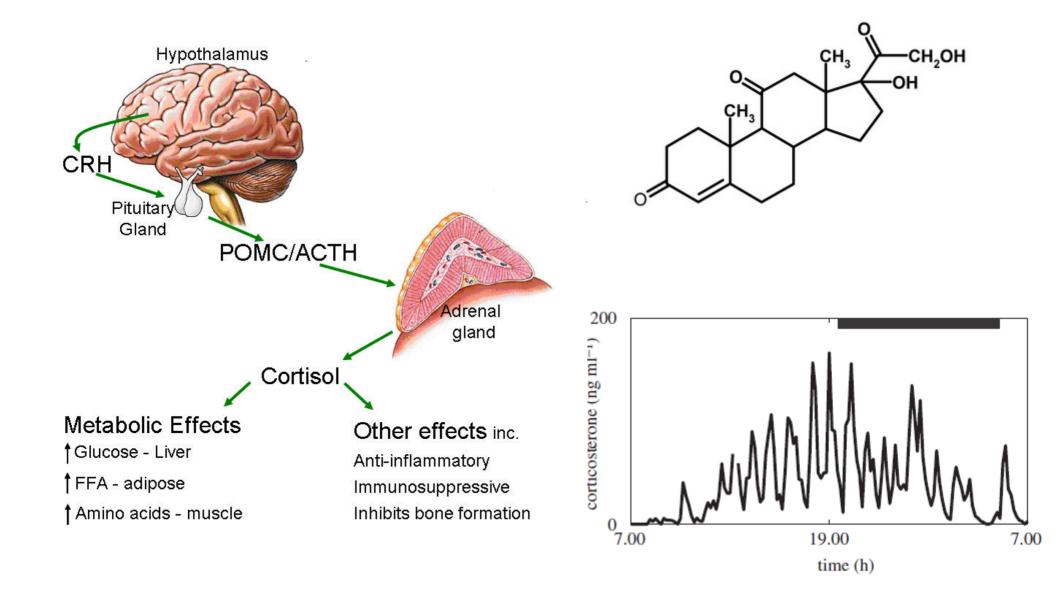
Regulatory pathways of pituitary corticotrophs







Corticosteroid hormone release under control of ACTH



Corticosteroid hormones have two transcription factor receptors: Mineralocorticoid Receptor and Glucocorticoid Receptor

Table 1. Two intracellular corticosteroid receptor types in the brain

1. Mineralocorticoid receptor (MR) High affinity for corticosterone ($K_D \approx 0.5 \text{ nm}$) In limbic brain structures Agonist: aldosterone Antagonist RU 26752, spironolactone

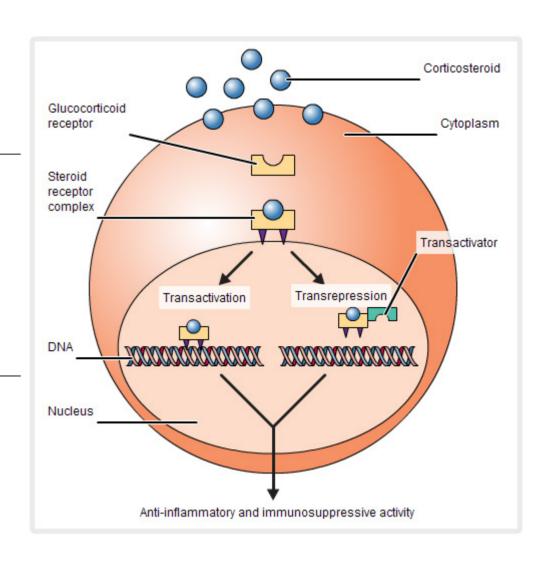
2. Glucocorticoid receptor (GR)

Lower affinity for corticosterone ($K_D \approx 5.0 \text{ nm}$)

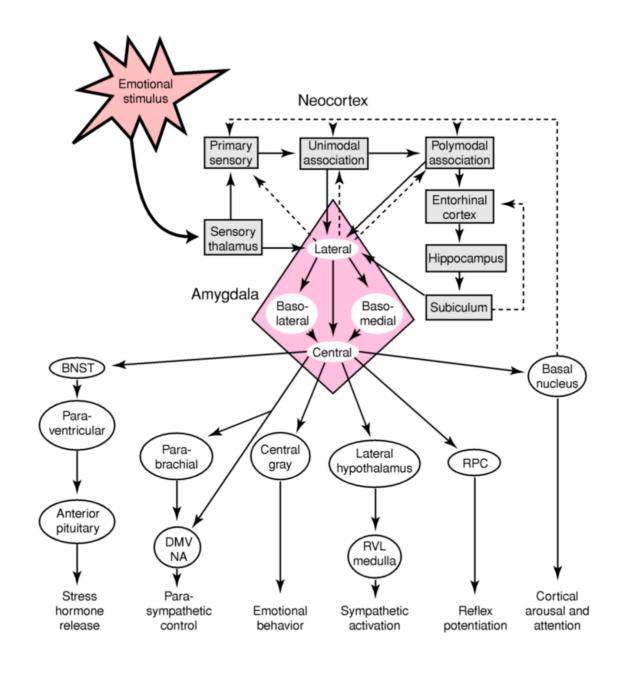
Ubiquitous

Agonist: dexamethasone, RU 28362

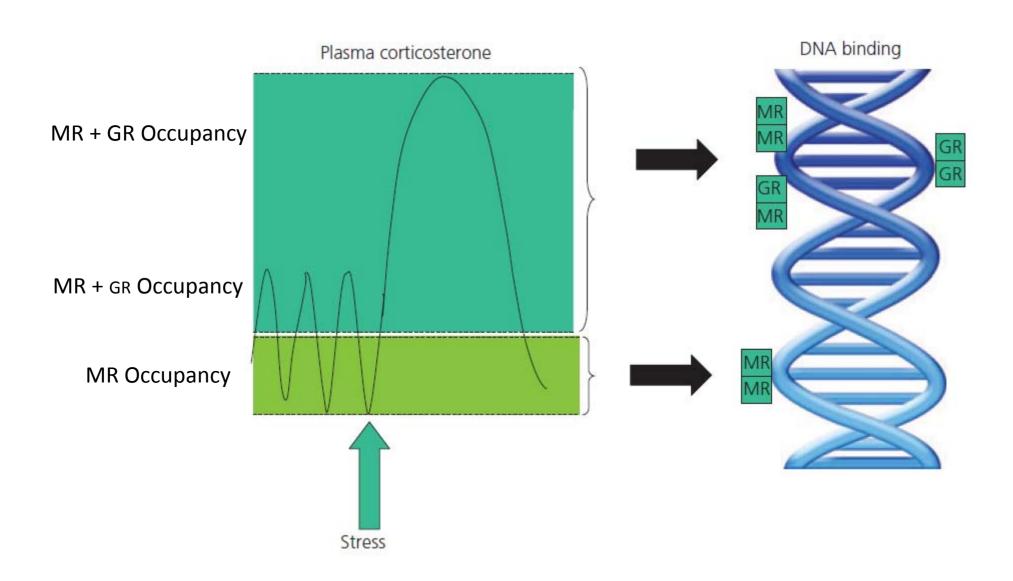
Antagonist: RU 38486



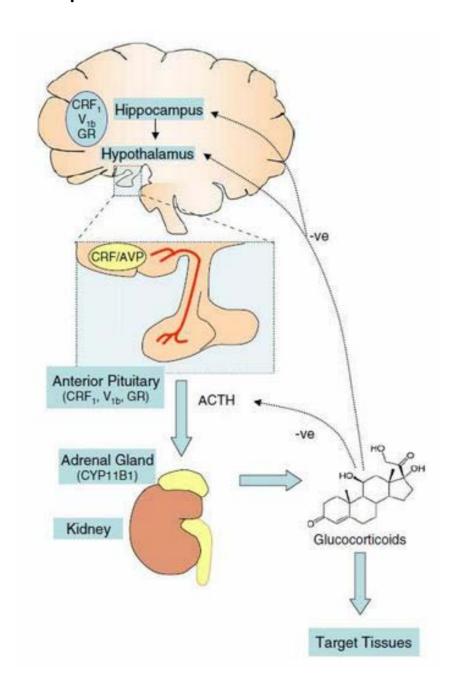
The HPA axis is a major Stress response system



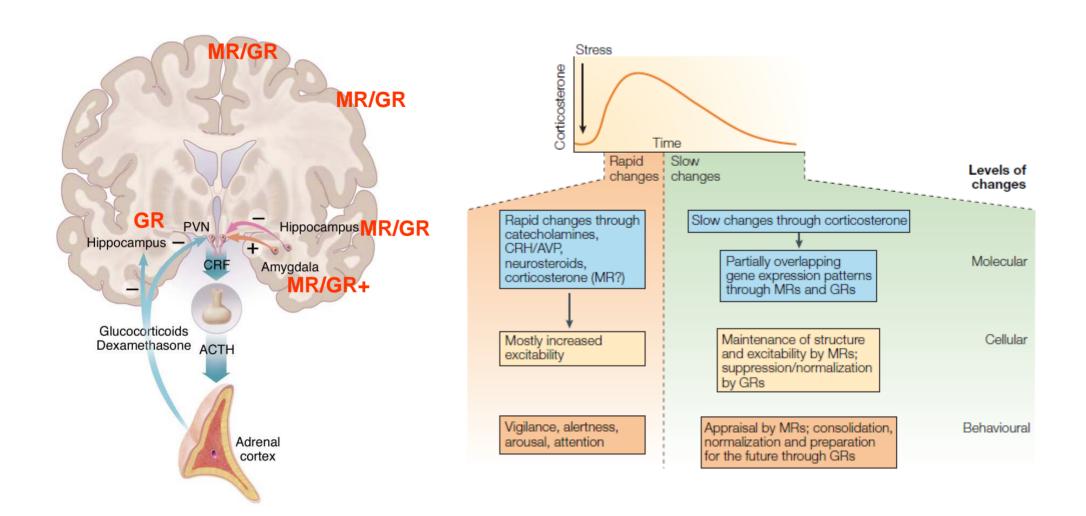
MR and GR affinities determine their state-dependent occupancy and transcription factor functioning



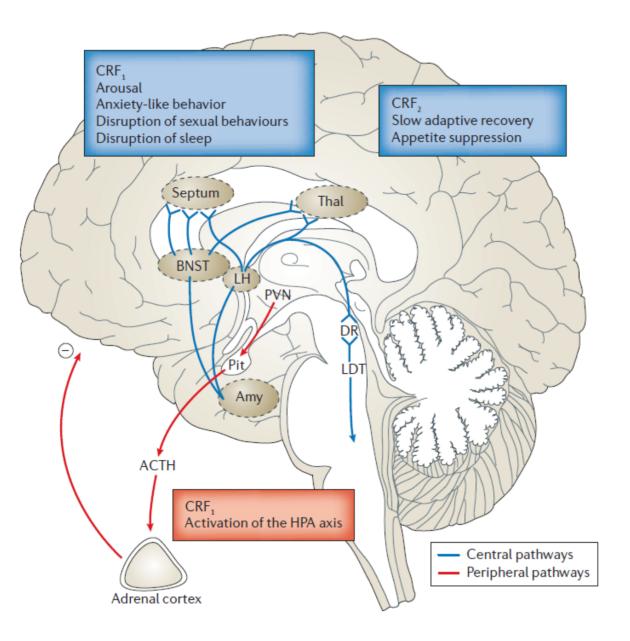
Glucocorticoid Receptor is expressed in hypothalamic PVN neurosecretory cells and pituitary coricotrophs and mediates HPA axis negative feedback



Mineralocorticoid Receptor and Glucocorticoid Receptor are expressed in the Brain



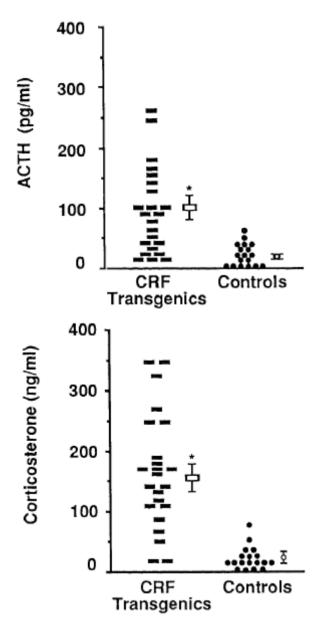
CRF is also a neurotransmitter and is important in CRF neuroendocrine release



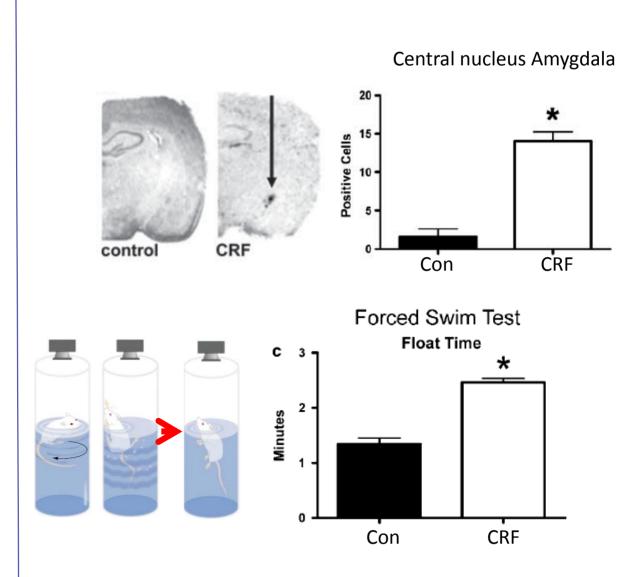
LH, Lateral hypothalamus BNST, Bed nucleus of stria terminalis Thal, Thalamus DR, Dorsal raphe nucleus Amy, Amygdala

CRF over-expression in rodents leads to stress-related phenotypes

Transgenic CRF over-expression in mouse



Viral-vector CRF over-expression in rat



"Increased immobility reflects depressive-like behaviour"

Keen-Rhinehart et al. (2009) Mol Psychiatry 14: 37