Physiology of the pituitary, thyroid, parathyroid and adrenal glands

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Abstract

The pituitary gland is made of clusters of cells producing specific hormones that control growth (growth hormone), thyroid function (triiodothyronine (T_3) and thyroxine (T_4)), adrenal function (adrenocorticotrophic hormone (ACTH)) and gonadal function (follicle-stimulating hormone and luteinizing hormone). In addition, the neurons that join the posterior pituitary (neurohypophysis) secrete vasopressin — the antidiuretic hormone involved in maintaining water balance.

The negative feedback loop is the basic mechanism to control the regulation of all endocrine glands. Hypothalamic peptides — releasing hormones (e.g. TRH, corticotrophin-releasing hormone) reach the hypophysis via the portal venous system and induce the secretion of specific stimulating hormones (e.g. thyroid-stimulating hormone, ACTH) that drive the end-target endocrine cells to secrete hormones (e.g. thyroid hormones — T_3 and T_4 or adrenal hormones — cortisol, dehydroepiandrosterone sulphate). The plasma levels of these circulating hormones inhibit the pituitary (short feedback) or the hypothalamus (long feedback) and limit the further release of releasing and stimulating hormones. The effects of circulating hormones on different tissues are mediated via specific receptors on the cell membrane (e.g. vasopressin receptors), in the cytoplasm (steroid receptor for cortisol) or in the nucleus (e.g. thyroid hormone receptors). Understanding the physiological effects of peripheral hormones helps understanding the mechanisms by which clinical signs and symptoms develop in diseases characterized by excessive hormone secretion (e.g. thyrotoxicosis, Cushing syndrome, phaeochromocytomas) or lack of hormone secretion (e.g. diabetes insipidus).

The parathyroid gland and adrenal medulla are not controlled by the pituitary but play important roles in calcium metabolism and the adrenergic (sympathetic nervous system) function respectively.

Keywords Catecholamines; cortisol; hormone secretion regulation; physiology; pituitary; thyroid hormones

Pituitary gland

The pituitary gland (hypophysis) lies beneath the hypothalamus, in the sella turcica and is composed of two parts (Figure 1): the anterior pituitary (adenohypophysis) is derived from ectoderm and secretes protein hormones; the posterior pituitary (neurohypophysis) is composed largely of hypothalamic neuronal axons which also form the pituitary stalk.

Secretion of hormones from the anterior pituitary is controlled by hypothalamic hormones reaching the pituitary via a portal system. The utility of this vascular system is that minute quantities of hypothalamic hormones are carried directly to their target cells in the anterior pituitary, and are not diluted in the systemic circulation.

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Growth hormone (GH)

GH is a 191-amino acid single-chain polypeptide synthesized in somatotroph cells of the anterior pituitary. There are about ten pulses of GH secretion per day. The predominant male 'pulsatile' secretion versus female 'continuous' secretion might explain the different patterns of gene activation in target tissues, for example induction of linear growth patterns and gain of body weight. GH secretion is controlled as follows.

- GH-releasing hormone (GHRH) secreted by the hypothalamus or as an ectopic secretion (e.g. from pancreatic cancers) stimulates GH secretion.
- Somatostatin (SST) inhibits GH secretion. In addition SST has multiple effects on pancreatic, liver and gastrointestinal function. It inhibits the secretion of CCK, glucagon, gastrin, secretin, GIP, insulin and vasoactive intestinal peptide (VIP) from the pancreas.
- Glucocorticoids have a biphasic effect on GH secretion: an initial acute stimulation within 3 hours, followed by suppression within 12 hours.
- Catecholamines: α-adrenergic pathways stimulate GH secretion. The α2-agonist clonidine can therefore be used as a provocative test of GH secretion. β-adrenergic pathways inhibit secretion by increasing somatostatin release.
- Acetylcholine: muscarinic pathways stimulate GH secretion by modulating somatostatinergic tone. Pyridostigmine, an indirect agonist which blocks acetylcholinesterase, increases the 24-hour secretion of GH. On the other hand, atropine (muscarinic antagonist) blunts GH release.
- Endogenous opioids: endorphins and enkephalins stimulate GH secretion in man and blockade with opiate antagonists can attenuate the GH response to exercise.
- Exercise is a powerful stimulus to secretion of GH.
- Hypovolaemic shock, elective surgery, hypo- and hyperglycaemia, and malnutrition all cause increased GH release. On the other hand, obesity is associated with lower GH levels, partially due to decreased frequency of GH pulses.
- GH release is stimulated by a protein meal. L-arginine, an essential amino acid, can be used as a provocative test for GH secretion.
- Sleep: the amount of GH secreted during sleep is approximately triple the daytime rate. The decline in GH secretion during ageing is parallelled by the decreasing proportion of time spent in sleep. After sleep deprivation (e.g. experimental or due to 'jet lag' when travelling across many time zones) the magnitude of secretory spikes is augmented and the major pulse of GH secretion occurs in late sleep.

Adrenocorticotrophic hormone (ACTH)

ACTH is released from corticotrophs. ACTH is derived from a larger amino acid precursor, pro-opiomelanocortin (POMC). POMC transcription is positively regulated by corticotrophin-releasing hormone (CRH) and negatively regulated by glucocorticoids. Like GH, ACTH is secreted in pulses from corticotrophs

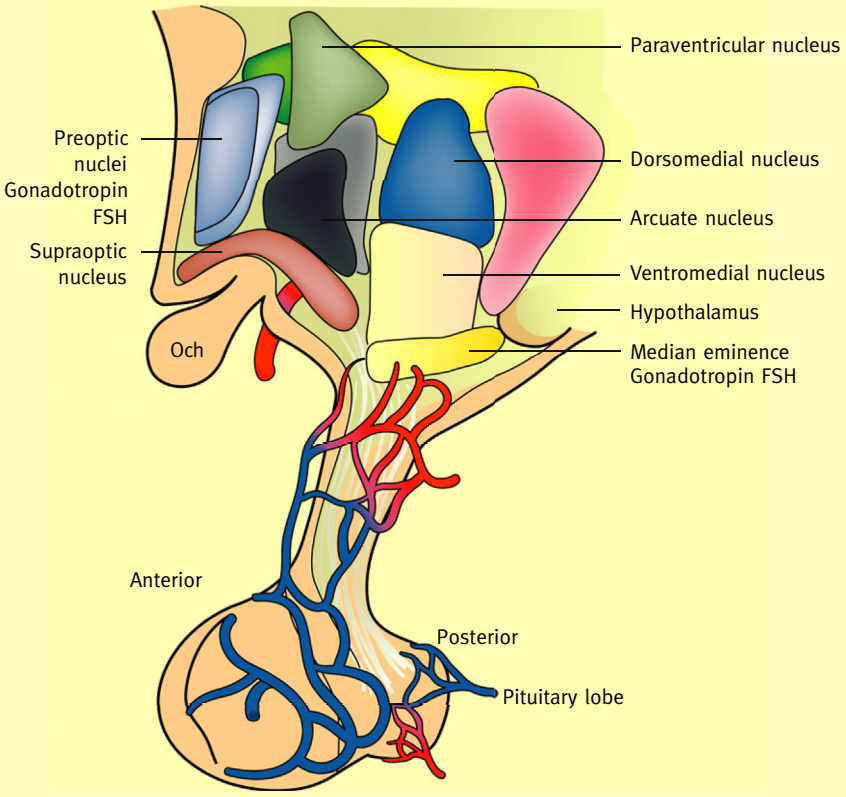

Figure 1

with about 40 pulses/24 hours, correlating with the pulsed secretion of cortisol. ACTH levels vary in circadian rhythm, with a peak at 0600–0900 hours and a trough at 2300–0200 hours.

Glucocorticoid feedback occurs at multiple levels: at the pituitary (inhibition of POMC transcription), at the hypothalamus (inhibition of CRH and AVP synthesis and release in the PVN), and most importantly, centrally at the level of the hippocampus, which contains the highest concentration of glucocorticoid receptors in the central nervous system.

ACTH release is increased by several factors, such as follows.

- CRH is a neuropeptide mainly found in the paraventricular nuclei of the hypothalamus. Besides stimulating POMC transcription and ACTH synthesis, CRH stimulates the release of ACTH, leading to a biphasic response with the fast release of a pre-synthesized pool of ACTH, and the slower and sustained release of newly synthesized ACTH.
- VIP stimulates ACTH secretion, a mechanism which may explain the increase in ACTH after eating.
- Catecholamines stimulate CRH release via central α1-adrenergic receptors.
- Interleukins (IL-1, IL-6 and possibly IL-2) – via short-term effects on the hypothalamus.
- Stress induces the release of ACTH. The hypoglycaemia during the insulin tolerance test is one such stressor.

Antidiuretic hormone (ADH)/vasopressin (AVP)

Arginine-vasopressin is a nine-amino acid peptide synthesized within hypothalamic neurons and packaged in secretory vesicles with a carrier protein called neurophysin, to be released from the posterior pituitary. Vasopressin conserves body water by reducing the loss of water in urine. It binds to receptors on cells in the collecting ducts of the kidney and promotes the insertion of 'water channels' (aquaporins) into the membranes of kidney tubules, which transport solute-free water through tubular cells and back into blood (water reabsorbtion), leading to a decrease in plasma osmolarity and an increased osmolarity of urine. High concentrations of ADH also cause widespread constriction of arterioles, which leads to increased arterial pressure.

ADH secretion is modulated by plasma osmolarity, which is sensed in the hypothalamus by osmoreceptors. When plasma osmolarity increases above a threshold, osmoreceptors stimulate the neurons that secrete ADH. Hypothalamic osmoreceptors also control the thirst sensation. The osmotic threshold for ADH secretion is considerably lower than for thirst, hence thirst is only activated if ADH alone cannot handle the increase in osmolarity. Secretion of ADH is also simulated by decreases in blood pressure and volume, conditions sensed by stretch receptors in the heart and large arteries. For example, loss of 15–20% of blood volume by haemorrhage results in massive secretion of ADH.