Chapter 15 – Hypothalamus, Pituitary, Adrenal, Thyroid, Sympathetic NS, and Stress

Objectives

Given the synopsis in this chapter, competence in each objective will be demonstrated by writing short essays, drawing diagrams, and responding to multiple choices or matching questions, at the level of 85% or greater proficiency for each student.

A. To compare and contrast the organization of the posterior pituitary and the anterior pituitary.
B. To explain the organization and control of the hypothalamic – pituitary axis in the control of metabolic hormones, and their role in the control of thyroid, adrenal cortical, and hepatic hormones.
C. To explain the organization and control of the hypothalamic – pituitary axis in the control of reproductive hormones, and their role in the control of the testes, ovaries, and mammary glands.
D. To explain the organization of the cerebral cortex, amygdala, hypothalamus, and brainstem in the integration of stress responses; including the role of CRF and the control and action of epinephrine, cortisol and T4/T3.

The hypothalamus, pituitary, thyroid, adrenal and sympathetic nervous system are central to the control and regulation of the body, especially the internal organs. In addition, each mediates critical components of the body's response to stress.

Pituitary Gland

As we saw in chapter 14 the pituitary gland is located at the base of the skull, is attached to the hypothalamus, and is separated into a posterior division and an anterior division.

Posterior Pituitary

The posterior pituitary is a direct continuation of the hypothalamus and contains axons of hypothalamic neurons that secrete vasopressin (antidiuretic hormone [ADH]) and oxytocin. As shown in Figure 15.1, magnocellular neurons of the hypothalamus synthesize and secrete vasopressin or oxytocin into the capillary network of the posterior lobe of the pituitary. From there the posterior pituitary hormones enter the systemic circulation by way of the pituitary vein. Accordingly, the posterior pituitary is as much hypothalamus as it is gland. The stimulus, source, and actions of each posterior pituitary hormone are summarized in Appendix A, Table A.1.

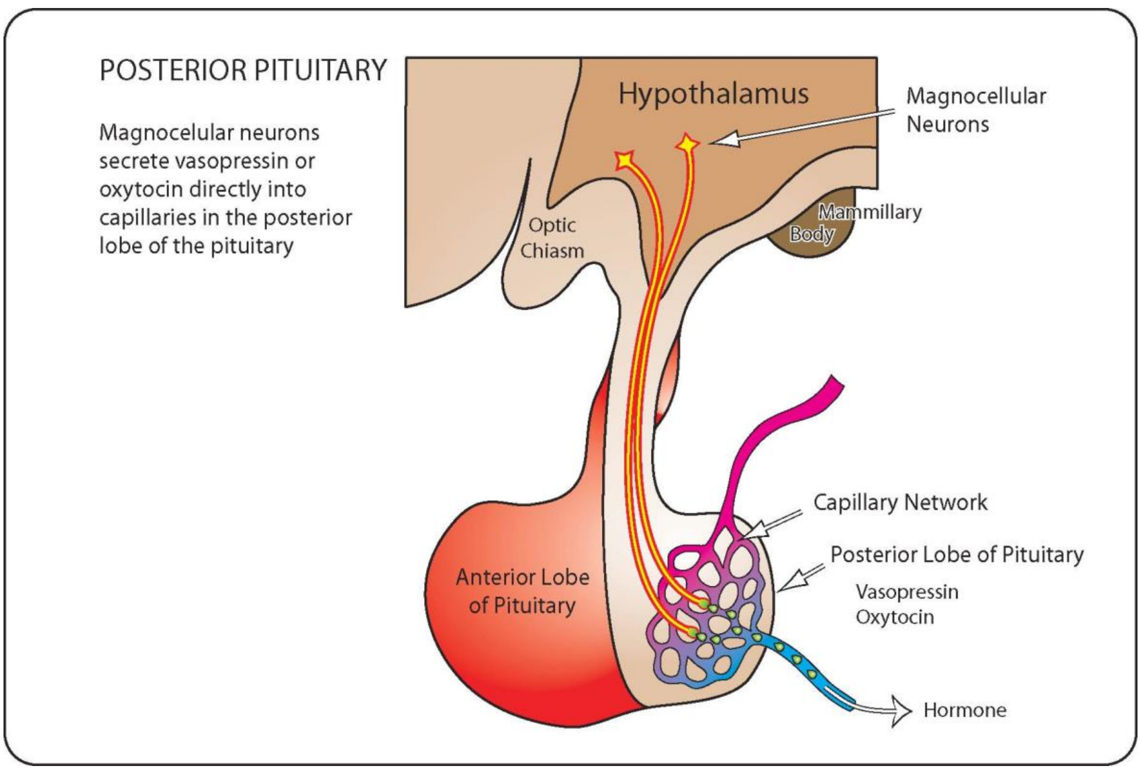

Figure 15.1 © 2007 David G. Ward, Ph.D.

Physical stress such as dehydration, hyper-osmolarity, and low blood volume stimulates magnocellular neurons and increases the secretion of vasopressin. In turn, vasopressin acts on V1a receptors to constrict blood vessels, on V1b receptors to enhance corticotropin secretion from the anterior pituitary, and on V2 receptors to increase the reabsorption of water by the kidney.

Sexual activity, childbirth, and suckling stimulate magnocellular neurons and increases the secretion of oxytocin. In turn oxytocin facilitates bonding and trust, stimulates uterine contraction, facilitates milk ejection from the mammary glands, and alters sodium excretion by the kidney

Anterior Pituitary

The anterior pituitary is a separate structure that is composed of endocrine cells rather than neurons. As shown in Figure 15.2, parvicellular neurons of the hypothalamus send their axons to the median eminence where chemical messengers (called hypothalamic regulatory hormones) are secreted into the capillary network of the median eminence. Pituitary portal vessels carry the regulatory hormones into the capillary network of the anterior pituitary where specific anterior pituitary cells respond to these hormonal signals. The pituitary cells that respond to the regulatory hormones will increase or decrease the secretion of their specific hormone into the capillary network of the anterior pituitary. From there the anterior pituitary hormones enter the systemic circulation by way of the pituitary vein. The stimulus, source, and actions of each hypothalamic regulatory hormone and each anterior pituitary hormone are summarized in chapter 14, Appendix A, Table A.3

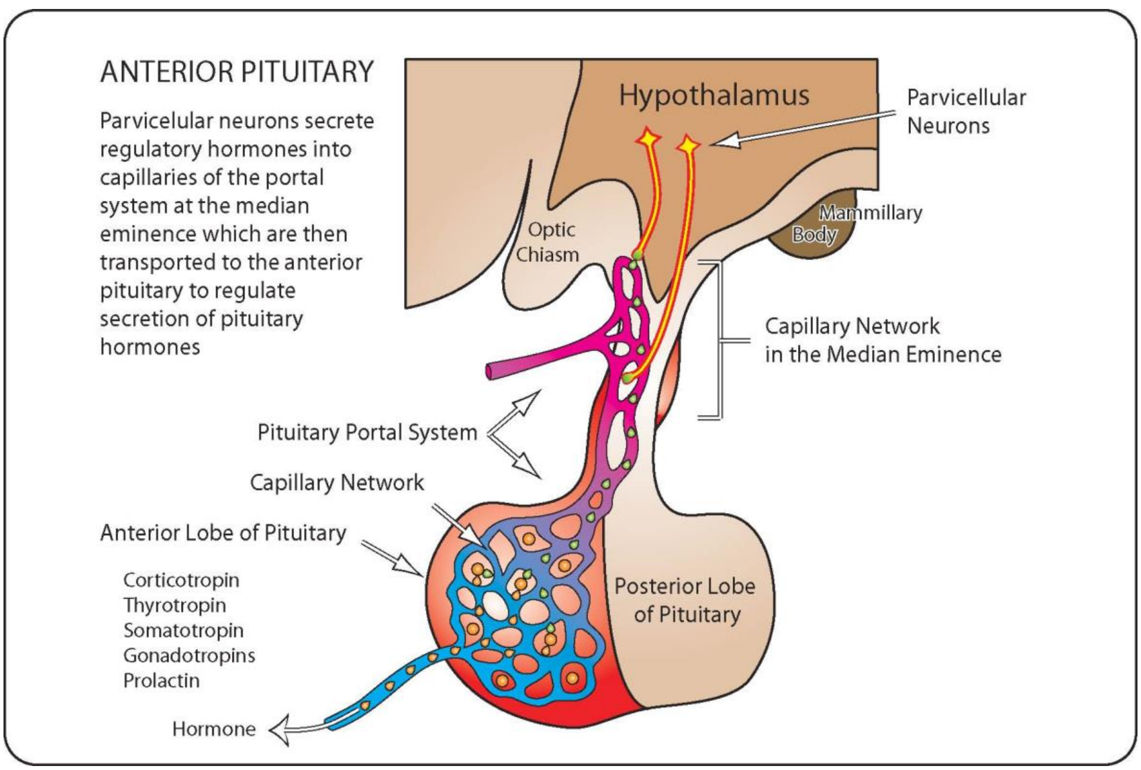

Figure 15.2 © 2007 David G. Ward, Ph.D.

There are five major types of cells in the anterior pituitary and each type of cell produces specific anterior pituitary hormones and is controlled by one or more specific hypothalamic regulatory hormone. The hormones can be divided into two categories: metabolic and reproductive.

Metabolic Anterior Pituitary Hormones

Three types of anterior pituitary cells produce hormones with metabolic actions, as shown in Figure 15.3

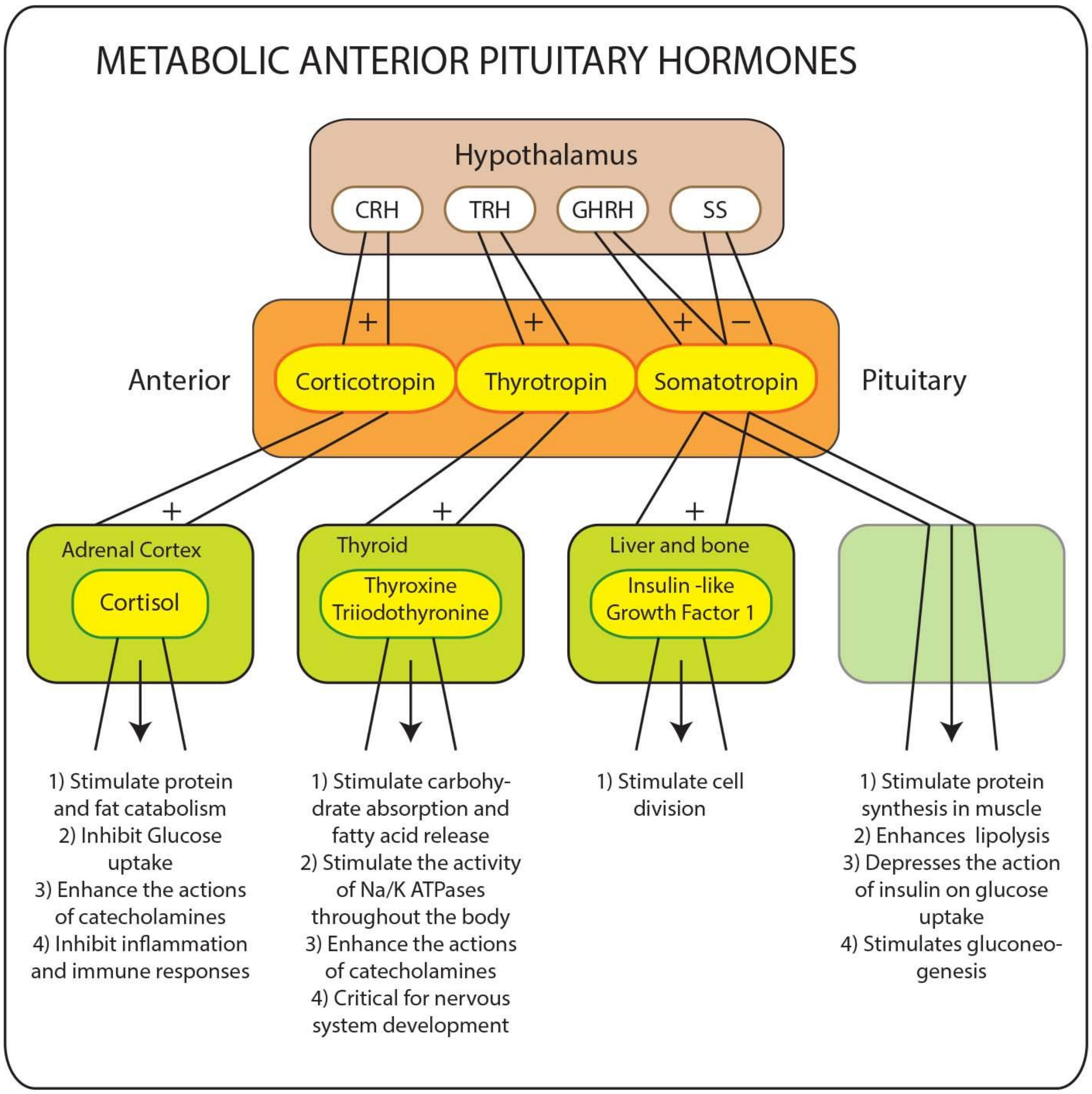

Figure 15.3 © 2020 David G. Ward, Ph.D.

- Corticotrophs secrete **corticotropin** (adrenocorticotropic hormone [ACTH]) and are stimulated by corticotropin releasing hormone (**CRH**) from the hypothalamus
- Thyrotrophs secrete **thyrotropin** (thyroid stimulating hormone [TSH]) and are stimulated by thyrotropin releasing hormone (**TRH**)
- Somatotrophs secrete **somatotropin** (growth hormone [GH]) and are stimulated by growth hormone releasing hormone (**GHRH**) or are inhibited by somatostatin (**SS**)

Physical stress such as low blood volume, cold, or low metabolism are among the factors that stimulate the hypothalamic neurons, which in turn secrete CRH, TRH, and GHRH. Elevated metabolism is one of the factors that stimulate the hypothalamic neurons that secrete SS. (Refer to chapter 14, Appendix, Table 14.2.)

Corticotropin and the adrenal cortex

Corticotropin acts on the zona fasciculata of the adrenal cortex to increase the synthesis and release of **cortisol**, as shown in Figure 15.3 and summarized in Appendix A, Table A.7. Major actions of cortisol include

- Stimulating protein and fat catabolism
- Inhibiting glucose uptake
- Enhancing the secretion and actions of catecholamines
- Inhibiting inflammation and immune responses
- Helping to maintain blood volume

Corticotropin acts on the zona reticularis of the adrenal cortex to increase the synthesis and release of **androstenedione**, as summarized in Appendix A, Table A.7. Major actions of adrenal androstenedione and its metabolic product testosterone include

- Stimulating muscle growth
- Increasing bone density
- Increasing libido to varying degrees
- Providing about 50% of the androgens in women

Thyrotropin and the thyroid

Thyrotropin acts on the follicles of the thyroid to increase the synthesis and release of **triiodothyronin (T3) and thyroxin (T4)**, as shown in Figure 15.3 and summarized in Appendix A, Table A.4. Major actions of T3 and T4 include

- Increasing the synthesis and quantity of Na^+/K^+ pumps
- Increasing the synthesis and quantity of mitochondrial and cellular respiratory enzymes
- Increasing oxygen and food consumption, carbohydrate absorption and substrate use
- Enhancing metabolic responses to epinephrine
- Increasing cardiac output and heart rate

Somatotropin and the liver and organs

Somatotropin acts on the hepatocytes of the liver to increase the synthesis and release of **insulin-like growth factor-1 (IGF-1)**, as shown in Figure 15.3. Major actions of IGF-1 include

- Acting on most cells of the body muscle, cartilage, bone, liver, kidney, nerves, skin, and lungs
- Stimulating cell division (proliferation)
- Inhibiting cell death (apoptosis)
- Achieving maximal growth
- Acting like a weaker form of insulin by binding to insulin receptors

Somatotropin also acts directly on most cells of the body, as shown in Figure 15.3. Major direct actions of somatotropin include

- Stimulating protein synthesis in muscle
- Enhancing lipolysis
- Depressing the action of insulin on glucose uptake
- Stimulating gluconeogenesis

Reproductive Anterior Pituitary Hormones

Two types of anterior pituitary cells produce hormones with reproductive actions, as shown in Figure 15.4

- Gonadotrophs secrete gonadotropins (**follicle stimulating hormone** [FSH] and **luteinizing hormone** [LH]) and are stimulated by gonadotropin releasing hormone (**GnRH**) from the hypothalamus
- Prolactotrophs secrete **prolactin** (PRL) and are stimulated by prolactin releasing hormone (**PRH**) or are inhibited by dopamine (**DA**)

Intrinsic neural pacemakers play a critical role in stimulating the hypothalamic neurons that secrete GnRH, and DA. Pregnancy and suckling are among the factors that stimulate the hypothalamic neurons that secrete PRH. (Refer to Appendix A, Table A.2.)

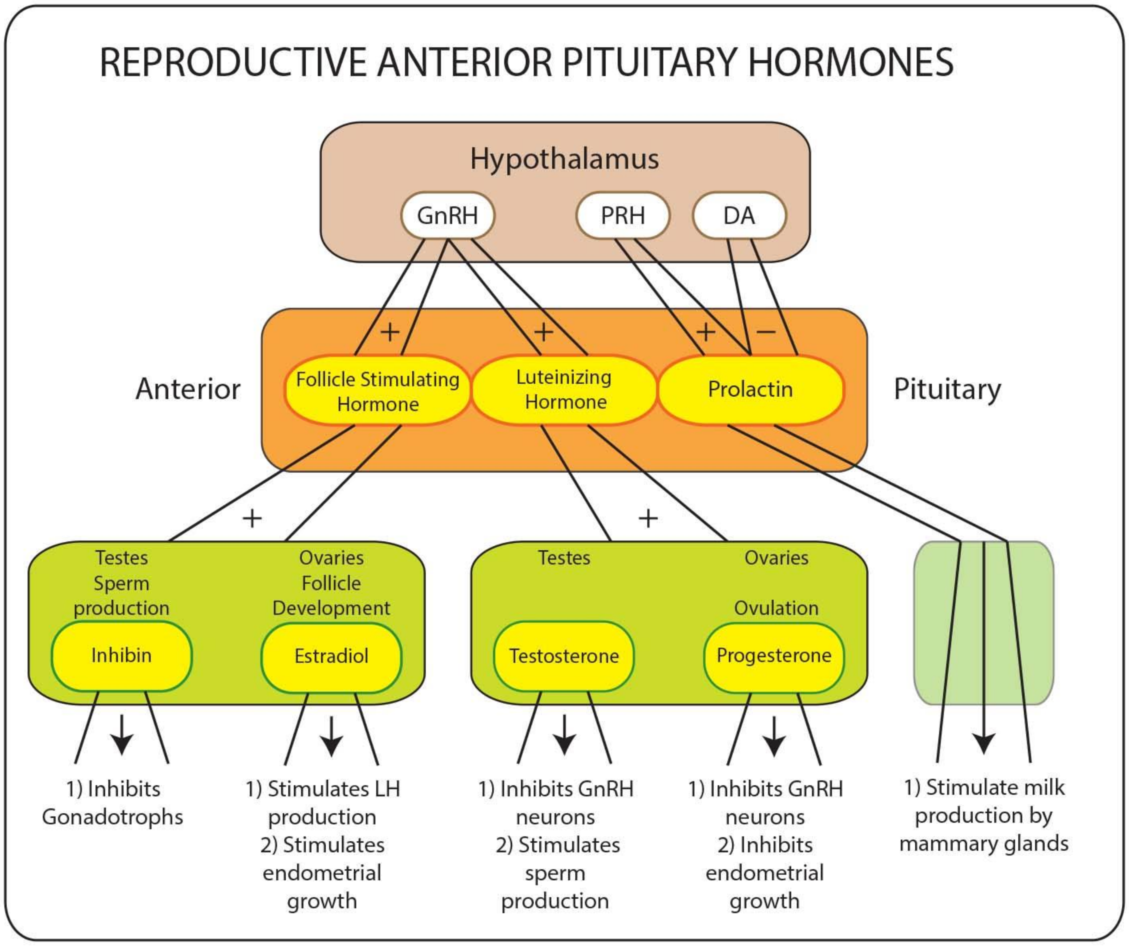

Figure 15.4 © 2020 David G. Ward, Ph.D.

Gonadotropins and the testes

Follicle stimulating hormone acts on the testes to increase androgen binding globulin and the secretion of **inhibin**, as shown in Figure 15.4 and summarized in Appendix A, Table A.12. Major actions of inhibin include

- Inhibiting gonadotrophs in the anterior pituitary

Luteinizing hormone acts on the testes to increase the synthesis and release of **testosterone**, as shown in Figure 15.4 and summarized in Appendix A, Table A.12. Major actions of testosterone include

- Inhibiting GnRH neurons in the hypothalamus
- Stimulating sperm production

Gonadotropins and the ovaries

Follicle stimulating hormone acts on the ovaries to stimulate follicle development and the synthesis and release of **estradiol**, as shown in Figure 15.4 and summarized in Appendix A, Table A.11. Major actions of estradiol include

- Stimulating luteinizing hormone secretion by gonadotrophs in the anterior pituitary
- Stimulating growth of the endometrium of the uterus

Luteinizing hormone acts on the ovaries to stimulate ovulation, the conversion of the empty follicle to the corpus luteum, and the synthesis and release of **progesterone**, as shown in Figure 15.4 and summarized in Appendix A, Table A.11. Major actions of progesterone include

- Inhibiting GnRH neurons in the hypothalamus
- Inhibiting and stabilizing growth of the endometrium of the uterus

Stress

Hans Selye (1974), who first used the term “stress”, called stress the "non-specific response of the body to any demand." The stress reaction can range from assuring peak performance during a physical or intellectual task, to helping the body deal with stimuli perceived as a threat. These types of responses require that large amounts of stored energy are released quickly.

Stimuli leading to stress responses come from two general areas – sensory nerves and the brain, as shown in Figure 14.5. Signals about physical stress, such as trauma, blood loss, pain, or inflammation travel through sensory nerves and reach the brainstem and hypothalamus. The second source of stimuli is from the brain. Fear, anxiety, or other emotions may occur when one perceives situations similar to previous unpleasant experiences. Signals from the cortex and amygdala travel to the hypothalamus.

The hypothalamus is central because it is an integration region for the parasympathetic nervous system, the sympathetic nervous system and the endocrine system. The hypothalamus, especially the paraventricular nucleus, coordinates the stress response by releasing corticotropin-releasing hormone (CRH). CRH was discovered first as a hormone and later was found to act as a neurotransmitter. As a hormone, CRH controls the pituitary, and by way of corticotropin, the cortex of the adrenal gland. As a neurotransmitter, CRH appears to control the autonomic nervous system. The hypothalamus receives messages from peripheral nerves, the cortex, and the limbic system, and controls behavioral, autonomic, and endocrine responses to stress.

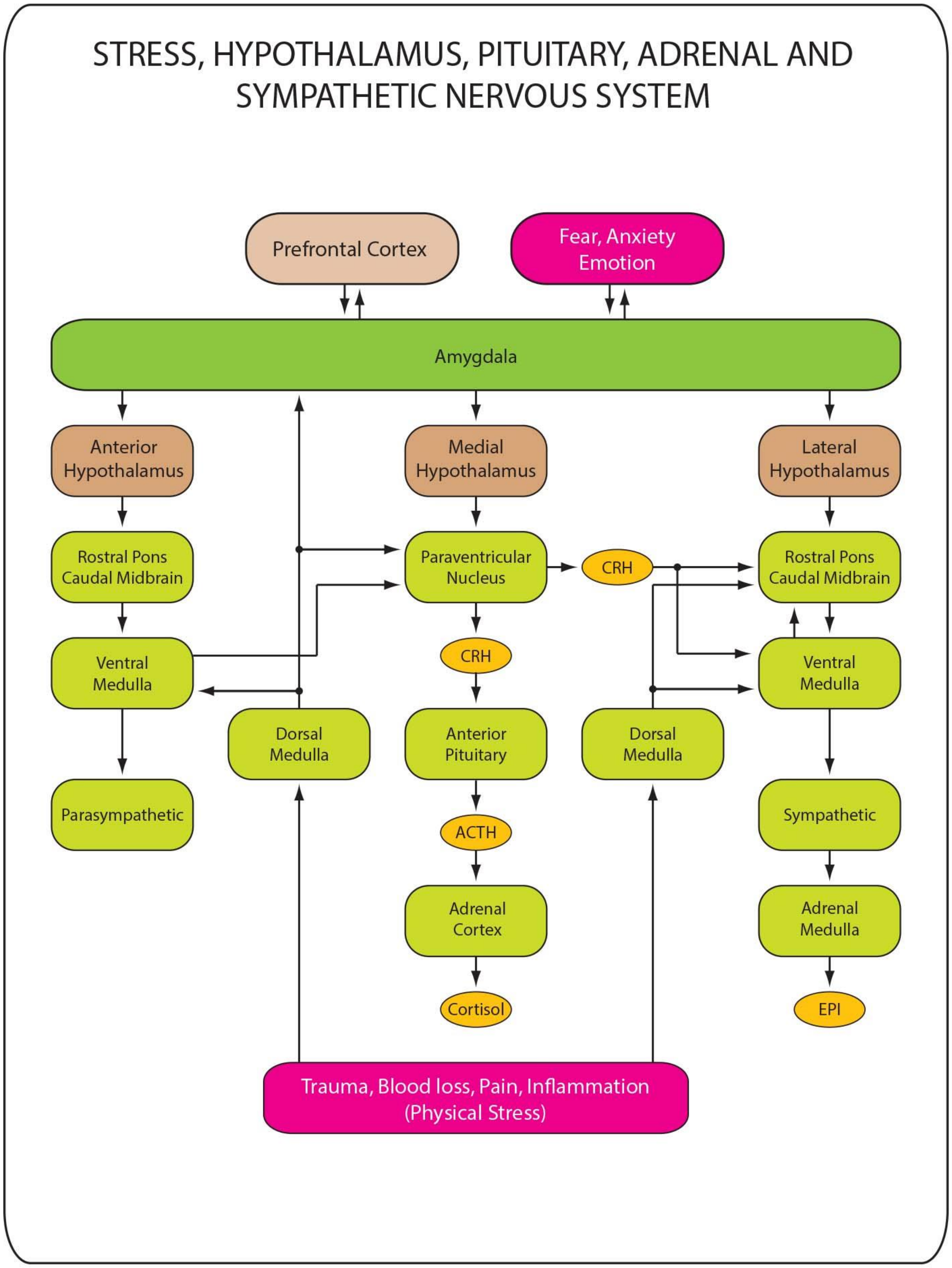

Figure 15.5 © 2020 David G. Ward, Ph.D.

The behavioral responses to stress are numerous, complex, and only partially understood. One behavioral response is nervous eating. Another is alternately freezing and running in the face of danger. In the classroom, nervous behavior may occur when a pop quiz is announced. The message enters the ears and goes to the cortex and limbic system where it is recognized as a cause for concern, especially if one has not studied. From here, the message is sent to the hypothalamus that returns messages to the limbic system to stimulate complex behavioral patterns, such as fidgeting, tremors, and increased talkativeness. Some of the hypothalamic messages are mediated by CRH, the same chemical that stimulates the endocrine and autonomic nervous systems. Consequently, students may also experience the autonomic symptoms of dilated pupils, sweaty palms, and increased heart and respiratory rates. The hypothalamus uses CRH as one of its messengers to coordinate the stress response to the pop quiz.

The autonomic responses to stress are stimulated by the hypothalamus, especially the paraventricular nucleus, and in part mediated by CRH. The autonomic responses are often easy to identify and may include increased heart rate and breathing, accelerated passage of food through the gastrointestinal tract, and hyperactive bladder. Most of the autonomic nerve activity in the stress response is due to sympathetic nerves that secrete the neurotransmitter norepinephrine. The sympathetic nervous system also stimulates the adrenal medulla to secrete the hormone epinephrine.

The endocrine responses to stress are stimulated by the hypothalamus. In reaction to continued stress, the hypothalamus secretes CRH, thyrotropin-releasing hormone (TRH), and growth hormone releasing hormone (GHRH). As we have seen these hypothalamic regulatory hormones lead to the secretion of corticotropin, thyrotropin and somatotropin from the anterior pituitary. The anterior pituitary hormones in turn lead to the synthesis and release of cortisol, T3, and T4 from the adrenal cortex and thyroid gland, respectively. The hypothalamus also stimulates the sympathetic nervous system which by way of acetylcholine in the adrenal medulla stimulates the secretion of epinephrine. Together, the body's cells are stimulated to use fat and protein, rather than glucose, for energy and to use glucose at a faster rate. Together epinephrine, cortisol, T3, and T4 help to supply energy to cells that are stimulated by stress stimuli and to cope with the increased metabolic demands on the cells brought on by increased activity.

All three stress response systems -- behavior, autonomic, and endocrine -- are coordinated in part by the hypothalamic release of CRH. These systems work together to help the body work at peak performance during physically, intellectually, physiologically, or emotionally stressful activities. Acute stress is generally seen as beneficial in this way. However, during prolonged stress, the stress response may damage certain body tissues and functions. Cortisol acts as a negative feedback mechanism to prevent overreaction of the several CRH-stimulated stress response systems. This is fairly effective with acute stress, but long-term or chronic stress is still associated with harmful effects. It is generally best if one can manage a lifestyle with intermittent acute stress rather than continuous stress.

Quiz Yourself

1-5. Matching

A) anterior pituitary
B) posterior pituitary
C) none of the above

contains thyrotrophs 1) _____
contains corticotrophs 2) _____
contains gonadotrophs 3) _____
contains pituitary portal vessels 4) _____
contains axons of hypothalamic neurons 5) _____

6-10. Matching

A) CRH
B) TRH
C) GHRH
D) GnRH

stimulates the release of ACTH by the pituitary 6) _____
stimulates the release of TSH by the pituitary 7) _____
stimulates the release of FSH by the pituitary 8) _____
stimulates the release of GH by the pituitary 9) _____
stimulates the release of LH by the pituitary 10) _____

11-15. Place in order the signals and structures involved in release of cortisol.

A) Pituitary portal vessels carry hormone 11) _____
B) Central nervous system detects stress 12) _____
C) Hypothalamic CRH neurons secrete CRH 13) _____
D) Anterior pituitary corticotrophs secrete corticotropin 14) _____
E) Adrenal fasciculata cells synthesize and release cortisol 15) _____

16-20. Place in order the signals and structures involved in release of T3 and T4.

A) Pituitary portal vessels carry hormone 16) _____
B) Central nervous system detects stress 17) _____
C) Hypothalamic TRH neurons secrete TRH 18) _____
D) Anterior pituitary corticotrophs secrete thyrotropin 19) _____
E) Thyroid follicles release T3 and T4 20) _____

Fill in

21. The posterior pituitary is an extension of the _______________ and contains _______________ (cells) that secrete hormones.

22. The anterior pituitary responds to _______________ and _______________ hormones and contains _______________ cells that secrete hormones.

23. _______________ (a hormone) inhibits cellular uptake of glucose and increases use of fatty acids and amino acids as an energy source.

24. Fear and anxiety leading to stress is mediated by the _______________ of the brain.

25. The neural and endocrine responses to stress are integrated in part by the _______________ _______________ of the hypothalamus which secretes _______________________.

Study Questions

1. Compare and contrast the organization of the posterior pituitary and the anterior pituitary.
2. Explain how the hypothalamus controls the anterior pituitary, which in turn controls other endocrine glands.
3. Explain the role of CRH in the control and integration of neural and endocrine responses to stress.