6 Diencephalon and Autonomic Nervous System

6 Diencephalon and Autonomic Nervous System

The diencephalon lies between the brainstem and the telencephalon. It has four components: the thalamus, epithalamus, subthalamus, and hypothalamus.

The **thalamus** is found on both sides of the third ventricle and consists of numerous nuclei with different functions. It is the relay station for most of the afferent pathways that ascend to the cerebral cortex. Some types of impulses (e.g., nociceptive impulses) may already be perceived, integrated, and given an affective coloring, in an imprecise way, in the thalamus, but actual conscious experiences do not seem to be generated until sensory impulses reach the cerebral cortex. Moreover, the thalamus has extensive connections with the basal ganglia, brainstem, cerebellum, and motor cortical areas of the cerebrum and is thus a major component of the motor regulatory system.

The most important nucleus of the **subthalamus** is the subthalamic nucleus, which is closely functionally related to the basal ganglia.

The **epithalamus** is mainly composed of the epiphysis (pineal gland/pineal body) and the habenular nuclei; it plays a role in the regulation of circadian rhythms.

The most basal portion of the diencephalon is the **hypothalamus**, which coordinates vital bodily functions such as respiration, circulation, water balance, temperature, and nutritional intake and is thus the hierarchically uppermost regulatory organ of the autonomic nervous system. It also influences the activity of the endocrine glands by way of the hypothalamic–pituitary axis.

The **autonomic nervous system** is responsible for the nerve supply of the internal organs, blood vessels, sweat glands, and salivary and lacrimal glands. It is called "autonomic" because it functions largely independently of consciousness; it is alternatively (less commonly) called the vegetative nervous system. Its efferent arm in the periphery is composed of two anatomically and functionally distinct parts, the sympathetic and parasympathetic nervous systems. The afferent arm is not divided in this way.

Because of the multiplicity of functions that the diencephalon performs, **diencephalic lesions** can have very diverse effects, depending on their site and extent. Thalamic lesions produce hemiparesis and hemisensory deficits, movement disorders, disturbances of consciousness, and pain syndromes, while hypothalamic lesions impair various vital functions singly or in combination, and cause endocrine dysfunction.

Location and Components of the Diencephalon

Location. The position of the diencephalon is just oral to that of the midbrain; the diencephalon does not continue along the brainstem axis, but rather takes a rostral bend, so that it comes to lie nearly in the longitudinal axis of the cerebrum (Fig. 6.**1**). It is located in the middle of the brain, ventrally and caudally to the frontal lobe, and encloses the lower portion of the third ventricle from both sides (Fig. 6.**2**).

The *thalamus* forms the **upper** portion of the third ventricular wall, the *hypothalamus* its **lower** portion. **Dorsally**, the diencephalon is enclosed by the corpus callosum, the lateral ventricles, and the cerebral hemispheres (Fig. 6.**2**). The roof of the third ventricle is formed by the thin tela choroidea and the attached choroid plexus. The **rostral** extent of the diencephalon is delimited by the lamina terminalis and anterior commissure, its **caudal** extent by the posterior commissure, habenular commissure, and pineal body (epiphysis). The interventricular foramen of Monro, which connects the lateral ventricle with the third ventricle, is found on either side anterior to the rostral portion of the thalamus, just below the genu of the fornix. The basal portion of the diencephalon is its only externally visible part: it can be seen on the undersurface of the brain between the optic chiasm, the optic tract, and the cerebral peduncles. The visible diencephalic structures in this area are the mamillary bodies and the tuber cinereum, together with

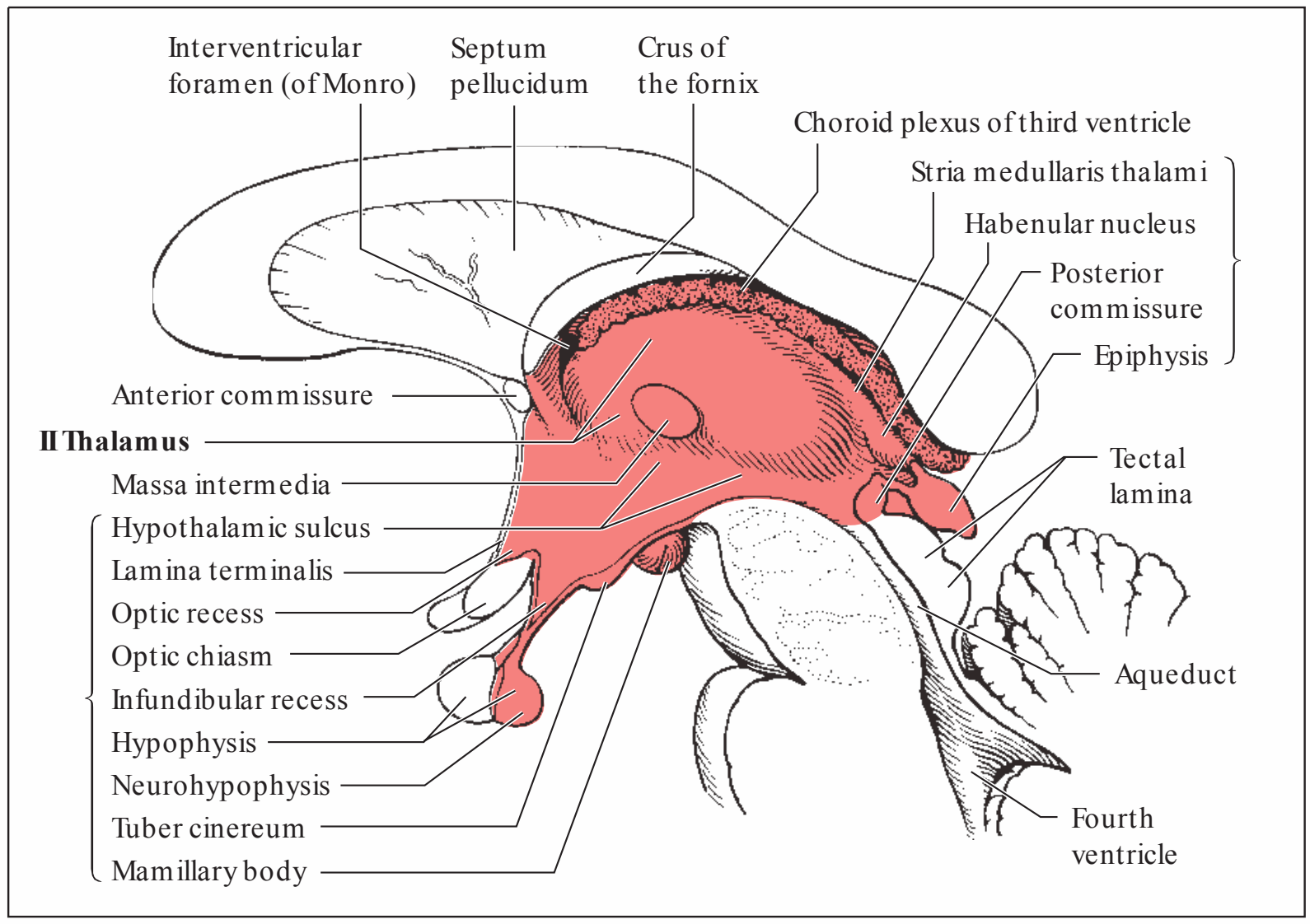


Fig. 6.**1** **Sagittal section through the diencephalon and the brainstem** showing the midbrain–diencephalic junction and the structures surrounding the third ventricle

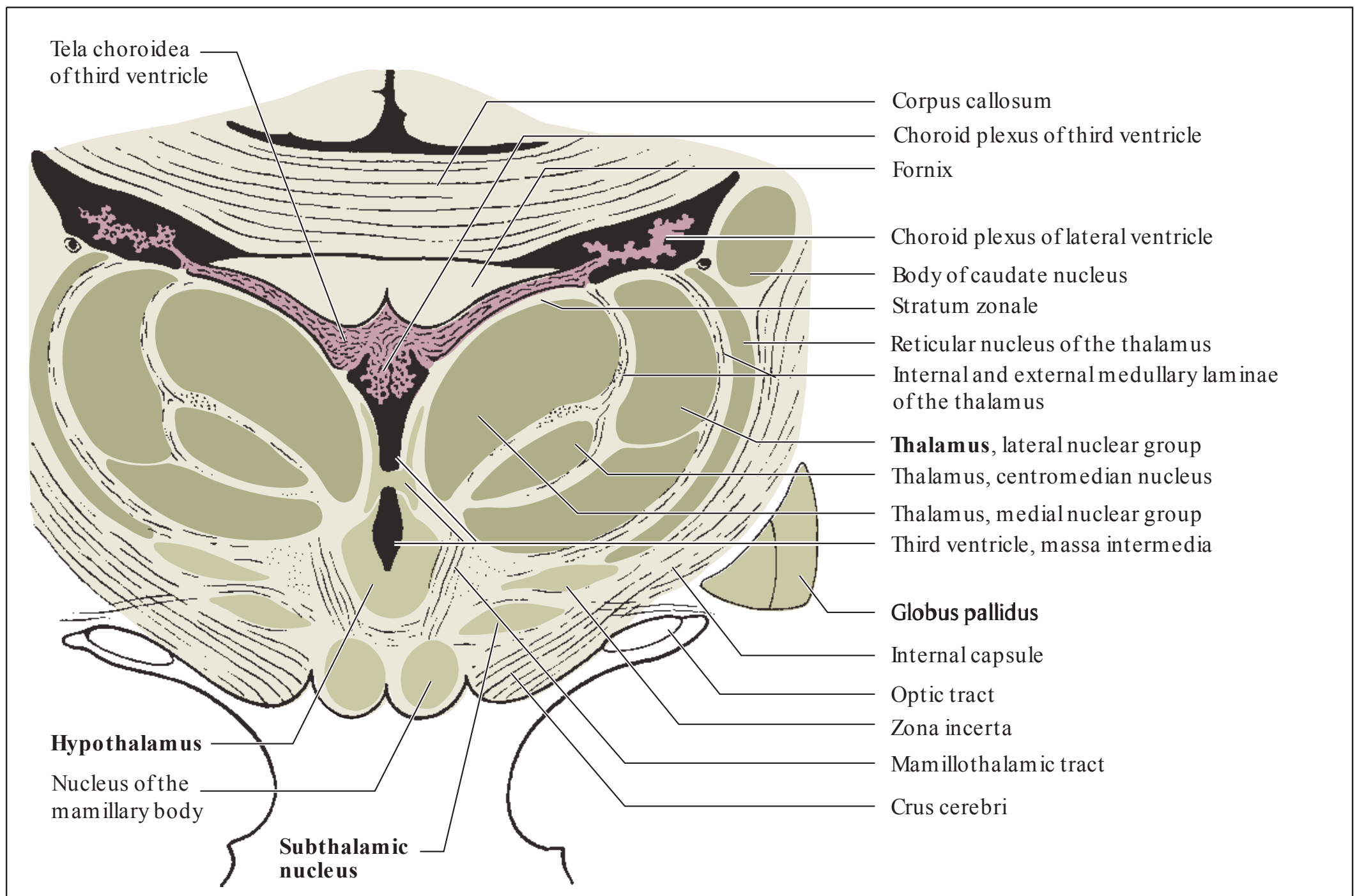


Fig. 6.**2** **Coronal section through the diencephalon**

its infundibulum (pituitary stalk), which leads downward to the pituitary gland (cf. Fig. 4.**8**, p. 83.

The two halves of the thalamus facing each other across the third ventricle are connected in 70–80 % of cases by the interthalamic adhesion (*massa intermedia*) (Fig. 6.**1**), which is not a fiber pathway but rather a secondary adhesion of the gray matter coming from either side. **Laterally**, the diencephalon is delimited by the internal capsule.

The globus pallidus is embryologically a part of the diencephalon, though it is separated from it by the internal capsule (Fig. 8.**4**, p. 216) and is thus located in the basal ganglia. It will be discussed along with the rest of the basal ganglia in Chapter 8 (p. 214). Likewise, a discussion of the hypophysis (pituitary gland), which is linked to the hypothalamus by the infundibulum, will be deferred to the section on the peripheral autonomic nervous system (p. 188).

Subdivisions. The diencephalon has the following components (Fig. 6.**1**):

- The **epithalamus**, which consists of the habenula and habenular nuclei, the habenular commissure, the epiphysis, and the epithalamic (posterior) commissure.
- The **thalamus**, a large complex of neurons that accounts for four-fifths of the volume of the diencephalon.
- The **hypothalamus**, which is demarcated from the thalamus by the hypothalamic sulcus, and contains various functionally distinct groups of neurons. It is the hierarchically uppermost center ("head ganglion") of the autonomic nervous system; on each side, the column of the fornix descends through the lateral wall of the hypothalamus to terminate in the mamillary body (see Fig. 6.**8**).
- The **subthalamus**, which mainly consists of the subthalamic nucleus (corpus luysii, Fig. 6.**2**) and is located beneath the thalamus and dorsolateral to the mamillary body.

Thalamus

Nuclei

Flanking the third ventricle, on either side of the brain, there is a large, ovoid complex of neurons measuring about 3 × 1.5 cm in diameter. This complex, the thalamus, is not a uniform cluster of cells but rather a conglomerate of numerous, distinct nuclei, each with its own function and its own afferent and efferent connections. Each half of the thalamus (left and right) is divided into three major regions by sheetlike layers of white matter taking the form of a Y (the internal medullary laminae, Fig. 6.**3**). The **anterior nuclei** sit in the angle of the Y, the **ventrolateral nuclei** laterally, and the **medial nuclei** medially. The ventrolateral nuclei are further subdivided into *ventral* and *lateral nuclear groups*. The ventral nuclei include the *ventral anterior nucleus* (*VA*), the *ventral lateral nucleus* (*VL*), the *ventral posterolateral nucleus* (*VPL*), and the *ventral posteromedial nucleus* (*VPM*). The lateral nuclei consist of a *lateral dorsal nucleus* and a *lateral posterior nucleus*. Further caudally, one finds the **pulvinar**, with the **medial** and **lateral geniculate bodies** attached to its underside. There are a few small groups of neurons within the internal medullary laminae (the **interlaminar nuclei**), as well as one larger, centrally located cell complex, the **centromedian nucleus** (or *centre médian*). Laterally, the external medullary lamina separates the thalamus from the internal capsule; the **reticular nucleus of the thalamus** is a thin layer of cells closely applied to the external medullary lamina (Fig. 6.**2**).

The three major nuclear groups (anterior, ventrolateral, and medial) have been cytologically and functionally subdivided into about 120 smaller nuclei, the most important of which are shown in Fig. 6.**3**. There is still no uniform standard for the subdivision and nomenclature of the thalamic nuclei; the nomenclature followed in Fig. 6.**3** is that found in *Nomina Anatomica*.

Position of the Thalamic Nuclei in Ascending and Descending Pathways

In the preceding chapters, the pathways that ascend from the spinal cord, brainstem, and cerebellum to the cerebral cortex have been traced upward as far as the thalamus. The thalamus is the last major relay station for all ascending impulses (except olfactory impulses) before they continue, via thalamocortical fibers, to the cortex. Figure 6.**4** shows the termination of various afferent pathways in distinct thalamic nuclei, which then project to corresponding cortical areas (for further details, see p. 173).

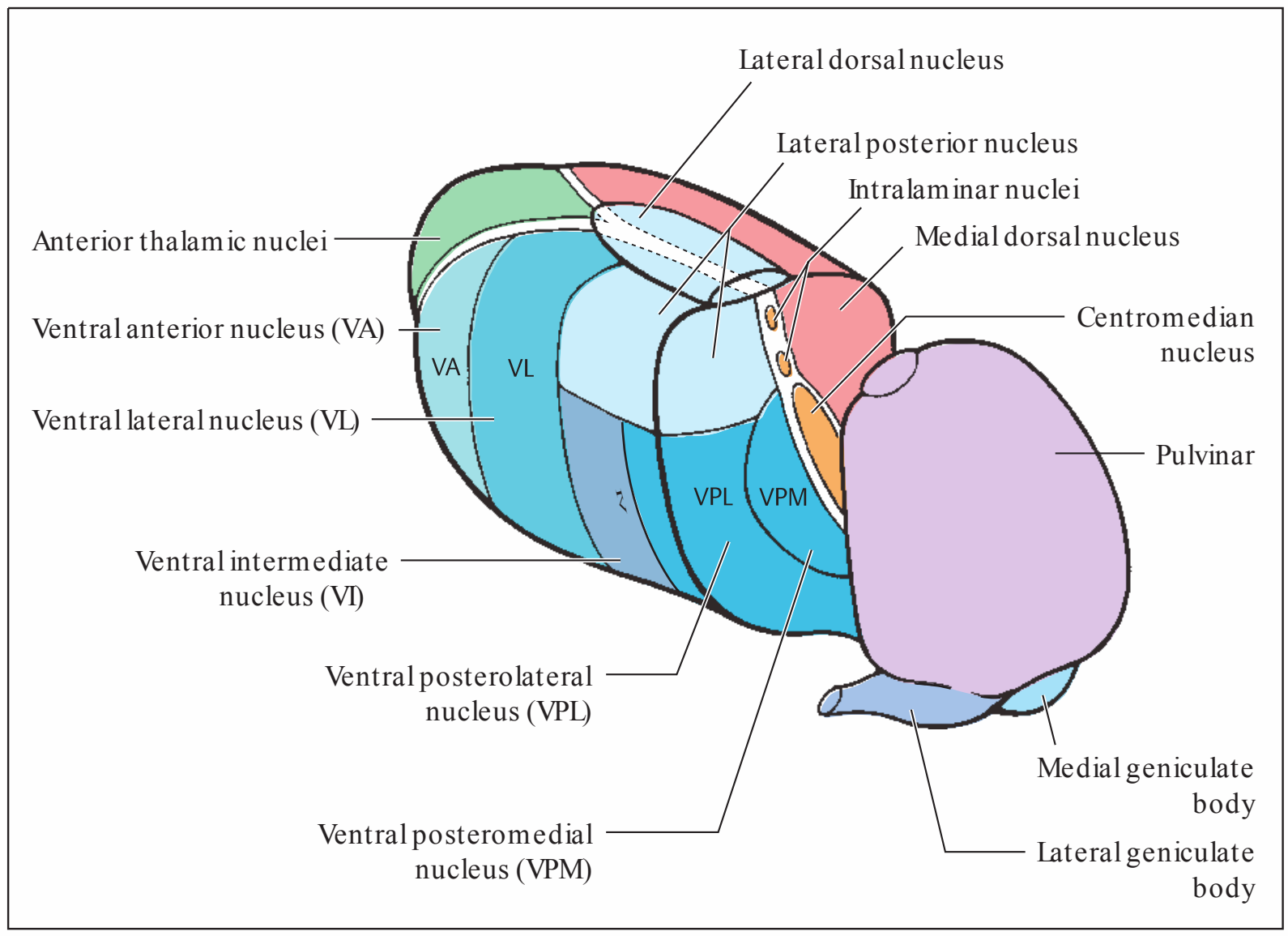


Fig. 6.**3** **Thalamic nuclei.** The four major nuclear groups are shown: the **anterior group** (green), the **ventrolateral group** (various shades of blue), the **medial group** (red), and the **dorsal group,** consisting of the pulvinar (violet) and the geniculate bodies (shades of blue).

Like the spinal cord and brainstem (e.g., the medial lemniscus), the thalamic nuclei and the thalamocortical projections maintain a strict **point-to-point somatotopic organization**.

Specific and nonspecific projections. Thalamic nuclei that receive input from circumscribed areas of the body periphery and transmit impulses to the corresponding circumscribed cortical areas (primary projective fields) are called **specific thalamic nuclei** (or primary thalamic nuclei). Thalamic nuclei projecting to the unimodal and multimodal cortical association areas (secondary and tertiary thalamic nuclei) are also counted among the specific nuclei. The distinguishing feature of the specific nuclei is thus a *direct projection to the cerebral cortex*.

In contrast, **nonspecific thalamic nuclei** receive their afferent input from multiple, distinct sense organs, usually after an intervening synapse in the reticular formation and/or one of the primary thalamic nuclei. They project only indirectly to the cerebral cortex (e.g., by way of the basal ganglia), including the association fields.

Specific Thalamic Nuclei and Their Connections

Nuclei with Connections to Primary Cortical Areas

Ventral posterolateral nucleus (VPL) and ventral posteromedial nucleus (VPM). All somatosensory fibers ascending in the medial lemniscus, spinothalamic tract, trigeminothalamic tract, etc., terminate in a relay station in the ventroposterior nuclear complex of the thalamus. The ventral posterolateral nucleus is the *relay station for the medial lemniscus*, while the ventral posteromedial nucleus is the *relay station for trigeminal afferents*. These nuclei, in turn, project fibers to circumscribed areas of the somatosensory cortex (areas 3a, 3b, 1, and 2, Fig. 6.**4**).

Furthermore, *gustatory fibers* from the nucleus of the tractus solitarius terminate in the medial tip of the ventral posteromedial nucleus, which, in turn, projects to the postcentral region overlying the insula (Fig. 6.**4**).

Medial and lateral geniculate bodies. The medial and lateral geniculate bodies, too, are among the specific nuclei of the thalamus. The optic tract terminates in the lateral geniculate body, which relays *visual impulses* retinotopically, by way of the optic radiation, to the visual cortex (area 17). *Auditory impulses* are carried in the lateral lemniscus to the

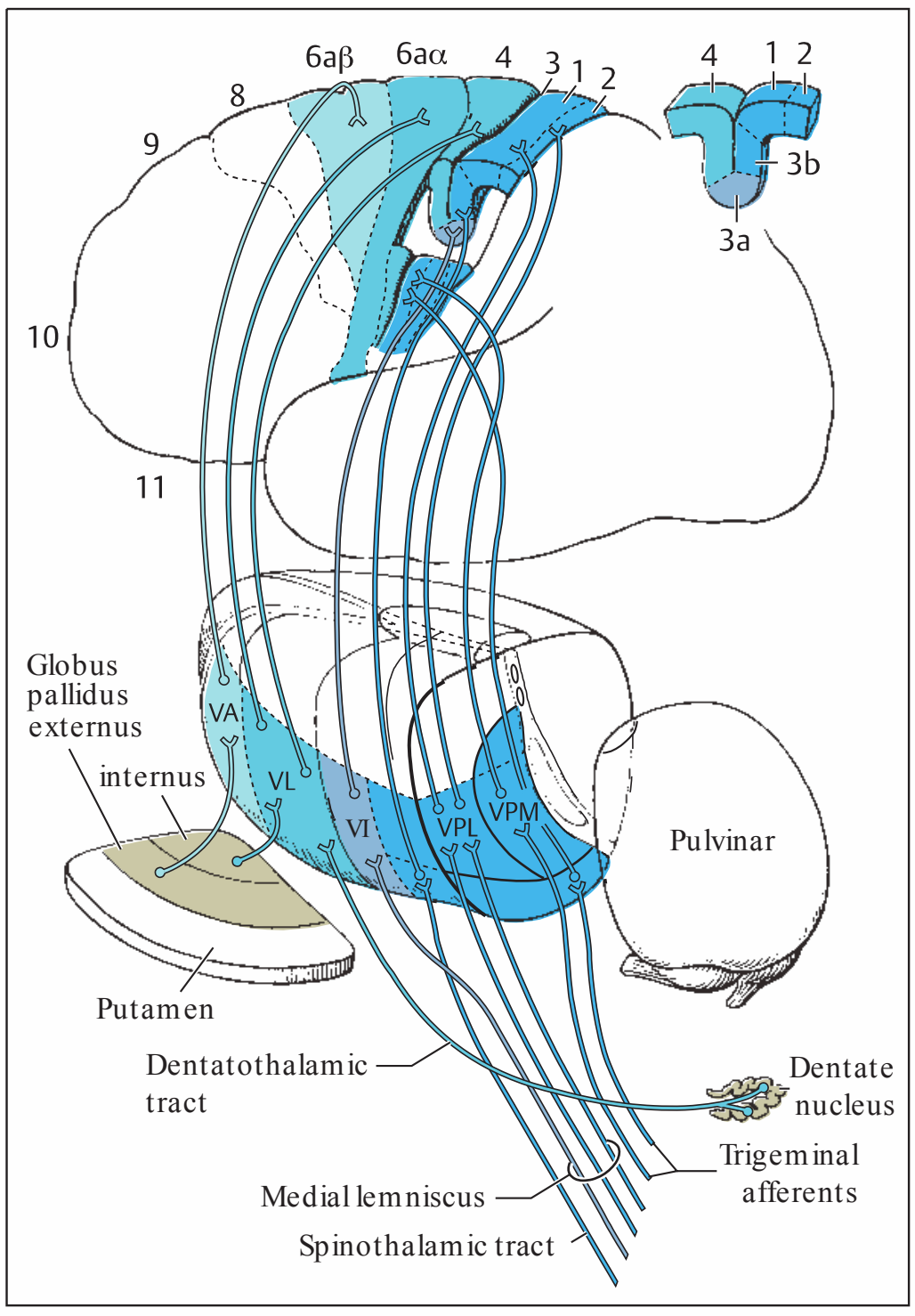


Fig. 6.4 **Afferent and efferent connections of the ventral nuclear group**

medial geniculate body and relayed tonotopically, by way of the auditory radiation, to the auditory cortex (transverse temporal gyri of Heschl, area 41) in the temporal lobe (Fig. 6.**5**).

Ventral oral nuclei and ventral anterior nucleus. The ventral oral posterior nucleus (V.o.p., a portion of the ventral lateral nucleus) receives input from the *dentate nucleus and red nucleus* by way of the dentatothalamic tract (Fig. 6.**4**) and projects to the *motor cortex* (area 4), while the ventral oral anterior nucleus (V.o.a.) and the ventral anterior nucleus (VA), both of which also belong to the ventral nuclear group, receive input from the *globus pallidus* and project to the *premotor cortex* (areas 6aα and 6aβ) (Fig. 6.**4**).

Nuclei Projecting to Association Areas of the Cerebral Cortex

The anterior nucleus, the medial nucleus, and the pulvinar are secondary and tertiary thalamic nuclei (Figs. 6.**5**, 6.**6**), i.e., specific thalamic nuclei projecting to the unimodal and multimodal cortical association fields (pp. 247). These nuclei mostly receive their input not directly from the periphery but rather after a synaptic relay, which is usually located in one of the primary thalamic nuclei described above.

The **anterior nucleus** (Fig. 6.**6**) is reciprocally connected to the mamillary body and fornix through the mamillothalamic tract (of Vicq d'Azyr); it possesses bidirectional, point-to-point connections with the cingulate gyrus (area 24) and is thus an integral part of the limbic system, whose structure and function are described in Chapter 7.

The **medial nucleus** of the thalamus has bidirectional, point-to-point connections with the *association areas of the frontal lobe* and the *premotor region*. It receives afferent input from other thalamic nuclei (ventral and intralaminar nuclei), and from the hypothalamus, midbrain nuclei, and globus pallidus (Fig. 6.**5**).

Destruction of the medial nucleus by a tumor or other process causes a **frontal brain syndrome** with a change of personality (loss of self-representation, as described by Hassler), just as has been described after frontal leukotomy—a psychosurgical procedure, now rarely, if ever, performed, in which a lesion is made in the deep white matter of the frontal lobe. The visceral impulses that reach this nucleus by way of the hypothalamus exert an influence on the affective state of the individual, leading to a sense of well-being or uneasiness, good or bad mood, etc.

The **pulvinar** possesses reciprocal, point-to-point connections with the association areas of the parietal and occipital lobes (Fig. 6.**5**). These association areas are surrounded by the primary somatosensory, visual, and auditory cortices and thus probably play a major role in the binding of these different types of incoming sensory information. The pulvinar receives neural input from other thalamic nuclei, especially the intralaminar nuclei.

Lateral nuclei. The lateral dorsal nucleus and the lateral posterior nucleus do not receive any neural input from outside the thalamus and are connected only to other thalamic nuclei. They are thus known as integrative nuclei.

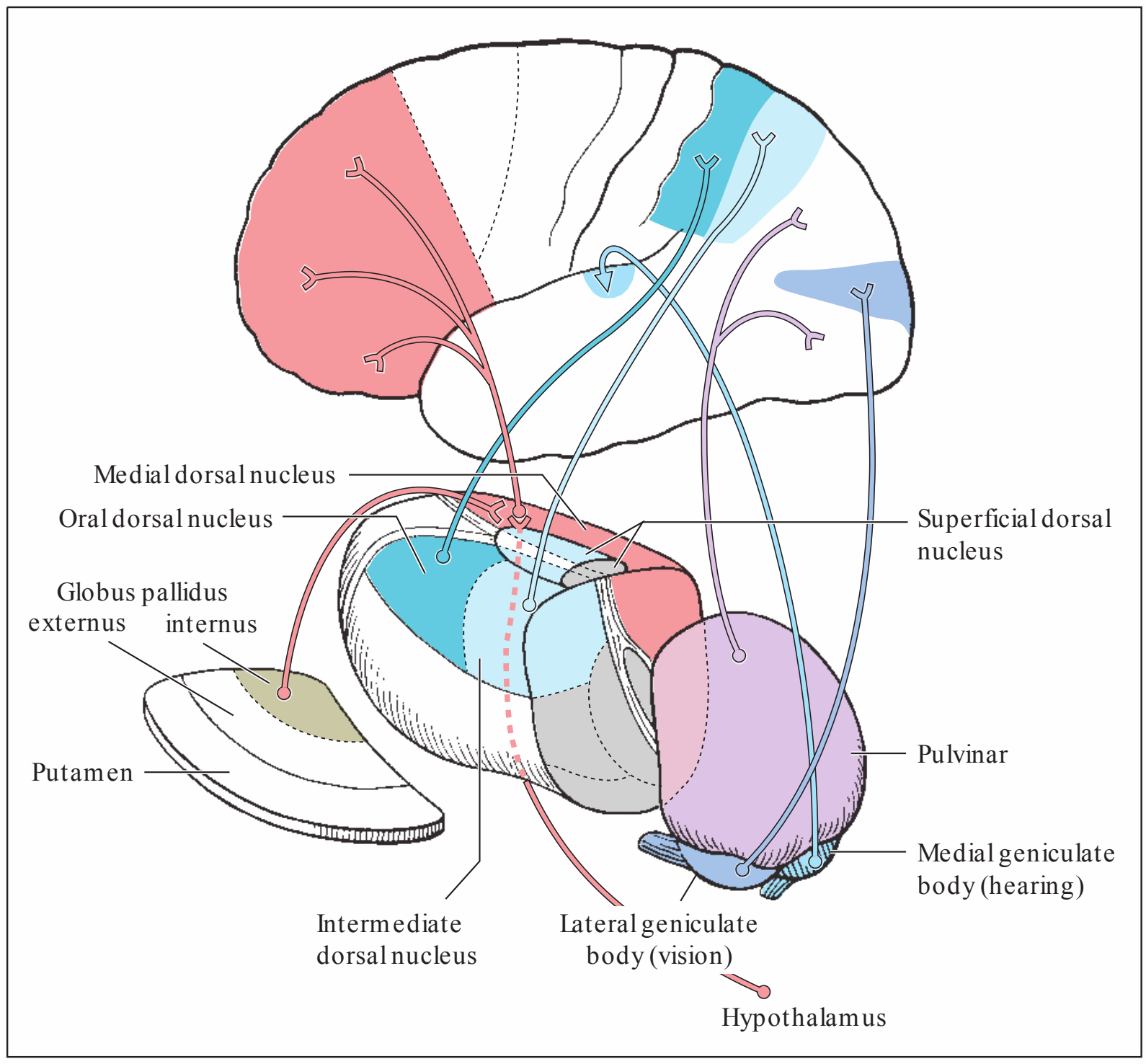


Fig. 6.**5** **Afferent and efferent connections of the medial** (red), **dorsal** (violet/blue), **and lateral** (blue) **nuclear groups**

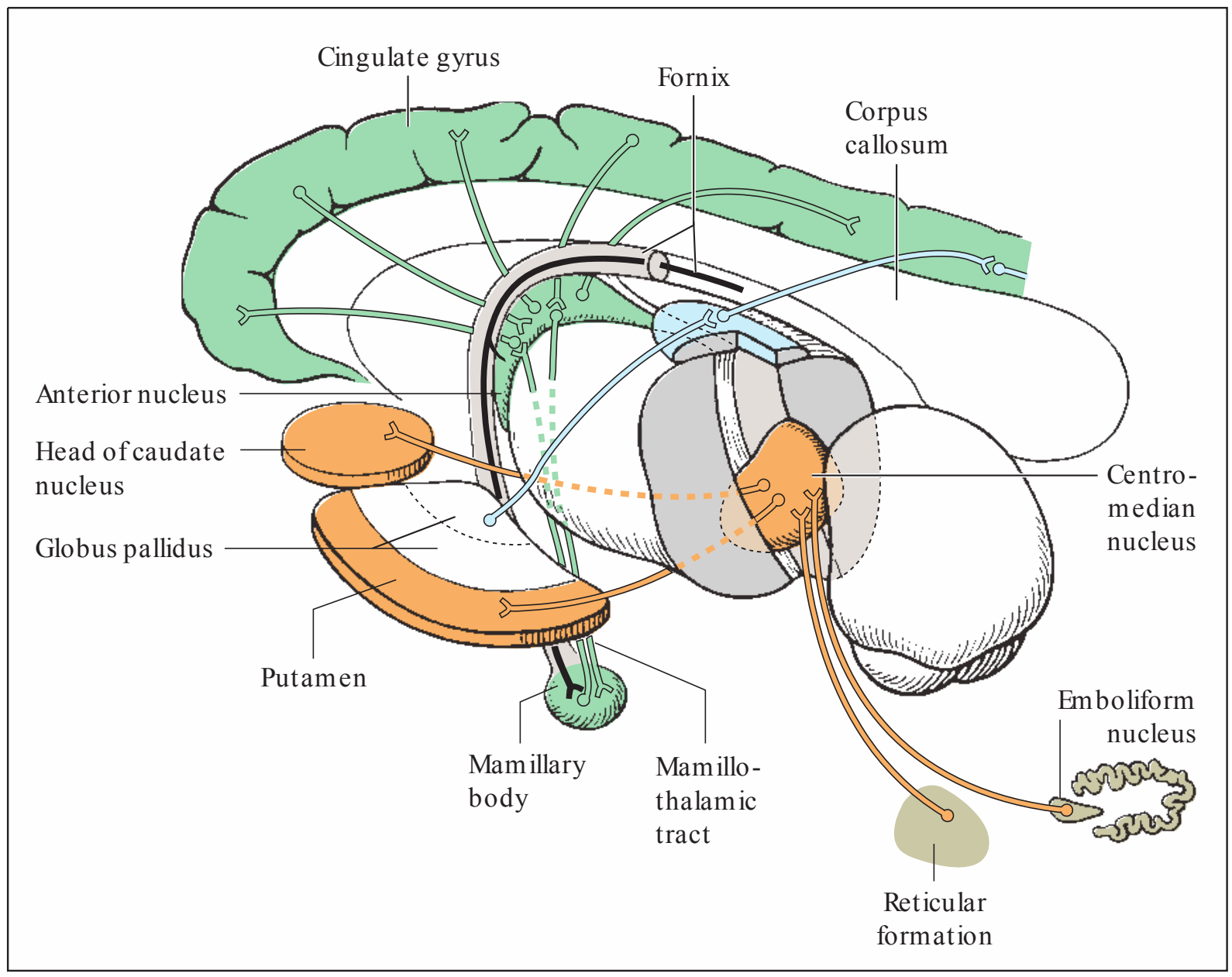


Fig. 6.**6** **Afferent and efferent connections of the anterior nucleus** (green) **and the centromedian nucleus** (orange)

Nonspecific Thalamic Nuclei and Their Connections

Intralaminar nuclei. The intralaminar nuclei are the most important component of the nonspecific thalamic projection system. These nuclei are located within the internal medullary lamina, and the largest among them is the **centromedian nucleus**. These cell complexes receive their afferent input through ascending fibers from the brainstem *reticular formation* and the *emboliform nucleus* of the cerebellum, as well as from the *internal pallidal segment* and other thalamic nuclei. They project not to the cerebral cortex but rather to the *caudate nucleus*, *putamen*, and *globus pallidus* (Fig. 6.**6**). They probably also send efferent impulses diffusely to all nuclei of the thalamus, which then, in turn, project to widespread secondary areas of the cerebral cortex. The centromedian nucleus is an important component of the intralaminar cell complex, which constitutes the thalamic portion of the ascending reticular activating system (*ARAS* or *arousal system*). Another portion of this arousal system probably involves the subthalamus and hypothalamus.

Functions of the Thalamus

The functions of the thalamus are highly complex because of the large number of nuclei it contains and their very diverse afferent and efferent connections.

- First of all, the thalamus is the largest subcortical **collecting point** for all exteroceptive and proprioceptive sensory impulses.
- Furthermore, it is a **relay station** for all impulses arising in cutaneous and visceral sensory receptors, for visual and auditory impulses, and for impulses from the hypothalamus, cerebellum, and brainstem reticular formation, all of which are processed in the thalamus before being transmitted onward to other structures. The thalamus sends a small efferent component to the striatum, but most of its output goes to the cerebral cortex. All sensory impulses (other than olfactory impulses) must pass through the thalamus before they can be consciously perceived. Thus, the thalamus was traditionally called "the gateway to consciousness," though the conscious perception of smell implies that this conception is flawed and perhaps misleading.
- The thalamus, however, is not merely a relay station, but an important **center for integration and coordination,** in which afferent impulses of different modalities, from different regions of the body, are integrated and given an affective coloration. A neural substrate of certain elementary phenomena such as pain, displeasure, and well-being is already present in the thalamus before being transmitted upward to the cortex.
- Through its reciprocal connections (feedback loops) with the motor cortex, some of which pass through the basal ganglia and cerebellum, the thalamus **modulates motor function.**
- Some thalamic nuclei are also **components of the ascending reticular activating system** (ARAS), a specific arousal system originating in nuclei that are diffusely located throughout the brainstem reticular formation. Activating impulses from the ARAS are relayed by certain thalamic nuclei (ventral anterior nucleus, intralaminar nuclei [particularly the centromedian nucleus], reticular nuclei) to the entire neocortex. An intact ARAS is essential for normal consciousness.

Syndromes of Thalamic Lesions

The clinical manifestations of thalamic lesions depend on their precise location and extent because the functions of the individual thalamic nuclei are so highly varied.

Lesions of the ventral anterior and intralaminar nuclei. The ventral anterior (VA), intralaminar, and reticular nuclei are nonspecific "activating" nuclei. They project diffusely to the frontal lobes (ventral anterior nucleus, cf. Fig. 6.**4**, p. 174) and the entire neocortex (intralaminar nuclei), and they serve to modulate cortical responses. These pathways are components of the ascending reticular activating system (ARAS). Lesions in this area, particularly bilateral lesions, cause *disturbances of consciousness and attention*, and, if they extend to the midbrain tegmentum, **vertical gaze palsy**. Less commonly, paramedian lesions can cause agitation, dysphoria, or acute confusion. Isolated lesions of the ventral anterior nuclei with impaired frontal cortical activation have been reported to cause disturbances of voluntary behavior; right-sided lesions in this area have also been reported to cause more complex

Case Presentation 1: Thalamic Pain Syndrome after Hemorrhage in the Basal Ganglia

This 51-year-old male schoolteacher was attending a friend's funeral when he suddenly fell and complained of nausea and a pulsatile headache. He had been standing in the hot sun during the eulogy, and the other funeral attendees at first thought he had simply fainted. When he was still unable to get up unaided and continued to complain of headache ten minutes later, they called an ambulance. The emergency physician on the scene found an arterial blood pressure of 220/120 mmHg and weakness of the left hand and the entire left lower limb, and the patient was transported to the hospital. Examination on admission revealed central-type left hemiparesis with increased deep tendon reflexes, as well as hypesthesia and hypalgesia near the midline, pallanesthesia, and a mild deficit of position sense on the left side of the body. A CT scan revealed an acute hemorrhage in the right basal ganglia.

Over the next six months, the patient's hemiparesis and hemisensory deficit largely resolved, and he was able to resume playing tennis. In the same period of time, however, he began to experience repeated bouts of paroxysmal pain and dysesthesia in the previously hypesthetic areas on the left side of the body. These abnormal sensations were partly electric in character. An MRI scan of the head at this time revealed only a small remnant of the initial hemorrhage, with formation of a cyst in the right thalamus. The pain improved considerably on treatment with carbamazepine and amitriptyline but returned promptly as soon as the patient tried to stop taking these medications. They could finally be discontinued with a slow taper after a further three years.

disturbances of mood, e.g., manic state and logorrhea, or, alternatively, delirium with confabulations and inappropriate behavior. Bilateral medial lesions can cause transient amnesia with or without anosognosia.

Lesions of the ventral nuclei. As described above, the **ventral posterior nuclei** are relay stations for specific sensory impulses, which are then sent onward to the corresponding primary cortical areas. Lesions of these nuclei produce specific deficits of one or more sensory modalities, as follows.

- Lesions of the **ventral posterolateral nucleus** produce *contralateral impairment of touch and proprioception,* as well as paresthesias of the limbs, which may feel as if they were swollen or abnormally heavy.
- Lesions affecting the **basal portion of the ventral posterolateral** and/or **posteromedial nucleus** can produce severe pain syndromes in addition to the sensory deficits just described ("thalamic pain," sometimes in anesthetic areas—"*anesthesia dolorosa*"; cf. Case Presentation 1).
- Lesions of the **ventral lateral nucleus** have mainly *motor* manifestations, as this nucleus is mainly connected to the primary and secondary motor areas of the cerebral cortex, and to the cerebellum and basal ganglia.
- **Acute lesions** of the ventral lateral nucleus and the neighboring subthalamic region can produce severe central "weakness," in which direct peripheral testing reveals no impairment of raw muscle strength (e.g., against resistance) ("thalamic astasia"). The patient falls to the side opposite the lesion and may be unable to sit unaided. Such manifestations appear either in isolation or in conjunction with transient thalamic neglect, in which both sensory and motor function is neglected on the side opposite the lesion. Thalamic neglect, due to involvement of thalamocortical fibers projecting to the parietal lobe, is usually short-lasting and almost always resolves completely.
- Lesions affecting the dentato-rubro-thalamic projections of the **ventral lateral nucleus** (VL) produce *contralateral hemiataxia* with action tremor, dysmetria, dysdiadochokinesia, and pathological rebound. Such findings may give the erroneous impression of a cerebellar lesion.

Thalamic Vascular Syndromes

The thalamus is supplied by four arteries (p. 277). Interruption of the arterial blood supply in each of these distributions causes a characteristic syndrome, as described in Chapter 11 on p. 299.

Epithalamus

The epithalamus consists of the **habenula** with its **habenular nuclei**, the **habenular commissure**, the **stria medullaris**, and the **epiphysis**. The habenula and the habenular nuclei constitute an important relay station of the olfactory system. Afferent olfactory fibers travel by way of the stria medullaris

thalami to the habenular nuclei, which emit efferent projections to the autonomic (salivatory) nuclei of the brainstem, thus playing an important role in nutritional intake.

The **epiphysis (pineal gland)** contains specialized cells, called pinealocytes. Calcium and magnesium salts are deposited in the epiphysis from approximately age 15 years onward, making this structure visible in plain radiographs of the skull (an important midline marker before the era of CT and MRI). Epiphyseal tumors in childhood sometimes cause *precocious puberty*; it is thus presumed that this organ inhibits sexual maturation in some way, and that the destruction of epiphyseal tissue can remove this inhibition. In lower vertebrates, the epiphysis is a *light-sensitive organ* that regulates circadian rhythms. In primates, light cannot penetrate the skull, but the epiphysis still indirectly receives visual input relating to the light–dark cycle. Afferent impulses travel from the retina to the **suprachiasmatic nucleus** of the hypothalamus, from which, in turn, further impulses are conducted to the **intermediolateral nucleus** and, via postganglionic fibers of the cervical sympathetic chain, to the epiphysis.

Subthalamus

Location and components. The subthalamus is found immediately caudal to the thalamus at an early stage of embryological development and then moves laterally as the brain develops. It comprises the **subthalamic nucleus**, part of the **globus pallidus** (cf. p. 217), and various **fiber contingents** that pass through it on their way to the thalamus, including the medial lemniscus, the spinothalamic tract, and the trigeminothalamic tract. All of these tracts terminate in the ventroposterior region of the thalamus (Fig. 6.**4**, p. 174). The substantia nigra and red nucleus border the subthalamus anteriorly and posteriorly. Fibers of the dentatothalamic tract travel in the prerubral field H1 of Forel to terminate in the ventro-oral posterior nucleus of the thalamus (a part of the ventral lateral nucleus, VL); fibers from the globus pallidus travel in the lenticular fasciculus (Forel's fasciculus H2) to the ventro-oral anterior nucleus (another part of VL) and the ventral anterior nucleus (VA). These tracts are

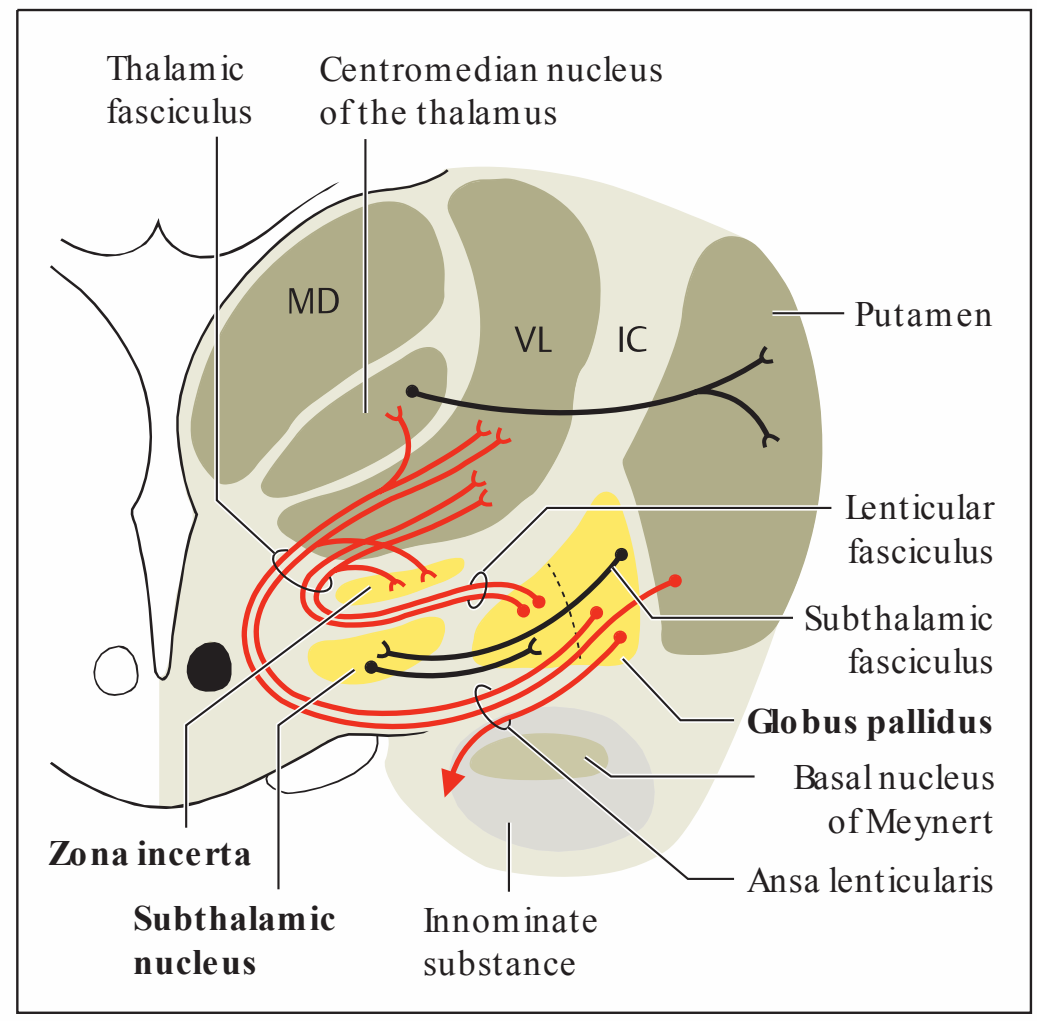


Fig. 6.7 **Fiber connections in the subthalamus.** MD = medial dorsal nucleus of the thalamus; VL = ventral lateral nucleus; IC = internal capsule.

joined more rostrally by the ansa lenticularis. The subthalamus also contains the zona incerta, a rostral continuation of the midbrain reticular formation. The major connections of the putamen, pallidum, subthalamus, and thalamus are depicted in Fig. 6.7.

Function. The subthalamic nucleus (corpus Luysii) is, functionally speaking, a component of the basal ganglia and has reciprocal connections with the globus pallidus (p. 217). Lesions of the subthalamic nucleus produce contralateral *hemiballism* (p. 223 f.).

Hypothalamus

Location and Components

The hypothalamus (Fig. 6.**8**) is composed of **gray matter in the walls of the third ventricle** from the hypothalamic sulcus downward and in the **floor of the third ventricle**, as well as the **infundibulum and the mamillary bodies**. The posterior pituitary lobe, or **neurohypophysis**, is also considered part of the hypothalamus; this structure is, in a sense, the enlarged caudal end of the infundibulum. The anterior pituitary lobe, on the other hand, is not derived from the neuroectoderm at all, but rather

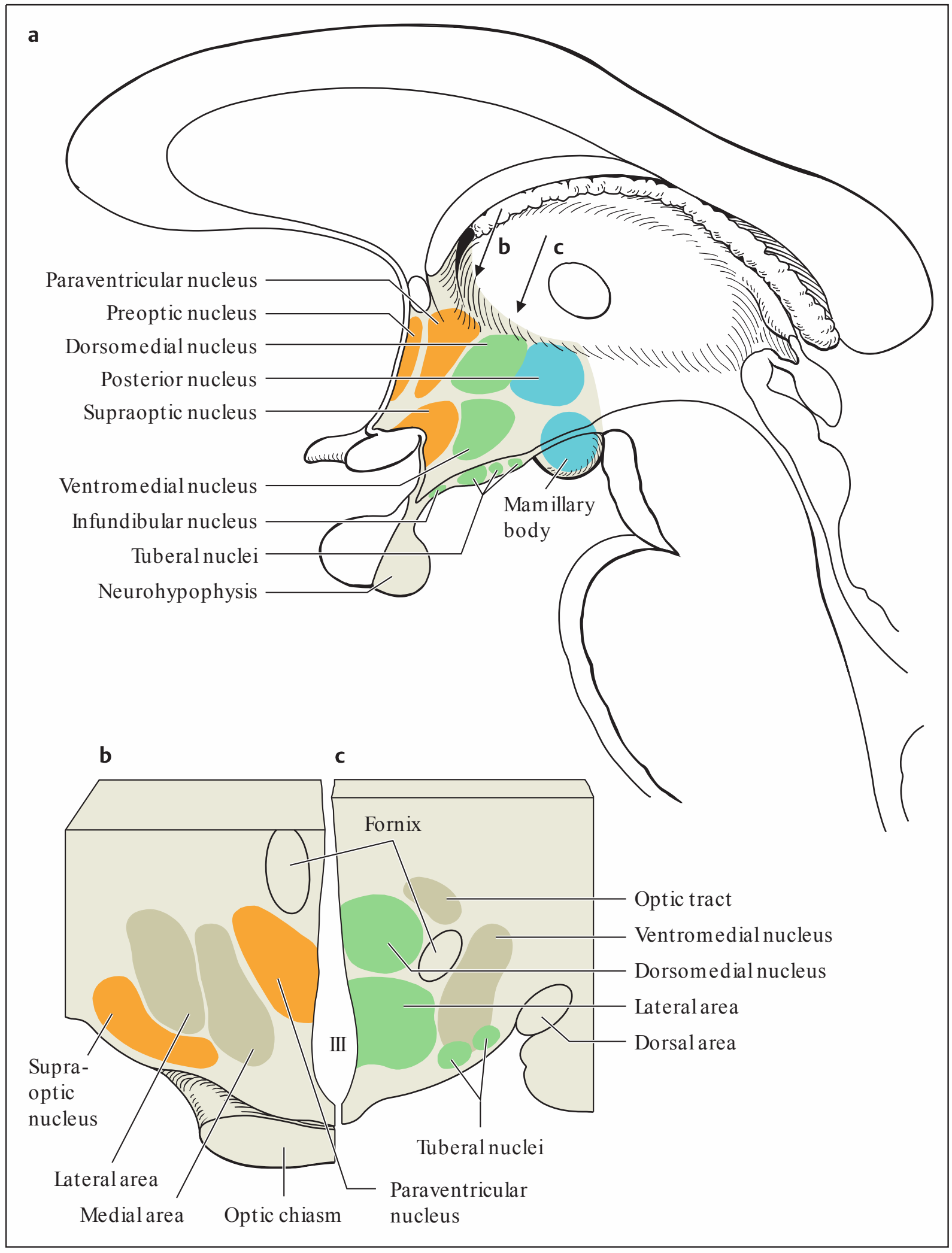


Fig. 6.**8** **Hypothalamic nuclei. a** Lateral view. **b** and **c** Coronal sections in two different planes.

from Rathke's pouch, an outcropping of the rostral end of the primitive alimentary tract. The two pituitary lobes, though adjacent to each other, are not functionally connected. Remnants of Rathke's pouch in the sellar region can grow into tumors, e.g., craniopharyngioma.

The columns of the fornix, as they descend through the hypothalamus to the mamillary bodies on either side, divide the hypothalamus of each side into a **medial** and a **lateral segment** (Fig. 6.**8**). The lateral segment contains various groups of fibers, including the *medial forebrain bundle*, which runs from basal olfactory areas to the midbrain. It also contains the lateral tuberal nuclei (see p. 180).

The medial segment, in contrast, contains a number of more or less clearly distinguishable nuclei (Fig. 6.**8a–c**), which are divided into an **anterior (rostral)**, a **middle (tuberal)**, and a **posterior (mamillary) nuclear group.**

Hypothalamic Nuclei

Anterior nuclear group. The important members of this group are the *preoptic*, *supraoptic*, and *paraventricular nuclei* (Fig. 6.**8**). The latter two nuclei project, by way of the supraoptico-hypophyseal tract, to the neurohypophysis (see Figs. 6.**10** and 6.**11**).

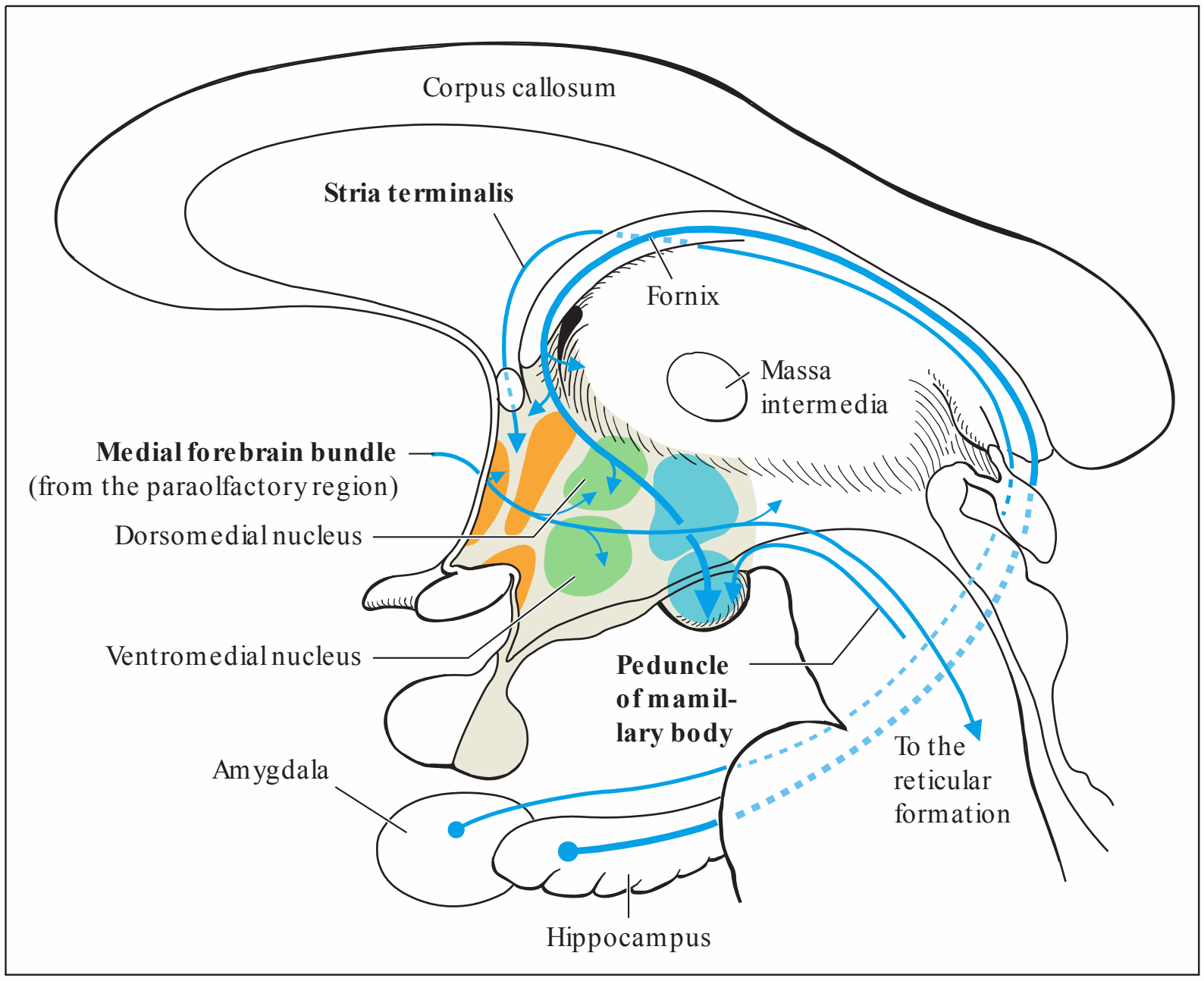


Fig. 6.**9** **Major afferent connections of the hypothalamus** (schematic drawing)

Middle nuclear group. The important members of this group are the *infundibular nucleus*, the *tuberal nuclei*, the *dorsomedial nucleus*, the *ventromedial nucleus*, and the *lateral nucleus* (or *tuberomamillary nucleus*) (Fig. 6.**8**).

Posterior nuclear group. This group includes the *mamillary nuclei* (the supramamillary nucleus, the mamillary nucleus, the intercalate nucleus, and others) and the *posterior nucleus* (Fig. 6.**8**). This area has been termed a dynamogenic zone (Hess), from which the autonomic nervous system can be immediately called into action, if necessary.

Afferent and Efferent Projections of the Hypothalamus

The neural connections of the hypothalamus (Figs. 6.**9** and 6.**10**) are multifarious and complex. In order to carry out its function as the coordinating center of all autonomic processes in the body (p. 190), the hypothalamus must communicate via afferent and efferent pathways with very many different areas of the nervous system. Information from the outside world reaches it through visual, olfactory, and probably also auditory pathways. The presence of cortical afferents implies that the hypothalamus can also be influenced by higher centers. The major connections of the hypothalamus are to the cingulate gyrus and frontal lobe, the hippocampal formation, the thalamus, the basal ganglia, the brainstem, and the spinal cord.

Some of the more important afferent connections (Fig. 6.**9**) will be described in the following section.

Afferent Pathways

The **medial forebrain bundle** originates in the basal olfactory areas and the septal nuclei and runs as a chain of neurons through the hypothalamus (lateral area) until it arrives in the midbrain reticular formation Along the way, it gives off collateral fibers to the preoptic nucleus, the dorsomedial nucleus, and the ventromedial nucleus. The medial forebrain bundle constitutes a reciprocal connection between olfactory and preoptic nuclear areas and the midbrain. It has olfacto-visceral and olfacto-somatic functions.

The **striae terminales** originate in the amygdala in the temporal lobe, then form an arch over the thalamus, terminating in the preoptic area and to

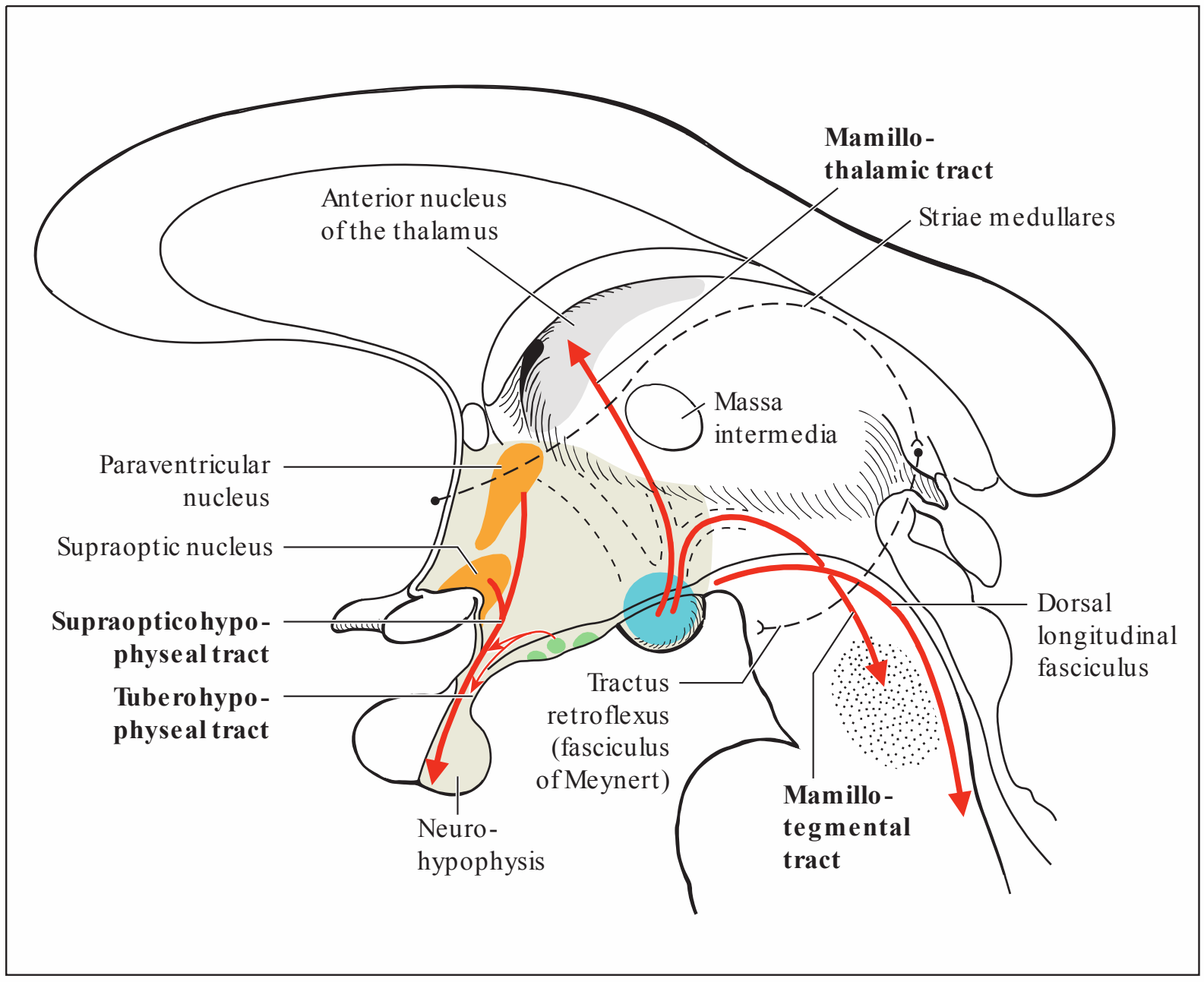


Fig. 6.**10** **Major efferent connections of the hypothalamus** (schematic drawing)

the anterior hypothalamic nuclei. These fiber bundles are thought to transmit olfactory information, as well as impulses relating to mood and drive.

The **fornix** transmits corticomamillary fibers originating in the hippocampus and subiculum and traveling to the mamillary body, with collaterals to the preoptic nucleus, the anterior nucleus of the thalamus, and the habenular nucleus. The fornix is an important pathway in the limbic system (p. 203). As it passes over the dorsal surface of the pulvinar, some of its fibers cross the midline to join the contralateral fornix (commissure of the fornices, psalterium).

At the level of the psalterium, the two fornices lie under the splenium of the corpus callosum, where they are usually not directly visible in an uncut brain specimen. Lesions in the area of the psalterium often affect both fornices, because these two thin structures are close together at this point. The serious functional deficits produced by bilateral limbic lesions are discussed below on p. 208 ff.

Ascending visceral impulses from the peripheral autonomic nervous system, and from the nucleus of the tractus solitarius (taste), reach the hypothalamus along various pathways: through relay nuclei in the brainstem reticular formation, from tegmental and interpeduncular nuclei, through reciprocal connections in the medial forebrain bundle, through the dorsal longitudinal fasciculus, and through the peduncle of the mamillary body (Figs. 6.**9** and 6.**10**). Somatosensory information from the erogenous zones (genitalia and nipples) also reaches the hypothalamus by these pathways and induces autonomic reactions.

Finally, **further afferent input** comes to the hypothalamus from the medial nucleus of the thalamus, the orbitofrontal neocortex, and the globus pallidus.

Efferent Pathways

Efferent fibers to the brainstem. The most important efferent projections from the hypothalamus to the brainstem are the **dorsal longitudinal fasciculus** (of Schütz), which contains fibers traveling in both directions, and the **medial forebrain bundle** (Figs. 6.**9** and 6.**10**). Hypothalamic impulses traveling in these pathways pass through multiple synaptic relays, mainly in the reticular formation, until they terminate in parasympathetic nuclei of the brain-

stem, including the oculomotor nucleus (miosis), the superior and inferior salivatory nuclei (lacrimation, salivation), and the dorsal nucleus of the vagus nerve. Other impulses travel to autonomic centers in the brainstem that coordinate circulatory, respiratory, and alimentary function (etc.), as well as to motor cranial nerve nuclei that play a role in eating and drinking: the motor nucleus of the trigeminal nerve (mastication), the nucleus of the facial nerve (facial expression), the nucleus ambiguus (swallowing), and the nucleus of the hypoglossal nerve (licking). Yet other impulses derived from the hypothalamus, relayed to the spinal cord through reticulospinal fibers, affect the activity of spinal neurons that participate in temperature regulation (shivering).

The **mamillotegmental fasciculus** (Fig. 6.**10**) runs from the mamillary body to the midbrain tegmentum, and then onward to the reticular formation.

The mamillothalamic tract (of Vicq d'Azyr) reciprocally connects the hypothalamus with the anterior nucleus of the thalamus, which, in turn, is reciprocally connected with the cingulate gyrus (Fig. 6.**6**). The anterior thalamic nucleus and the cingulate gyrus are important components of the limbic system. The main function of the limbic system is said to be the regulation of affective behavior so as to promote the survival of the individual and of the species (MacLean 1958; cf. p. 202).

The **supraoptico-hypophyseal tract** has already been mentioned as an efferent pathway to the neurohypophysis. Neurons in the supraoptic and paraventricular nuclei produce the hormones oxytocin and vasopressin (antidiuretic hormone), which are transported along the axons of the supraoptico-hypophyseal tract to the neurohypophysis, and are then released there, from the axon terminals, into the bloodstream (Figs. 6.**10** and 6.**11**). The neurons in these nuclei are thus comparable to the hormone-producing cells of other organs, and are referred to as neurosecretory cells. Oxytocin and vasopressin mainly exert their effects on cells outside the nervous system: oxytocin induces con-

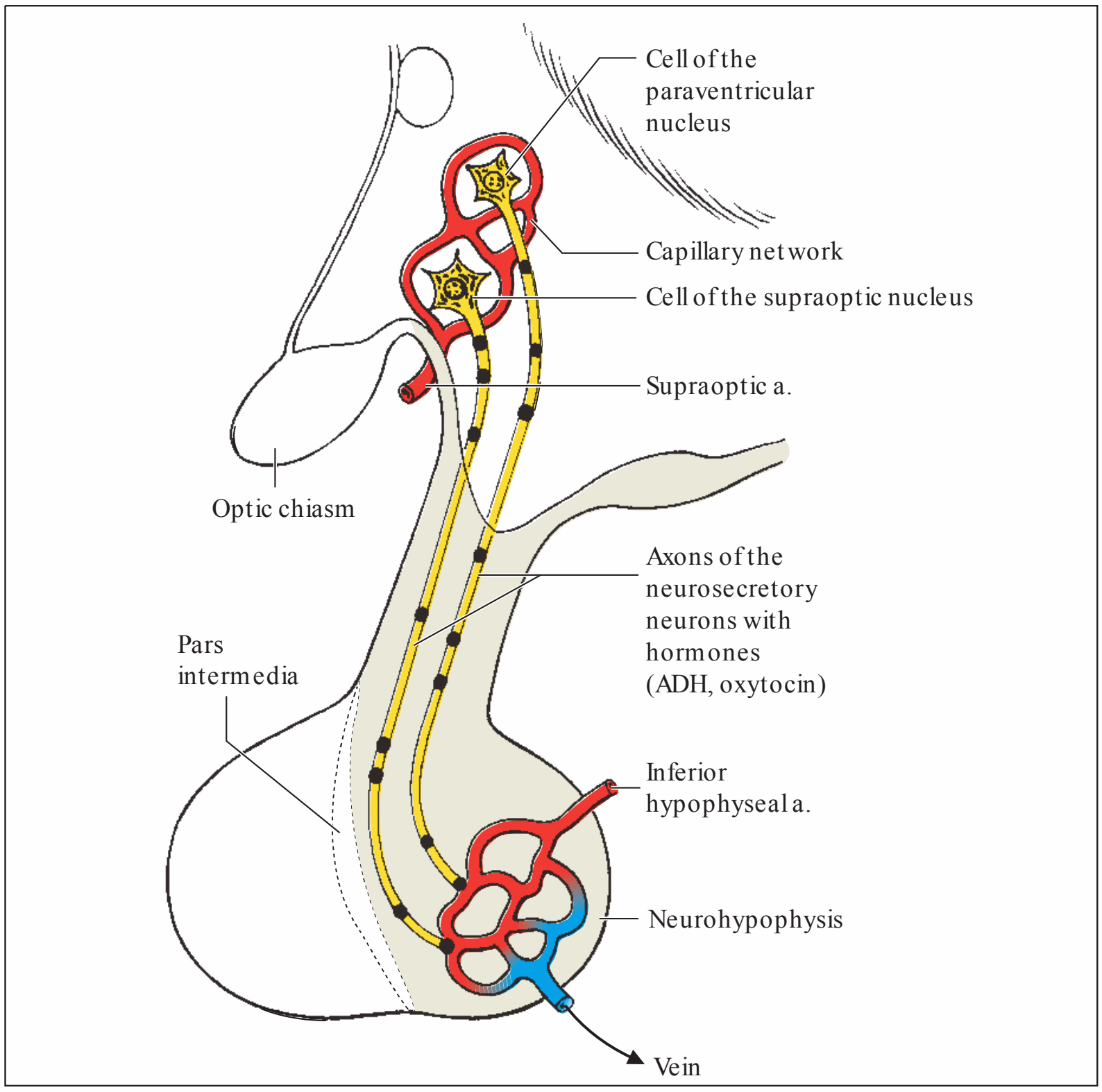


Fig. 6.**11** **Posterior lobe of the pituitary gland** (neurohypophysis). Neurosecretory fibers reach the posterior lobe directly by way of the supraoptico-hypophyseal tract.

traction of the smooth muscle of the uterus and the mammary gland, while vasopressin induces water reuptake through the renal tubular epithelial cells (see also p. 184).

Functional Connection of the Hypothalamus to the Adenohypophysis

There is no direct neural connection between the hypothalamic nuclei and the adenohypophysis. Nonetheless, it has long been recognized that the hypothalamus exerts a major influence on the adenohypophyseal endocrine cells. Fiber bundles from the tuberal nuclei carry *releasing factors* and *release-inhibiting factors* to the median eminence by intra-axonal transport; the median eminence, in turn, is connected to the adenohypophysis through a portal vascular network. The hypothalamus regulates adenohypophyseal hormone secretion by this mechanism (Fig. 6.**12**; cf. p. 185).

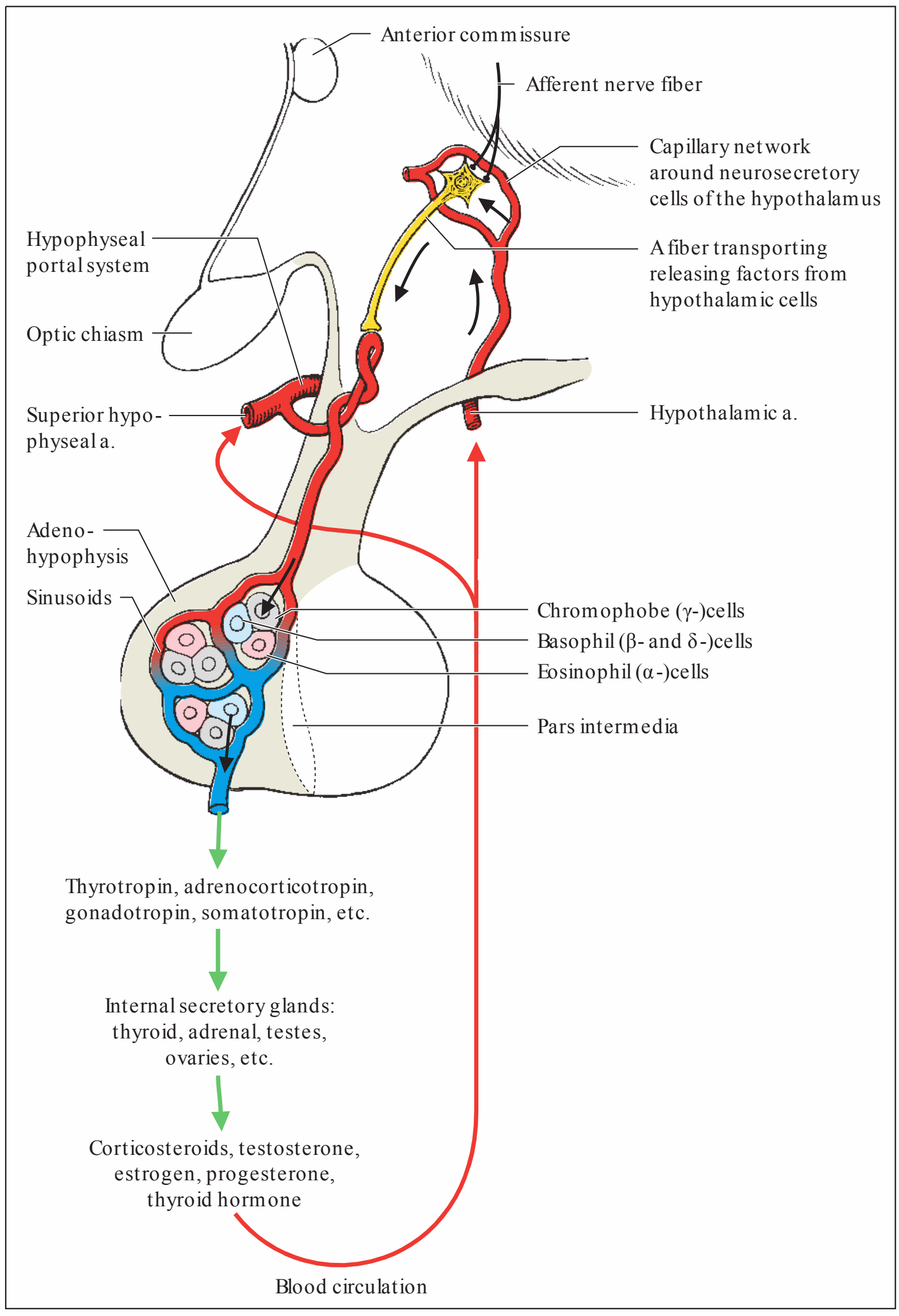


Fig. 6.**12** **Anterior lobe of the pituitary gland** (adenohypophysis). Releasing hormones and release-inhibiting hormones are produced by the hypothalamus and travel over neurosecretory fibers to the first capillary network in the area of the median eminence (neurohemal region), where they enter the bloodstream. They are transported in the bloodstream to the adenohypophysis, reaching it by a second capillary network immediately adjacent to the hormone-producing glandular cells (hypophyseal portal system). Thus, hormone secretion by the anterior lobe of the pituitary gland is regulated by way of the bloodstream.

Functions of the Hypothalamus

The hypothalamus is the hierarchically uppermost regulatory organ ("head ganglion") of the autonomic nervous system. It plays the leading role in a wide variety of regulatory circuits for **vital bodily functions** such as temperature, heart rate, blood pressure, respiration, and food and water intake. These regulatory functions are carried out largely independently of any conscious thought on the part of the individual, i.e., autonomically. The hypothalamus also regulates important hormone systems through the hypothalamic–pituitary axis and coordinates the interaction of the endocrine and autonomic nervous systems. The elementary functions controlled by the hypothalamus will be described, briefly and individually, in this section.

Temperature Regulation

The *anterior preoptic hypothalamus* contains specific receptors for the maintenance of a constant internal temperature (*temperature homeostasis*). Physiological responses to *temperature changes* (vasoconstriction and shivering at low temperature, vasodilation and sweating at high temperature) are regulated by circuits in the *posterior hypothalamus*.

Disturbances of temperature regulation. Dysfunction of the anterior preoptic region of the hypothalamus (caused, for example, by traumatic brain injury or hemorrhage) can lead to **central hyperthermia**. Dysfunction of the posterior region can lead to **hypothermia** or **poikilothermia** (rapid fluctuations of body temperature by more than 2°C); the possible causative lesions here include hypothalamic tumors (craniopharyngioma, glioma), Wernicke's encephalopathy, and hydrocephalus.

Regulation of Heart Rate and Blood Pressure

The hypothalamus influences the autonomic nervous system directly through descending pathways that will be discussed below in the section on the peripheral autonomic nervous system (p. 170).

The *sympathetic* nervous system is regulated by the ventromedial and posterior portions of the hypothalamus (p. 190). Stimulation of these areas induces a rise in heart rate and blood pressure, dilatation of the pupils, vasoconstriction in the capillary beds, vasodilation in the skeletal musculature, and expressions of fear or rage.

The *parasympathetic* nervous system (p. 192), on the other hand, is regulated by the paraventricular and anterior or lateral portions of the hypothalamus. Stimulation of these areas induces a fall in heart rate and blood pressure and constriction of the pupils. Stimulation of posterior parasympathetic areas increases blood flow to the bladder and diminishes blood flow to skeletal muscle.

Regulation of Water Balance

The *hypothalamic osmoreceptors* are located in the *supraoptic* and *paraventricular nuclei*. They are stimulated either by intracellular dehydration, with an elevated intracellular sodium concentration, or by extracellular dehydration, with an elevated concentration of angiotensin II in the hypothalamic capillary blood; stimulation leads to the *secretion of ADH* (antidiuretic hormone, vasopressin). Conversely, an increase of intravascular volume stimulates peripheral volume receptors, ultimately leading to the inhibition of ADH secretion.

Disturbances of water balance. If 90% or more of the neurons of the supraoptic and paraventricular nuclei are destroyed or rendered dysfunctional (e.g., by a granulomatous process, vascular lesion, trauma, or infection), then ADH is no longer secreted and **diabetes insipidus** results, manifested clinically by excessive thirst, polyuria, and polydipsia. The diagnosis is established by the demonstration of *hypo-osmolar polyuria*, i.e., the excretion of at least 3 liters of urine per day, with an osmolality between 50 and 150 mosm/l. ADH substitution is the treatment of choice. If the urine osmolality fails to rise by more than 50% after the administration of 5 IU of ADH, then the patient is suffering from renal diabetes insipidus (inadequate response of the kidney to circulating ADH), in which substitution therapy is of no help.

Many types of hypothalamic lesion impair the thirst response, and can thus cause severe hyponatremia.

The **syndrome of inappropriate ADH secretion** (**SIADH** or **Schwartz–Bartter syndrome**), usually caused by abnormal ectopic secretion of ADH (e.g., by bronchial carcinoma or other malignant

tumors), is manifested by hypervolemia, hyponatremia (□ 130 mmol/l), low serum osmolarity (□ 275 mosm/kg), and highly concentrated urine. The clinical manifestations include weight gain, weakness, nausea, and disturbances of consciousness, as well as epileptic seizures. SIADH is treated by eliminating the underlying cause, though it is often useful to treat the hypervolemia and hyponatremia symptomatically as well, by fluid restriction and correction of the sodium balance.

Regulation of Nutritional Intake

Lesions of the ventromedial hypothalamic nuclei may cause severe obesity through hyperphagia and poverty of movement. More lateral lesions can cause anorexia and abnormal weight loss.

Neurosecretion and Regulation of the Endocrine System

As mentioned above, the hypophysis (pituitary gland) has two components, the anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis). The hypothalamus controls each part differently.

Hormone secretion by the posterior lobe. Secretory neurons in the supraoptic and paraventricular nuclei produce oxytocin and ADH, which are transported intra-axonally to the neurohypophysis and released there into the bloodstream (neurosecretion). The functions of ADH have been described above. Oxytocin is secreted during the last few weeks of pregnancy; it induces the contraction of uterine smooth muscle as well as the secretion of milk from the mammary glands. Somatosensory stimulation (touching the nipple) produces afferent impulses that activate the neurosecretory neurons of the hypothalamus (by way of the thalamus and the cerebral cortex). The intimate connection between this regulatory circuit and emotion is illustrated by the fact that milk production decreases significantly when the mother suffers from fear or stress.

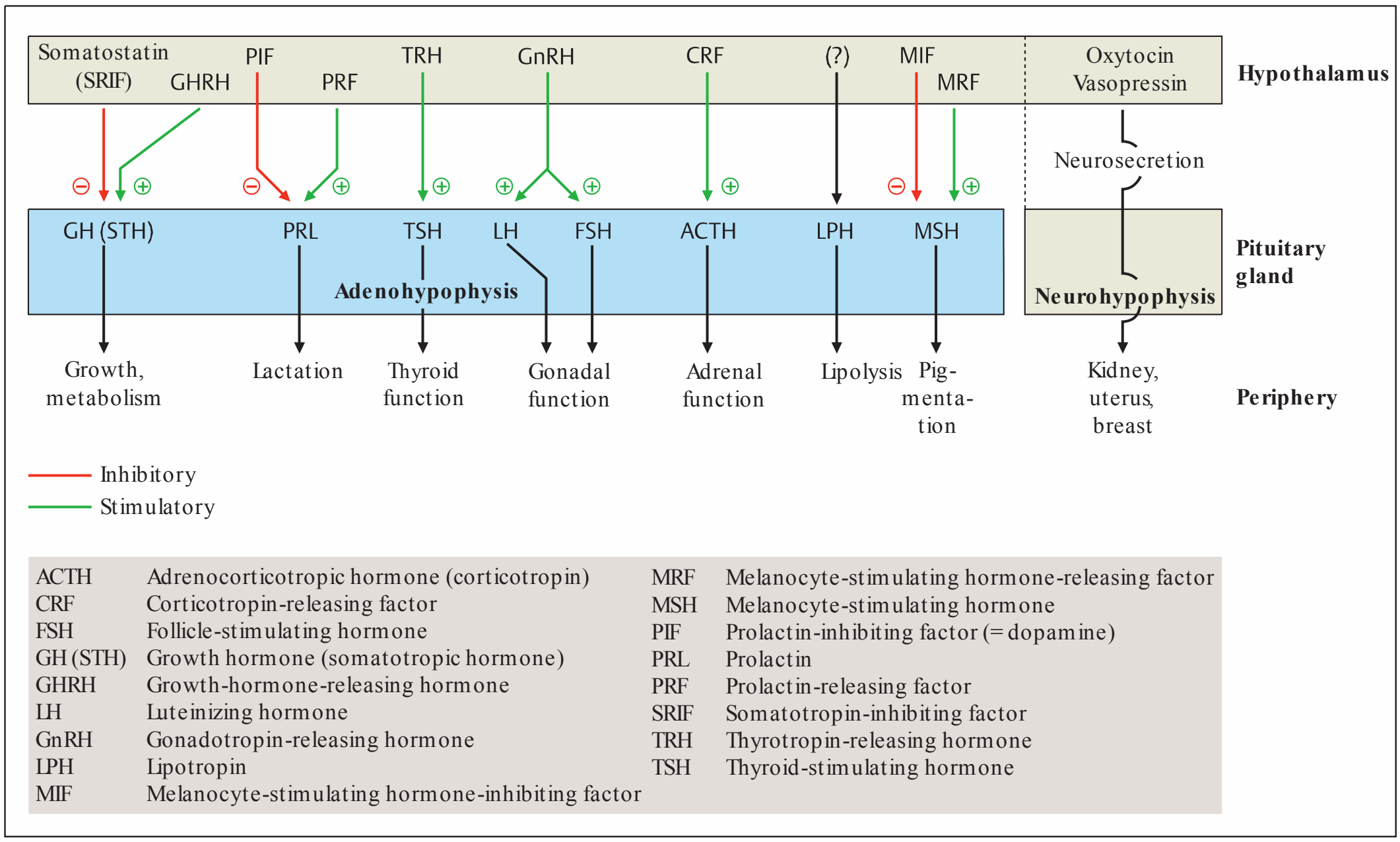
Hormone secretion by the anterior lobe. The parvocellular secretory neurons found in periventricular areas of the hypothalamus communicate with the adenohypophysis not by axonal connections (as in the case of the neurohypophysis) but rather through a portal vascular system (see p. 183). These parvocellular neurons secrete the "**hypophysiotropic**" hormones gonadotropin-releasing hormone (GnRH), thyrotropin-releasing hormone (TRH), corticotropin-releasing hormone (CRH), growth-hormone-releasing hormone (GHRH), and factors regulating the secretion of melanocyte-stimulating hormone (MSH), namely MIF and MRF. All of these hormones, in turn, control the release of the corresponding pituitary hormones from the adenohypophysis, once they arrive there by way of the portal vascular network (cf. Figs. 6.**12** and 6.**13**). In the adenohypophysis, **acidophil cells** (α cells) secrete growth hormone (GH, also called somatotropic hormone or STH) and prolactin (PRL, also called luteotropic hormone or LTH). **Basophil cells** (β cells) secrete thyrotropin (thyroid-stimulating hormone, TSH), corticotropin (also called adrenocorticotropic hormone or ACTH), melanocyte-stimulating hormone (MSH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). **Chromophobe cells** (γ cells) are not known to secrete any hormones, but some authors state that they play a role in ACTH synthesis.

The hormones produced by the pituitary secretory cells enter the bloodstream and induce the respective peripheral endocrine organs to secrete hormones. These peripheral hormones circulate in the blood, and their concentrations, in turn, influence the secretion of the corresponding hypothalamic and pituitary hormones, in a negative feedback loop.

Hormonal Disturbances: Disturbances of the Hypothalamic–Pituitary Axis

The endocrine function of the hypophysis can be impaired by hormone-secreting tumors (e.g., pituitary adenoma) or by destruction of pituitary tissue by non-hormone-secreting tumors.

Panhypopituitarism. The most severe clinical syndrome consists of **loss of all functions of the hypophysis** and is clinically manifested by lack of drive, decline of physical performance, loss of weight, loss of libido, bradycardia, lessened skin pigmentation, loss of axillary and pubic hair, and, sometimes, diabetes insipidus (if the neurohypophysis is involved). This syndrome may be caused by large, hormonally inactive tumors of the hypophysis, infundibulum, or hypothalamus (e.g., adenoma, metastasis, glioma, or craniopharyn-



ACTH	Adrenocorticotropic hormone (corticotropin)	MRF	Melanocyte-stimulating hormone-releasing factor
CRF	Corticotropin-releasing factor	MSH	Melanocyte-stimulating hormone
FSH	Follicle-stimulating hormone	PIF	Prolactin-inhibiting factor (= dopamine)
GH (STH)	Growth hormone (somatotropic hormone)	PRL	Prolactin
GHRH	Growth-hormone-releasing hormone	PRF	Prolactin-releasing factor
LH	Luteinizing hormone	SRIF	Somatotropin-inhibiting factor
GnRH	Gonadotropin-releasing hormone	TRH	Thyrotropin-releasing hormone
LPH	Lipotropin	TSH	Thyroid-stimulating hormone
MIF	Melanocyte-stimulating hormone-inhibiting factor		

Fig. 6.**13** **Endocrine Regulation along the Hypothalamic–Pituitary Axis**

gioma). The treatment of choice is surgical resection and hormone substitution. Hypopituitarism may also arise in the aftermath of trauma, or as a complication of neurosurgical procedures. Sudden loss of pituitary function with subsequent adrenal failure (addisonian crisis) is a life-threatening event.

Hormone-secreting pituitary tumors. A neoplasm arising from one of the cell types of the anterior pituitary lobe causes symptoms through an **excess of the corresponding hormone(s)**. If the tumor is large enough, the **suprasellar mass effect** will produce a characteristic visual field defect (usually bitemporal hemianopsia, because of compression of the optic chiasm; cf. p. 187).

Prolactinoma. Most pituitary adenomas (60–70 %) secrete prolactin. In female patients, the resulting excess of circulating prolactin (hyperprolactinemia) causes **secondary amenorrhea** through the inhibition of gonadotropin-releasing hormone secretion (when the serum prolactin concentration rises above 40–100 ng/ml), as well as **galactorrhea** and, less commonly, hirsutism. In male patients, hyperprolactinemia causes **impotence**, **gynecomastia**, and galactorrhea. Surgical resection (e.g., by the transsphenoidal route) is the treatment of choice for prolactinomas with mass effect; for smaller tumors with less severe manifestations, pharmacological treatment with a dopamine agonist such as bromocriptine can be tried. Dopamine agonists inhibit prolactin secretion.

Growth-hormone-secreting adenoma. Clinically, an excess of circulating growth hormone (□ 5 ng/ml) causes **acromegaly**: increased growth of acral portions of the skeleton (hands, feet, head circumference), osteoporosis, hyperhidrosis, glucose intolerance, hypertension, hypertrophic cardiomyopathy, goiter, compressive neuropathies such as carpal tunnel syndrome, other types of neuropathy, proximal myopathy, sleep disturbances (hypersomnia, sleep apnea syndrome), and neuropsychiatric disturbances (depression, psychosis). The standard diagnostic test is an oral glucose tolerance test, with a characteristic overshoot in the reflex rise of growth hormone concentration. Surgical resection is the treatment of choice.

ACTH-secreting adenoma causes **Cushing syndrome** with truncal obesity, moon facies, glucose intoler-

Case Presentation 2: Pituitary Tumor/Prolactinoma

This 40-year-old male office worker complained to his family physician of "peculiar" bodily changes that had been troubling him for some time. He had gained 50 kg in weight over the previous 2–3 years, and he now needed shoes two sizes larger than before. His hands also seemed to have become "rough." He had recently had an automobile accident caused by his failure to see another car approaching from the side, and a couple of days previously he had almost run over a pedestrian for the same reason. He could no longer trust himself to drive a car, both because of these occurrences and because he was always tired and could not concentrate. He had increasing difficulty on the job. He denied suffering from headache, loss of libido, or impotence.

The physician found his weight to be 132 kg (previously 82 kg), with an unchanged height of 193 cm. His hands and feet were disproportionately large (acromegaly), finger perimetry revealed severe bitemporal hemianopsia, and there was mild gynecomastia, though no galactorrhea could be induced. Laboratory testing revealed normal values of all thyroid parameters (T_3, T_4, basal TSH, and TRH test) as well as of ACTH and cortisol. The testosterone level, however, was very low (50 ng/ml) and the prolactin level extremely high (590 µg/dl). TRH administration caused the prolactin level to climb still further to 2020 µg/dl.

These findings suggested a prolactin-secreting adenoma of the pituitary gland with partial hypopituitarism affecting the anterior lobe hormones, particularly the gonadotropic axis. A plain radiograph of the head revealed massive expansion of the sella turcica with partial destruction of the dorsum sellae and the sellar floor. An MRI scan revealed a tumor measuring 5 × 5 × 4 cm (Fig. 6.**14**), too large to be removed through a transsphenoidal approach. A frontotemporal craniotomy was performed. Intraoperatively a firm, grayish-yellow tumor with some reddish areas was found; it was adherent to the floor of the middle cranial fossa, made contact with the terminal portion of the internal carotid artery, and compressed the optic chiasm. The histopathological finding was of a diffusely growing epithelial tumor, without lobular structure, in which the tumor cells occasionally showed a papillary organization. Immmunohistochemical study revealed an increased expression of prolactin in ca. 30–40 %of the tumor cells, while a few of them stained positive for ACTH, LH, or GH. Excessive GH secretion had presumably caused the patient's clinically evident acromegaly. Postoperatively, he had transient diabetes insipidus requiring treatment with desmopressin acetate. Anterior pituitary lobe insufficiency persisted in his subsequent course and he was treated with hydrocortisone and thyroxine substitution.

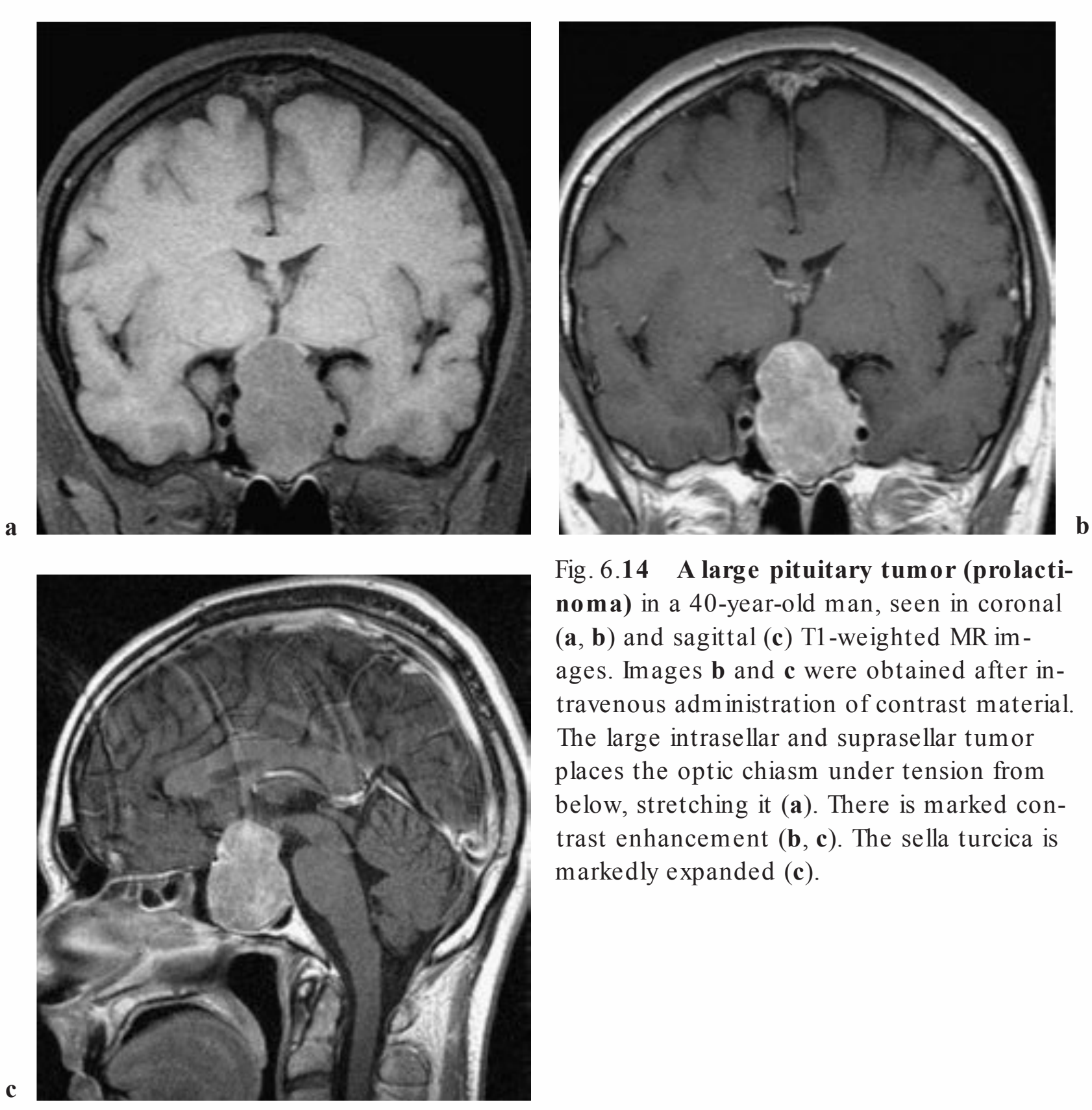


Fig. 6.**14** **A large pituitary tumor (prolactinoma)** in a 40-year-old man, seen in coronal (**a**, **b**) and sagittal (**c**) T1-weighted MR images. Images **b** and **c** were obtained after intravenous administration of contrast material. The large intrasellar and suprasellar tumor places the optic chiasm under tension from below, stretching it (**a**). There is marked contrast enhancement (**b**, **c**). The sella turcica is markedly expanded (**c**).

ance, hypertension, edema, amenorrhea, impotence, a tendency to thromboembolism, polyuria, steroid myopathy, and neuropsychiatric disturbances. The diagnosis is made endocrinologically by the demonstration of an elevated amount of cortisol in a 24-hour urine collection. Surgical resection is the treatment of choice.

Peripheral Autonomic Nervous System

Fundamentals

The autonomic nervous system, working in concert with the endocrine system (see p. 185 ff.) and various nuclei in the brainstem, regulates vital functions that are necessary for the maintenance of the internal environment (homeostasis), including respiration, circulation, metabolism, body temperature, water balance, digestion, secretion, and reproductive function. The designation "autonomic" is derived from the fact that these functions are controlled by unconscious (involuntary) mechanisms, as discussed above.

As already mentioned, the hypothalamus is the main regulatory center for the entire peripheral autonomic system. It exercises its control over many bodily functions partly through nerve impulses and partly through hormonal pathways, by means of the hypothalamic–pituitary system (see above and standard works on endocrinology, physiology, and anatomy).

The efferent arm of the autonomic nervous system is composed of two complementary systems, the **sympathetic** nervous system and the **parasympathetic** nervous system, whose effects are generally antagonistic to each other. The efferent fibers of both systems mainly innervate the smooth muscle of the viscera, blood vessels, and glands and are thus commonly called *visceral efferent (visceromotor) fibers*, to distinguish them from the sensory *visceral afferent fibers*. The latter, unlike the visceral efferent fibers, are not divided into two systems.

General scheme of the sympathetic and parasympathetic nervous systems. The final efferent pathway of both the sympathetic and the parasympathetic nervous systems consists of two neurons in series (Fig. 6.**15**). The cell body of the **first (preganglionic) neuron** lies within the central nervous system, while that of the **second (postganglionic) neuron** is found in a peripheral ganglion.

The first neurons of the sympathetic nervous system lie in the thoracic and lumbar segments of the spinal cord (intermediolateral cell column, T1–L2); for this reason, the sympathetic nervous system is sometimes called the **thoracolumbar system**. Some of the first neurons of the parasympathetic nervous system are found in the nuclei of cranial nerves III, VII, IX, and X (see below), while the remainder are found in the lateral horns of the sacral segments of the spinal cord (pelvic parasympathetic system, S2–S4). Thus, the parasympathetic nervous system is sometimes called the **craniosacral system.**

The second neurons of the sympathetic nervous system are arranged in prevertebral and paravertebral chains of ganglia (the sympathetic chains), while those of the parasympathetic nervous system generally lie in the walls of the innervated organs (intramural ganglia). The first neurons of both systems use acetylcholine as their neurotransmitter. The second neurons of the parasympathetic nervous system also use acetylcholine as their neurotransmitter (a further alternative name for the parasympathetic nervous system is, therefore, the **cholinergic system**). The neurotransmitter of the postganglionic sympathetic neurons, however, is norepinephrine (**adrenergic system**). The sweat glands are an exception to this rule: the second sympathetic neuron innervating them is cholinergic, like a second neuron in the parasympathetic nervous system.

Hypothalamic control of the sympathetic and parasympathetic nervous systems. Stimulation of the **rostral** hypothalamus induces **increased parasympathetic (trophotropic) activity**, including reduction of the cardiac minute volume, hypotonia, slowing of the heartbeat, reduction of the respiratory volume, lowering of the basal metabolic rate, vasodilatation, sweating, salivation, contraction of the bladder, reduced secretion of epinephrine, increased peristalsis, and pupillary constriction. Stimulation of the **caudal** hypothalamus, on the other hand, induces **increased sympathetic (ergotropic) activity**, including a rise in blood pressure, acceleration of the heartbeat, increased blood supply to the skeletal muscle and lungs, vasocon-

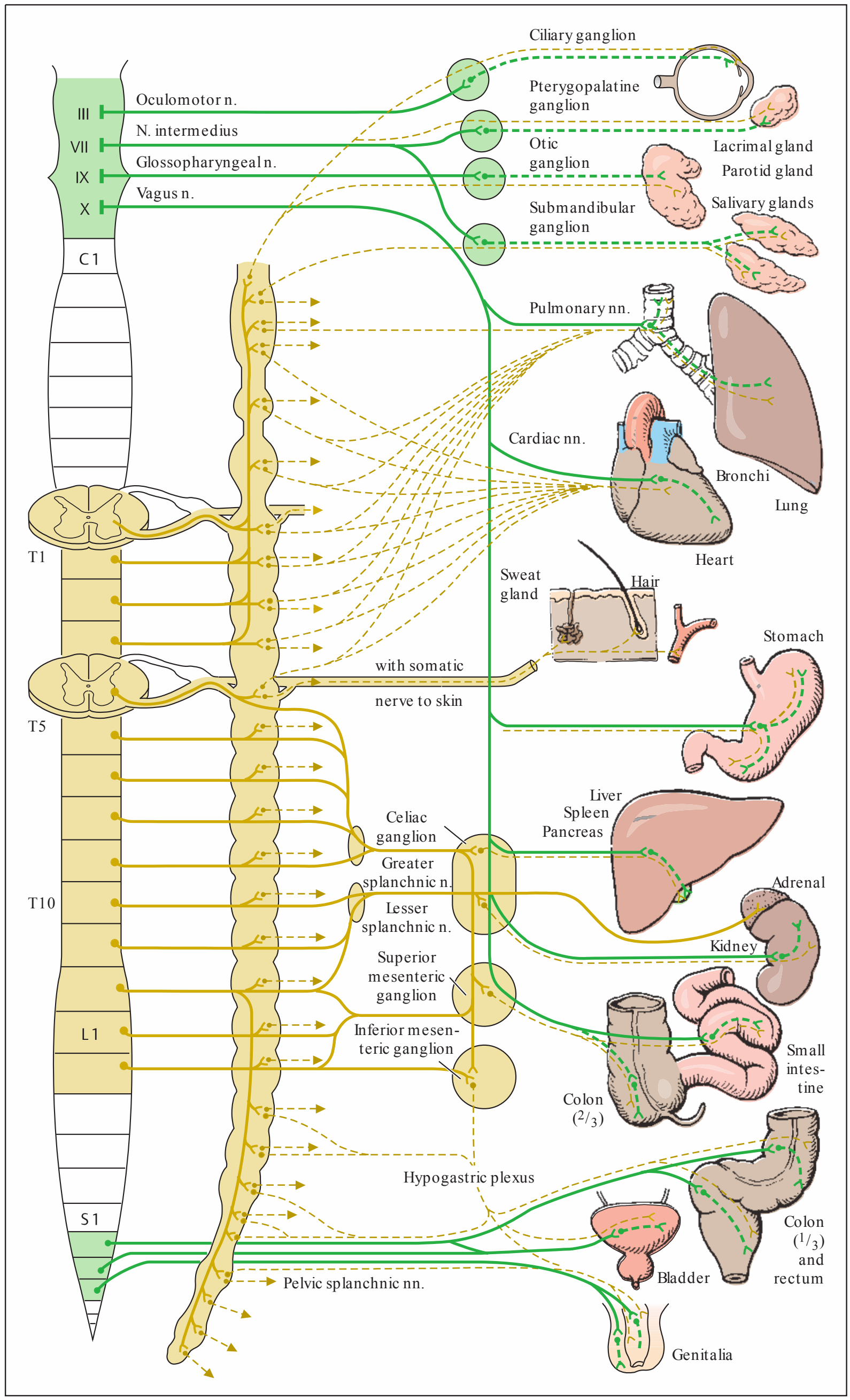


Fig. 6.**15** **The sympathetic and parasympathetic nervous system** (schematic diagram). Yellow: sympathetic. Green: parasympathetic.

striction in blood depots such as the capillary bed of the digestive tract, decreased blood supply to the abdominal viscera, increased respiratory volume, a rise in the blood glucose level, inhibition of peristalsis, urinary retention, increased secretion of epinephrine, widening of the palpebral fissure, and pupillary dilatation. A mass reaction thus occurs in the entire body, directed toward physical exertion and therefore enabling the whole organism to deal optimally with situations of attack

and stress. While the sympathetic, ergotropic reaction is directed toward physical exertion, the parasympathetic, trophotropic reaction is directed toward rest and recovery. Despite these general principles, however, the distinction between parasympathetic and sympathetic activity is not always clear-cut.

Neural connections of the hypothalamus to the peripheral autonomic nervous system. The hypothalamus exerts its regulating and controlling functions over the sympathetic and parasympathetic nervous systems by means of descending pathways including the *medial forebrain bundle* (Fig. 6.**9**), the *mamillotegmental tract*, and the *dorsal longitudinal fasciculus* (of Schütz) (Fig. 6.**10**).

These three fiber pathways connect the hypothalamus to the *descending midbrain reticular system*, which, in turn, carries the central impulses to the various components of the parasympathetic and sympathetic nervous systems.

Sympathetic Nervous System

The sympathetic nervous system innervates the smooth musculature of the blood vessels, abdominal viscera, bladder, rectum, hair follicles, and pupils, as well as the cardiac muscle, the sweat glands, and the lacrimal, salivatory, and digestive glands. The smooth musculature of the abdominal viscera, bladder, rectum, and digestive glands is inhibited, while that of all other target organs is stimulated to contract.

The caliber of the body's arteries is mainly regulated by the sympathetic nervous system. Increased sympathetic activity leads to vasoconstriction, and decreased sympathetic activity to vasodilatation.

Anatomy. The origin of the preganglionic fibers from thoracic segments T1 through T12 and from the first two lumbar segments is shown in Fig. 6.**15**. Some of the preganglionic fibers terminate on second neurons in the right and left sympathetic chains (only the left sympathetic chain is depicted in the figure). The remainder pass through the sympathetic chain without a synapse and terminate on a second neuron in a prevertebral ganglion. In either case, the postganglionic fiber of the second neuron transmits the sympathetic impulses onward to the target organ.

Sympathetic chain. As shown in Fig. 6.**16**, the preganglionic fibers emerge from neurons in the lateral horn of the spinal cord (intermediolateral cell column) and then join the axons of the somatic motor neurons to exit from the spinal cord in the anterior root. At the level of the spinal ganglion, the autonomic fibers separate from the somatic fibers once again and enter the sympathetic chain by way of the *white ramus communicans*, which is white because its fibers are myelinated. Some preganglionic fibers already terminate on the second neuron in the pathway at the same segmental level, but others travel one or more levels up or down the sympathetic chain before making a synapse onto their second neuron. Yet other fibers traverse the sympathetic chain without making a synapse and then terminate on a second neuron in a prevertebral ganglion. In all cases, the unmyelinated postganglionic fibers leave the sympathetic chain in the *gray ramus communicans*, which rejoins the spinal nerve at the same segmental level, so that its fibers travel to the corresponding cutaneous dermatome. In the skin, the autonomic fibers innervate the cutaneous vessels, the piloerector muscles, and the sweat glands.

Sympathetic innervation of the head and neck. As mentioned above, some postganglionic fibers reach their targets in the periphery by way of the segmental spinal nerves, but others do so by traveling along the blood vessels and their branches, particularly in the head and neck. The cervical spinal cord contains no sympathetic nuclei; thus, the sympathetic innervation of the head and neck is derived from the intermediolateral cell column of the upper four or five thoracic segments. Postganglionic fibers from these segments ascend in the sympathetic chain, and terminate in three ganglia at its rostral end: the *superior cervical ganglion*, the *middle cervical ganglion*, and the *cervicothoracic (stellate) ganglion*. These ganglia are the sites of the synaptic relay onto the second neurons, which emit the postganglionic fibers. Some of these fibers travel with the spinal nerves to the cervical cutaneous dermatomes. Other, unmyelinated fibers from the superior cervical ganglion form the *external carotid plexus*, which accompanies the external carotid artery and its branches to the head and the face, innervating the sweat glands, the smooth muscle of the hair follicles, and the blood vessels. Yet other fibers accompany the internal carotid

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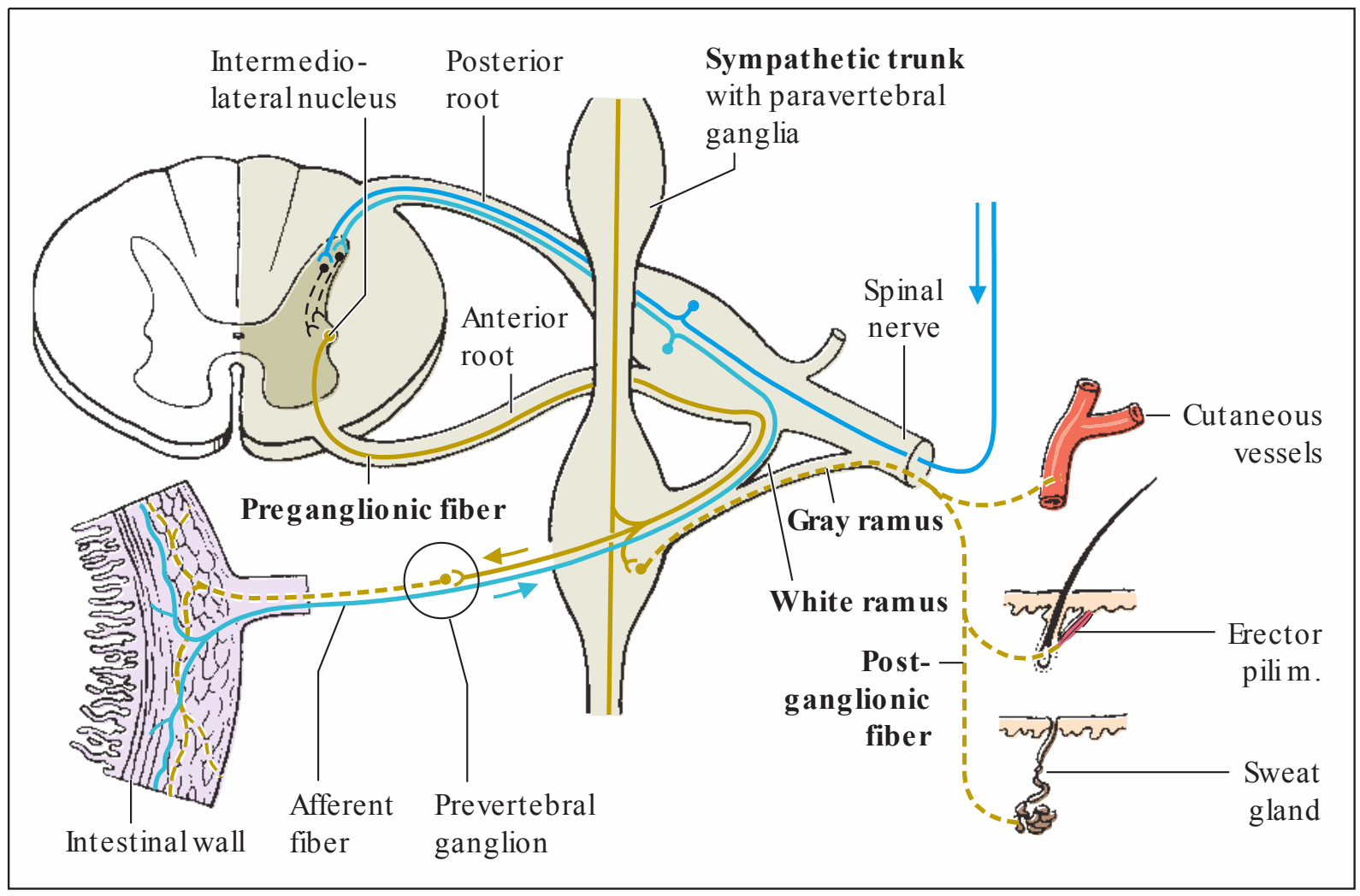

Fig. 6.**16** **The sympathetic trunk and the preganglionic and postganglionic sympathetic fibers** (schematic diagram)

artery as the *internal carotid plexus*, which innervates the eye (dilator pupillae muscle, orbitalis muscle, and tarsal muscle) as well as the lacrimal and salivary glands (Figs. 4.**27** and 4.**28** [pp. 103, 104] and 6.**15**).

Sympathetic innervation of heart and lungs. Postganglionic fibers from the cervical and upper four or five thoracic ganglia run in the *cardiac nerves* to the *cardiac plexus*, which innervates the heart. *Pulmonary nerves* innervate the bronchi and lungs (Fig. 6.**15**).

Sympathetic innervation of the abdominal and pelvic organs. Preganglionic fibers arise in thoracic segments T5 through T12 and travel, by way of the *greater* and *lesser splanchnic nerves*, to the unpaired prevertebral ganglia (the *celiac*, *superior mesenteric*, and *inferior mesenteric ganglia*), which are located along the aorta at the levels of origin of the correspondingly named aortic branches. Within these ganglia, the splanchnic fibers make synapses onto the second sympathetic neurons, which, in turn, emit the postganglionic fibers for the abdominal and pelvic viscera. In contrast to the parasympathetic fibers, the sympathetic postganglionic fibers are very long and form various plexuses before reaching their target organs (Fig. 6.**15**).

Adrenal medulla. The adrenal medulla occupies a special position in the sympathetic nervous system. It is analogous to a sympathetic ganglion, in that it is directly innervated by preganglionic fibers. These fibers form synapses onto modified second neurons within the adrenal medulla, which, rather than possessing an axon, secrete epinephrine and norepinephrine into the bloodstream (Fig. 6.**15**). Sympathetic activation induces the adrenal medulla to secrete epinephrine and norepinephrine, which then exert sympathetic effects in the periphery. This is particularly important under conditions of stress.

Clinical Symptoms of Sympathetic Lesions

Horner syndrome. As mentioned in Chapter 4 (p. 102 ff.), lesions affecting the ciliospinal center, the cervical sympathetic chain (cervicothoracic ganglion), or the autonomic plexuses along the blood vessels of the head and neck cause ipsilateral Horner syndrome. This consists of the clinical triad of a constricted pupil/**miosis** (due to loss of contraction of the dilator pupillae muscle), a hanging eyelid/**ptosis** (due to loss of contraction of the tarsal muscle), and an inwardly sunken globe/**enophthalmos** (due to loss of contraction of the orbitalis muscle). There is also loss of sweating (**anhidrosis**) and **vasodilatation** (due to loss of the vasoconstrictive effect of the sympathetic nerves) on the ipsilateral half of the face, which therefore appears dry and reddened.

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Causes of Horner syndrome. Interruption of the sympathetic pathway to the head and neck at any point can cause Horner syndrome. One common cause is a bronchial carcinoma at the apex of the lung (**Pancoast tumor**) impinging on the cervical sympathetic chain. Such tumors may present with Horner syndrome before becoming otherwise symptomatic.

Dissection of the internal carotid artery is another important cause of Horner syndrome. When the intima of the artery is torn, blood enters the vessel wall and the lumen is narrowed or occluded; rupture of the artery with pseudoaneurysm formation is rare. Carotid dissection has many possible etiologies; dissection may be *traumatic* or due to an *intrinsic abnormality* of the tissue of the vessel wall, e.g., fibromuscular dysplasia, which predisposes to the development of an intimal tear. In most cases, however, the etiology of carotid dissection cannot be determined.

The pathogenesis of sympathetic dysfunction in carotid dissection is not yet fully understood. According to one current hypothesis, *compression* of the sympathetic nerve branches by an intramural hematoma leads to nerve injury and dysfunction. According to another hypothesis, *ischemia* of the sympathetic nerve branches is the major cause of their dysfunction, as these nerve branches are supplied by small perforating branches of the internal carotid artery, which can be displaced or occluded by the dissection. Neither hypothesis is fully satisfactory.

Horner syndrome also arises as a result of brainstem lesions affecting the central sympathetic pathway, as in Wallenberg syndrome (p. 147 ff.)

Vasomotor phenomena in sympathetic dysfunction. The vasodilatation that follows a sympathetic lesion can be exploited therapeutically: *sympathectomy* is sometimes performed to increase regional blood flow, e.g., in Raynaud disease.

The vasodilatation due to a sympathetic lesion is also evident after interruption of the splanchnic nerves, which leads to a large increase of intravascular volume in the blood vessels of the bowel, i.e., to pooling of blood in the splanchnic area, with the risk of internal hemorrhage.

Parasympathetic Nervous System

In contrast to the sympathetic nervous system, the parasympathetic nervous system does not evoke any systemic responses, but instead produces its effects in individual, circumscribed areas, as reflected in the fact that its second (postganglionic) neurons lie near their target organs. Furthermore, acetylcholine, which is released as a neurotransmitter at the parasympathetic nerve terminals, is rapidly broken down by cholinesterases, and its effect is thus relatively short-lived.

The preganglionic fibers of the parasympathetic nervous system are long (unlike the short preganglionic fibers of the sympathetic nervous system). They emerge from nuclei in the brainstem and sacral spinal cord (S2, S3, S4) (Fig. 6.**15**).

Cranial Portion of the Parasympathetic Nervous System

Parasympathetic innervation of the head. The cell bodies of the preganglionic neurons lie in various *brainstem nuclei*, and their axons are found in *cranial nerves III, VII, IX, and X*. (The anatomy and course of these nerves was described in Chapter 4.) The preganglionic fibers travel to a number of ganglia that lie very close to their respective end organs (the *ciliary*, *pterygopalatine*, *submandibular*, and *otic ganglia*). These ganglia are relay stations in which the preganglionic fibers form synapses onto the second (postganglionic) neurons. The parasympathetic postganglionic fibers in the head are short, as they have only a short distance to travel before they reach their end organs. Like the sympathetic postganglionic fibers, they innervate smooth muscle, sweat glands, and lacrimal and salivary glands (Fig. 6.**15**). The smooth muscle of the blood vessel walls receives no parasympathetic innervation.

Parasympathetic innervation of the thoracic and abdominal organs. The parasympathetic portion of the *vagus nerve* (Fig. 4.**49**, p. 129) originates in the *dorsal nucleus of the vagus nerve* and carries preganglionic fibers for the innervation of the heart, lungs, and abdominal viscera down to the distal third of the transverse colon (Fig. 6.**15**). The second (postganglionic) neurons are found in autonomic plexuses located immediately adjacent to their end organs, or else within the bowel wall (myenteric

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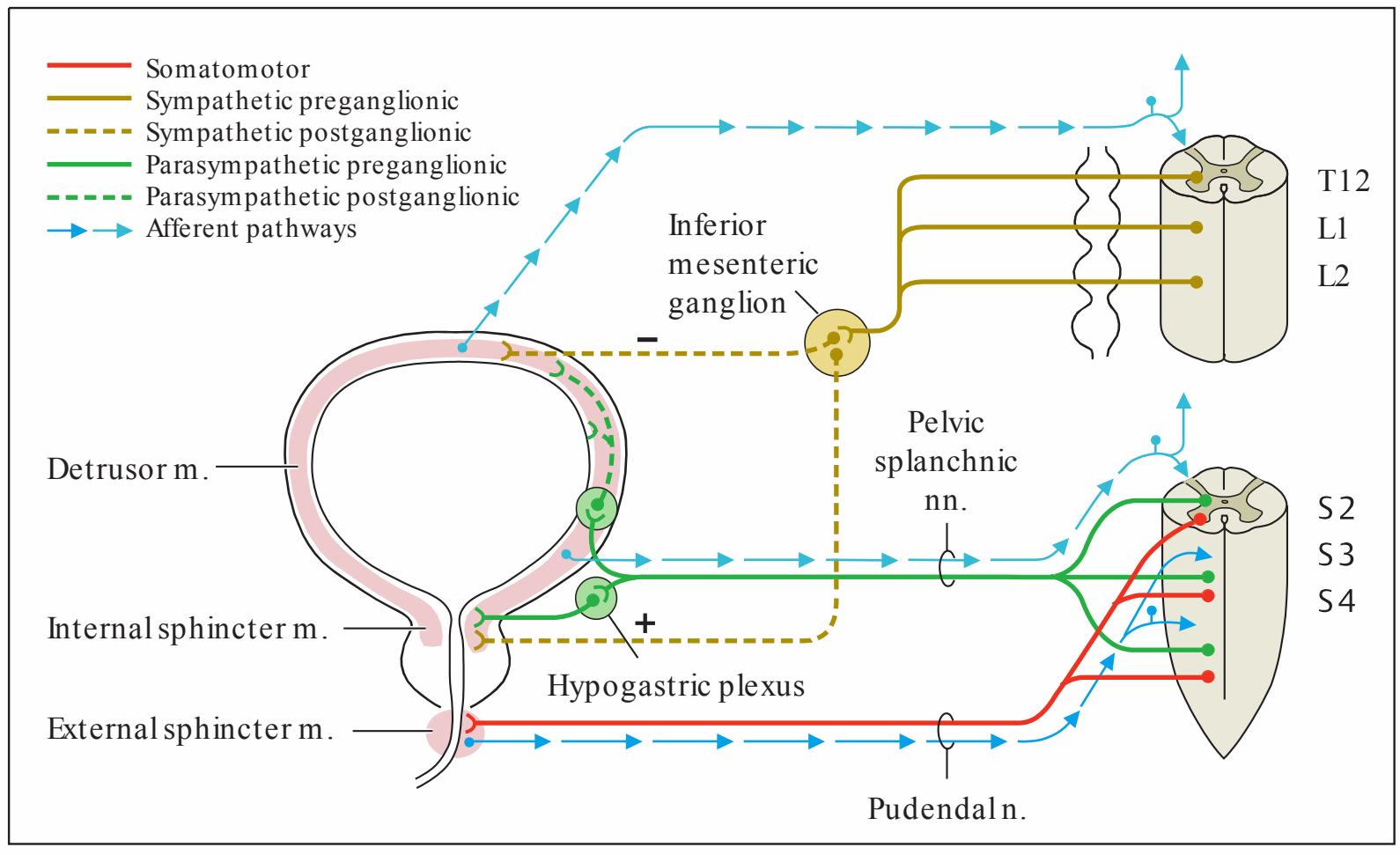

Fig. 6.**17** **Innervation of the bladder**

plexus of Auerbach, submucosal plexus of Meissner).

Sacral Portion of the Parasympathetic Nervous System

Parasympathetic innervation of the pelvic organs and genitalia. The sacral portion of the parasympathetic nervous system carries impulses in the *pelvic splanchnic nerves* and the *superior and inferior hypogastric (pelvic) plexuses* to ganglia in the muscular wall of the colon (from the distal third of the transverse colon onward), rectum, bladder, and genitalia (Fig. 6.**15**). In the pelvic area, the parasympathetic nervous system is responsible for the emptying of the rectum and bladder. It also brings about penile erection, while sympathetic fibers are responsible for ejaculation, which occurs through contractions of the ductus deferens and the seminal vesicles.

Autonomic Innervation and Functional Disturbances of Individual Organs

The sympathetic and parasympathetic innervation of individual organs is summarized in Table 6.**1**. The innervation of the pelvic organs will be discussed in greater detail in the following sections, because the function of these organs is commonly impaired in disturbances of the autonomic nervous system. Bladder dysfunction is the most important problem of this type.

Innervation of the Bladder

Parasympathetic innervation. The motor innervation of the urinary bladder is mostly parasympathetic. The pelvic splanchnic nerves, derived from segments S2, S3, and S4, travel to parasympathetic ganglia in the bladder wall and to the smooth muscle of the internal urethral sphincter (Figs. 6.**15** and 6.**17**). Parasympathetic stimulation induces contraction of the smooth detrusor muscle of the bladder wall and simultaneous relaxation of the internal urethral sphincter. Micturition results.

Sympathetic innervation. The sympathetic fibers innervating the bladder are derived from neurons in the intermediolateral cell column of the lower thoracic and upper lumbar spinal cord (segments T12, L1, and L2). These fibers travel through the caudal portion of the sympathetic chain and the inferior splanchnic nerves to the inferior mesenteric ganglion. Postganglionic sympathetic fibers then travel, by way of the inferior hypogastric plexus, to the bladder wall (tunica muscularis) and to the smooth muscle of the internal urethral sphincter (Fig. 6.**15** and 6.**17**).

Sensory innervation. Afferent fibers originate in nociceptors and proprioceptors of the bladder wall, which respond to stretch. As the bladder fills, there is a reflexive increase in muscle tone in the bladder wall and internal sphincter, which is mediated by the sacral segments (S2–S4) and the pelvic

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Table 6.1 **The Sympathetic and Parasympathetic Nervous System**

	Sympathetic			Parasympathetic		
Organ	Preganglionic neuron	Postganglionic neuron	Activity	Preganglionic neuron	Postganglionic neuron	Activity
Eye	T1–T2	Superior cervical ganglion	Mydriasis	Edinger–Westphal nucleus (accessory oculomotor nucleus)	Ciliary ganglion	Miosis, contraction of the ciliary muscle (accommodation)
Lacrimal, sublingual, and submandibular glands	T1–T2	Superior cervical ganglion	Vasoconstriction Secretion (viscous)	Superior salivatory nucleus	Pterygopalatine ganglion	Lacrimation, salivation (watery), vasodilation
Parotid gland	T1–T2	Superior cervical ganglion	Vasoconstriction Secretion	Inferior salivatory nucleus	Otic ganglion	Salivation
Heart	T1–T4 (T5)	Superior, middle, and inferior cervical ganglia and upper thoracic ganglia	Acceleration Dilation of coronary arteries	Dorsal nucleus of the vagus nerve	Cardiac plexus	Bradycardia, constriction of coronary arteries
Small intestine and ascending colon	T6–T10	Celiac ganglion, superior mesenteric ganglion	Inhibition of peristalsis and secretion	Dorsal nucleus of the vagus nerve	Myenteric plexus (of Auerbach), submucosal plexus (of Meissner)	Peristalsis, secretion, vasodilation
Pancreas	T6–T10	Celiac ganglion	—	Dorsal nucleus of the vagus nerve	Periarterial plexus	Secretion
Descending colon and rectum	L1–L2	Inferior mesenteric ganglion, hypogastric ganglion	Inhibition of peristalsis and secretion	S2–S4	Myenteric plexus (of Auerbach), submucosal plexus (of Meissner)	Secretion, peristalsis, evacuation
Kidney **Bladder**	L1–L2	Celiac ganglion, renal and hypogastric plexuses	Activation of internal sphincter muscle, vasoconstriction	S2–S4	Hypogastric plexus (vesical plexus)	Relaxation of the internal sphincter muscle, contraction of the detrusor muscle, vasodilation
Adrenal gland	T11–L1	Adrenal cells	Secretion (norepinephrine, epinephrine)	—	—	—
Male genitalia	L1–L2 (pelvic splanchnic nerves)	Superior and inferior hypogastric plexuses (pelvic plexus)	Ejaculation Vasoconstriction	S2–S4	Hypogastric plexus (pelvic plexus)	Erection, vasodilation, secretion

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Table 6.1 **The Sympathetic and Parasympathetic Nervous System** (continued)

		Sympathetic		Parasympathetic		
Skin of head and neck	T2–T4	Superior and middle cervical ganglia	Vasoconstriction Sweating Piloerection	—	—	—
Arms	T3–T6	Inferior cervical ganglion and upper thoracic ganglia		—	—	—
Legs	T10–L2	Lower lumbar and upper sacral ganglia		—	—	—

splanchnic nerves. Increasing tension on the bladder wall is consciously perceived, as some of the afferent impulses travel centrally, by way of the posterior columns, to the so-called pontine micturition center, which lies in the reticular formation near the locus ceruleus. From the micturition center, impulses travel onward to the paracentral lobule on the medial surface of the cerebral hemispheres, and to other brain areas.

Regulation of Bladder Function: Continence and Micturition

The bladder performs its two major functions, the **continent storage of urine** and **periodic**, **complete emptying**, as follows.

Urinary continence is achieved by *activation of the internal and external urethral sphincters*, and, in women, mainly by activation of the *muscles of the pelvic floor*. Sympathetic efferent fibers from T11–L2 activate alpha-receptors of the internal sphincter and are also thought to inhibit the detrusor muscle by a mechanism that has not yet been determined. The external urethral sphincter is a striated muscle that, like the muscles of the pelvic floor, receives its somatic innervation through efferent fibers of the pudendal nerve (S2–S4, see p. 193).

As the bladder is filled and the tension on the bladder wall increases, involuntary reflex contraction of the detrusor muscle is effectively countered by activation of the external sphincter by the sacral somatic motor neurons. At the same time, lumbar sympathetic activation induces closure of the internal sphincter as well as relaxation of the detrusor muscle.

Micturition. The most important stimulus for micturition is *stretching of the bladder wall*, which excites visceral sensory afferent neurons, induces the urge to void, and, with the cooperation of higher nervous centers, leads to *contraction of the detrusor muscle*. This hollow muscle receives its parasympathetic innervation from the sacral spinal cord by way of the pelvic nerve. Bladder emptying is further promoted by somatic, voluntarily controlled *abdominal pressing* and by *simultaneous relaxation of the internal and external urethral sphincters*.

At a supraspinal level, micturition is controlled by the *pontine micturition center*, which projects descending efferent fibers in the medial and lateral reticulospinal tracts to coordinate the simultaneous relaxation of the internal and external sphincters and contraction of the detrusor muscle. The neurotransmitter glutamate may play a role in this pathway. The pontine micturition center is anatomically poorly characterized. It can be inhibited through afferent fibers from higher centers, including the frontal cortex, cingulate gyrus, paracentral lobule, and basal ganglia.

Bladder Dysfunction

As discussed in the last section, the regulation of continence and micturition requires the perfect functional cooperation of numerous anatomical structures, some of which are very distant from others. Lesions at many different sites in the central or peripheral nervous system can have far-ranging deleterious effects on bladder function.

Bladder dysfunction may be due to structural/anatomical lesions of the bladder or urethra (**bladder dysfunction of urological origin**: vesical

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tumors, infravesical obstruction by urethral stricture or prostatic hypertrophy), or it may be due to a lesion of the neural structures innervating the bladder (**neurogenic bladder dysfunction**). The responsible neural lesion may lie in the peripheral nerve pathways, the autonomic plexuses, the spinal cord, or higher centers.

Impairment of supraspinal control mechanisms frequently causes bladder dysfunction in patients with multiple sclerosis, for example. Disturbances of the interaction between the pontine micturition center and other, higher centers that modulate it play an important role in the types of neurogenic bladder dysfunction seen in neurodegenerative diseases, including Parkinson disease.

Neurogenic Bladder Dysfunction

Typical manifestations of neurogenic bladder dysfunction include *urinary frequency and urgency*, *incontinence*, *difficult and incomplete bladder emptying*, and *recurrent urinary tract infections*.

The first step toward the successful treatment of neurogenic bladder dysfunction is a correct clinical diagnosis. Various aspects of urinary function must be taken into account, including the answers to the following questions: When and how frequently is the bladder emptied? Is it emptied completely? Is the urge to void normal, diminished, or abnormally severe (urinary urgency)? Has a urinary tract infection been ruled out? Is the patient continent?

Detrusor instability and detrusor hyperreflexia are characterized by premature detrusor contractions during the vesical filling phase. The term "instability" refers to a lack of the normal inhibition of detrusor contraction; the term "hyperreflexia" implies that a neurological disease is causing the bladder emptying disorder. Thus, clinical entities such as uninhibited neurogenic bladder, automatic bladder, and motor instability of the bladder all belong within the etiological category of detrusor hyperreflexia. In such cases, *the lesion lies above the sacral spinal cord* and impairs the function of suprasacral inhibitory projections to the detrusor muscle. The major symptom of isolated detrusor hyperreflexia is **imperative urinary urgency with urge incontinence and low residual volume**. The more common causes are multiple sclerosis, cerebrovascular diseases, normal pressure hydrocephalus, Parkinson disease, spinal cord trauma, and trauma or tumor affecting the frontal lobes of the brain.

Detrusor–sphincter dyssynergia is defined as involuntary detrusor contraction without relaxation of the external urethral sphincter. The lesion lies *between the sacral spinal cord and the pontine micturition center*. The major symptom is **imperative urinary urgency with incomplete emptying of the bladder**. Detrusor–sphincter dyssynergia causes complications (in particular, ascending urinary tract infections) more frequently in men than in women, because women have a lower bladder outlet resistance than men. The more common causes are multiple sclerosis, cervical myelopathy, spinal tumors, vascular malformations, and trauma. This entity should be distinguished from the rare *functional obstruction of the bladder neck*, a disorder of unknown etiology that is associated with increased residual volume and can impair renal function.

Detrusor areflexia results from deficient afferent or efferent innervation of the detrusor muscle. Afferent and efferent disturbances hardly ever occur in isolation, presumably because both afferent and efferent impulses travel through the pelvic parasympathetic nerves and the sacral spinal segments, so that any lesion impairing one type of impulse necessarily impairs the other. The clinical manifestations of detrusor areflexia are **reduced urge to void**, **inability to initiate micturition**, **and overflow incontinence** with an increased bladder volume (up to 2000 ml). *The lesion lies within the sacral spinal cord or the peripheral nerves that enter and emerge from it*. Causes include tumors involving the conus medullaris and/or cauda equina, lumbar spinal stenosis and disk herniation, polyradiculitis (including Guillain–Barré syndrome), diabetic or alcoholic polyneuropathy, tabes dorsalis, pelvic surgery and radiation therapy, myelodysplasia, and tethered cord syndrome.

Detrusor areflexia due to sacral spinal cord dysfunction is found in 20–30 % of patients with multiple sclerosis. Most of these patients have markedly elevated residual volumes because the attempt to urinate is further thwarted by lack of relaxation of the external urethral sphincter.

Genuine stress incontinence is said to be present when detrusor function is normal and stress incon-

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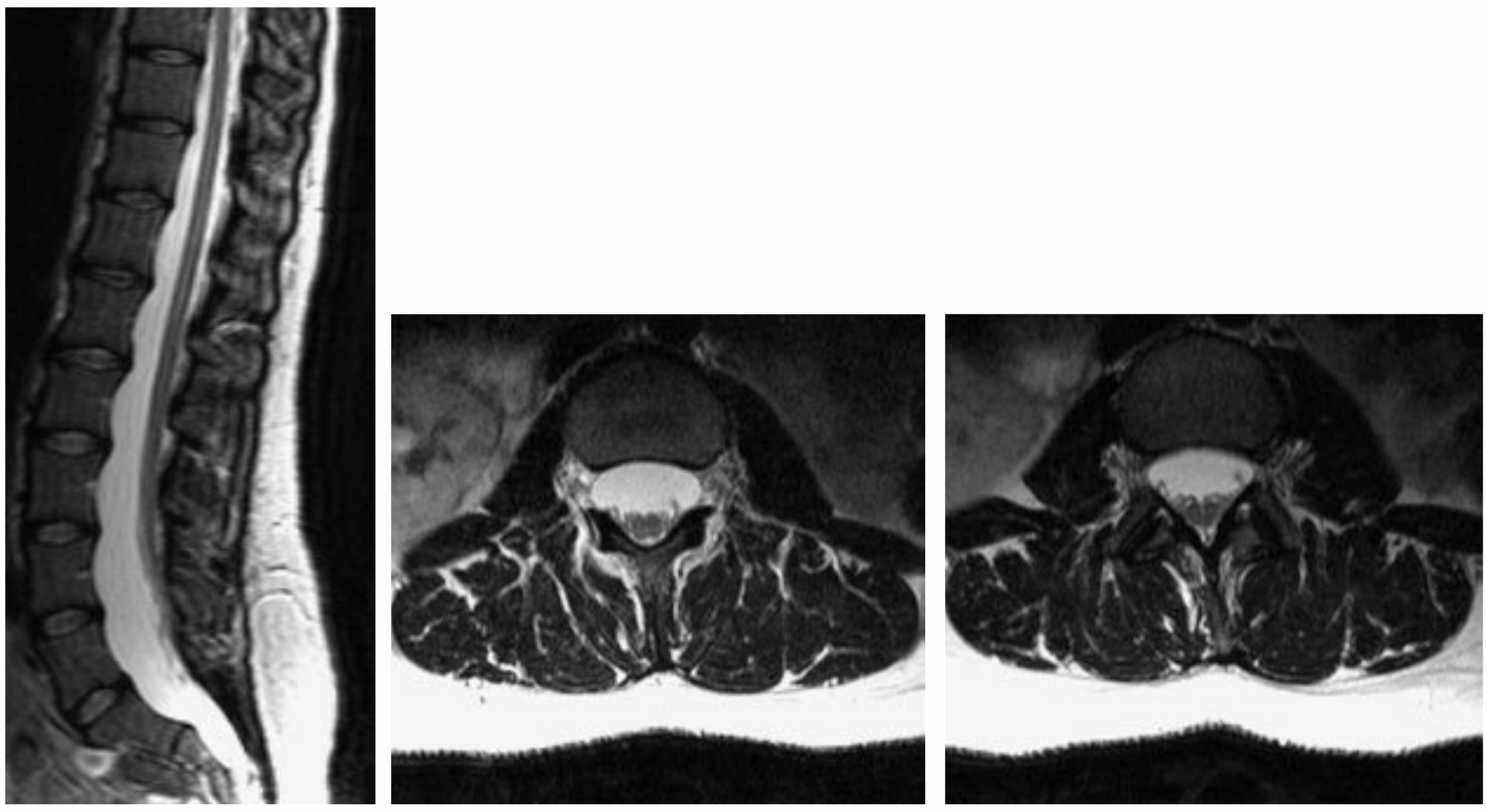
Case Presentation 3: Tethered Cord Syndrome

This previously healthy 27-year-old nurse complained to her family physician of difficulty urinating. She had trouble initiating the flow of urine, needed to strain to urinate, and felt that her bladder was still full afterward. At other times, she passed small amounts of urine involuntarily. Finally, she had also had a single episode of stool incontinence. She was very worried and embarrassed, was afraid to leave the house, and had stopped going to work. She denied having pain or any history of trauma.

Neurological examination revealed hypesthesia in the sacral dermatomes (saddle hypesthesia), normal strength in the lower limbs, and markedly diminished sphincter tone. An MRI scan was ordered to rule out a mass compressing the conus medullaris or cauda equina (Fig. 6.**18**). This study revealed a developmental anomaly in the lumbosacral spinal canal, in which the conus medullaris lay at an abnormally low level (tethered cord syndrome).

In this disorder, the conus, because it lies immediately under the dorsal dura mater and adheres to it, cannot ascend normally to the L1–2 level over the course of development. The resulting neurological deficits may not arise until later in life, and their pathogenesis remains incompletely understood. Because of her progressive neurological deficits, the patient presented here was treated neurosurgically, with an operative detachment of the conus from the dura mater. Her deficits resolved completely thereafter.



a **b** **c**

Fig. 6.**18** **Tethered cord syndrome. a** The sagittal T2-weighted image shows an enlarged lumbar spinal canal with the conus medullaris lying at an abnormally low position (L4) immediately underlying the dorsal dura mater. In this case, there were no associated anomalies such as a dermal sinus, lipoma, or meningomyelocele. **b**, **c** The T2-weighted axial sections through the spinal canal at T12 (**b**) and L2 (**c**) reveal spinal cord at both levels. Even at the L2 level, the cord has a greater diameter than the cauda equina. It adheres to the dorsal dura mater.

tinence is due solely to deficient activation of the external urethral sphincter. Genuine stress incontinence, the most common type of bladder emptying disorder in women, occurs mainly after hysterectomy and in multiparous women with uterine prolapse. Its incidence rises with age. It also occurs as a manifestation of various neurogenic bladder emptying disorders, including detrusor hyperreflexia and detrusor–sphincter dyssynergia.

Nonneurogenic Bladder Dysfunction

Infravesical obstruction usually occurs in men, often as the result of benign prostatic hyperplasia, and is manifested clinically with urinary urgency, pollakiuria, nocturia, urinary retention, and overflow incontinence.

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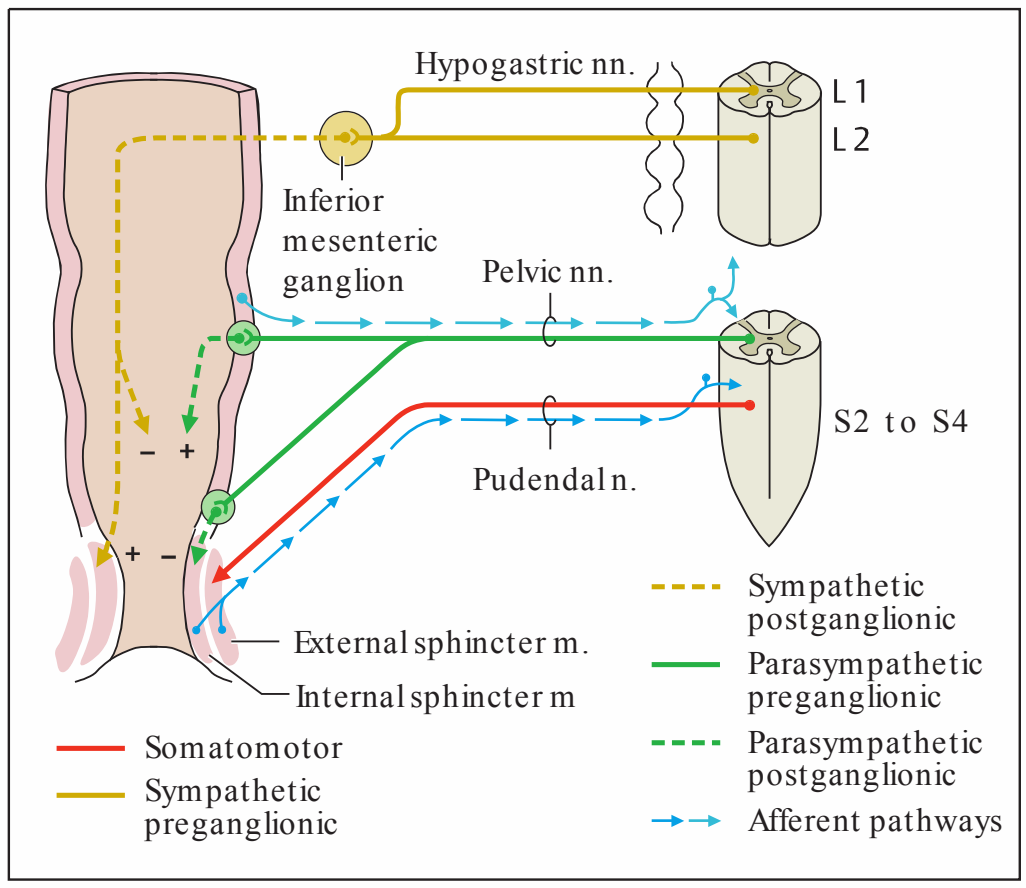

Fig. 6.**19** **Innervation of the rectum**

Dysfunction of the external urethral sphincter, preventing adequate relaxation of the sphincter muscle, has been found to be a common cause of obstructive bladder emptying disturbances in young women. It is characterized by myotoniform discharges in the EMG. Electromyographic study is necessary to distinguish this disorder from two important alternative diagnoses in young women with bladder emptying disturbances, namely, multiple sclerosis and psychogenic bladder dysfunction.

Enuresis is defined as bedwetting, by day or night, in individuals over the age of 4 years, in the absence of any demonstrable causative lesion. Enuresis is thus, by definition, not a neurogenic disturbance. The important differential diagnoses include *organic* neurological and urological causes of bedwetting, including epilepsy, spina bifida occulta, and malformations of the urogenital tract. A 24-hour EEG recording is indicated in some cases.

Innervation of the Rectum

Emptying of the rectum is analogous to emptying of the bladder in many respects (Fig. 6.**19**).

Filling of the rectum activates stretch receptors in the rectal wall, which transmit impulses by way of the inferior hypogastric plexus to segments S2 through S4 of the sacral spinal cord. Afferent impulses then ascend the spinal cord to higher control centers, which are probably located in the pontine reticular formation and the cerebral cortex.

Rectal peristalsis is induced by parasympathetic activation from segments S2 through S4, which also induces relaxation of the internal sphincter. The sympathetic nervous system inhibits peristalsis. The external sphincter consists of striated muscle and is under voluntary control.

Rectal emptying is mainly accomplished voluntarily by abdominal pressing.

Rectal Emptying Disorders

Fecal retention. Transection of the spinal cord above the lumbosacral centers for defecation leads to fecal retention. Interruption of the afferent arm of the reflex pathway for defecation deprives higher centers of information about the filling state of the rectum, while interruption of descending motor fibers impairs voluntary abdominal pressing. Sphincter closure is often inadequate because of spastic weakness.

Fecal incontinence. Lesions of the sacral spinal cord (S2–S4) abolish the anal reflex and produce fecal incontinence. If the stool is watery, involuntary loss of stool occurs.

Innervation of the Male Genitalia

Efferent sympathetic fibers from the upper lumbar spinal cord travel by way of a periarterial nervous plexus (the hypogastric plexus) to the seminal vesicles, prostate, and ductus deferentes. Stimulation of the plexus causes ejaculation (Fig. 6.**20**).

Parasympathetic fibers from segments S2 through S4 travel through the pelvic splanchnic nerves (the nervi erigentes) to the corpora cavernosa. Parasympathetically induced vasodilatation in the corpora cavernosa brings about penile erection (Fig. 6.**20**). The urethral sphincter and the ischiocavernosus and bulbospongiosus muscles are innervated by the pudendal nerve.

Genital function is ultimately under the control of hypothalamic centers, which exert their effects partly through neural connections (reticulospinal fibers) and partly by humoral means (hormones).

Genital Dysfunction

Spinal cord transection at a thoracic level causes impotence. Reflex priapism may occur, and occasional ejaculation is also possible. Paraplegia has

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been reported to be associated with testicular atrophy.

Lesions of the sacral spinal cord from S2 to S4 also cause impotence. In these cases, neither erection nor ejaculation is possible.

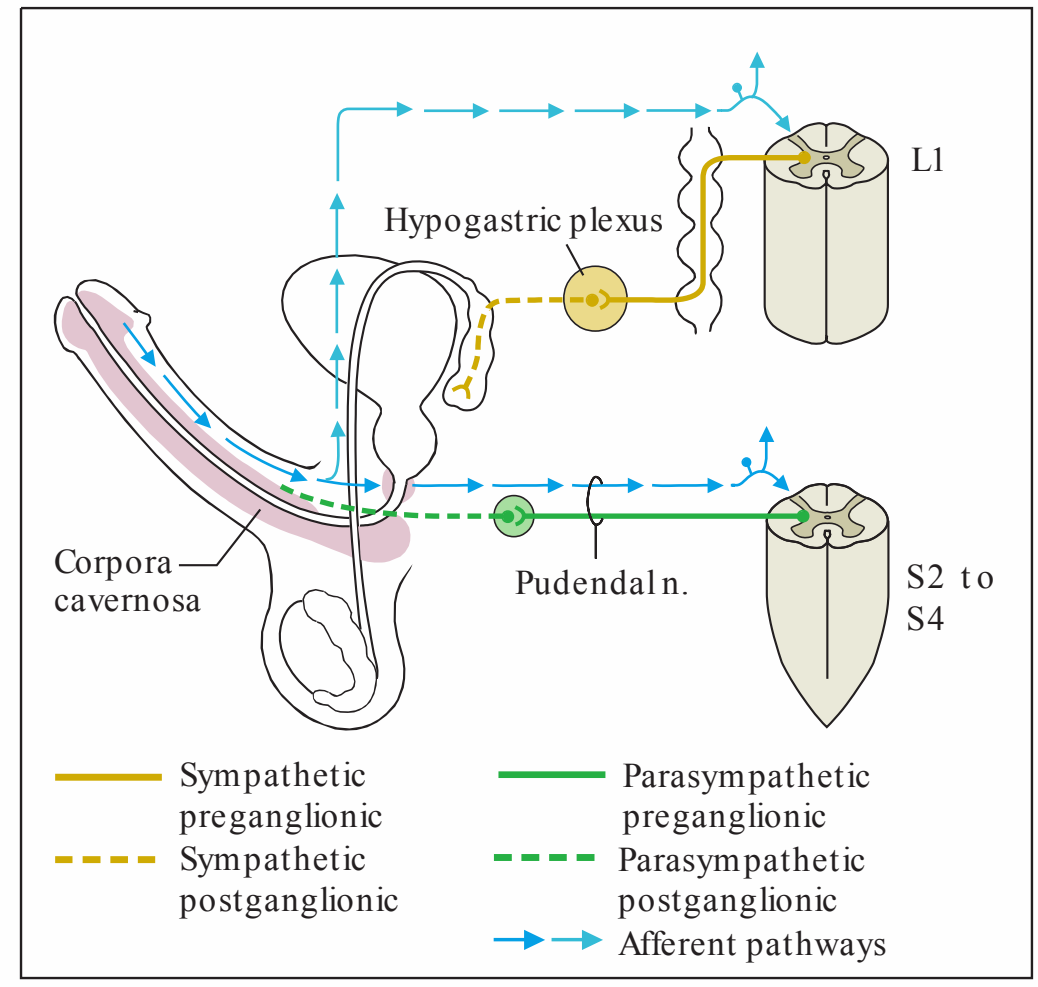

Fig. 6.**20** **Innervation of the male genitalia** (erection and ejaculation)

Visceral and Referred Pain

Afferent autonomic fibers participate in a large number of autonomic regulatory circuits. Most of the impulses traveling in these fibers do *not* rise to consciousness.

Visceral pain. The individual *can*, however, consciously perceive the filling state of the hollow viscera, which is reported to the central nervous system through afferent autonomic fibers arising from pressure or stretch receptors in the visceral wall. Overfilling of a hollow viscus is perceived as pain. Moreover, irritation of the wall of a viscus can cause reflex spasm of smooth muscle, which also gives rise to pain (biliary colic due to gallstones, renal colic due to kidney stones). Visceral inflammation or ischemia is also painful, e.g., angina pectoris.

Pain originating in the internal organs is diffuse and poorly localizable. Furthermore, the patient may report feeling pain not in the organ itself but in a related zone of the body surface (these are the zones of Head, cf. Fig. 6.**21**).

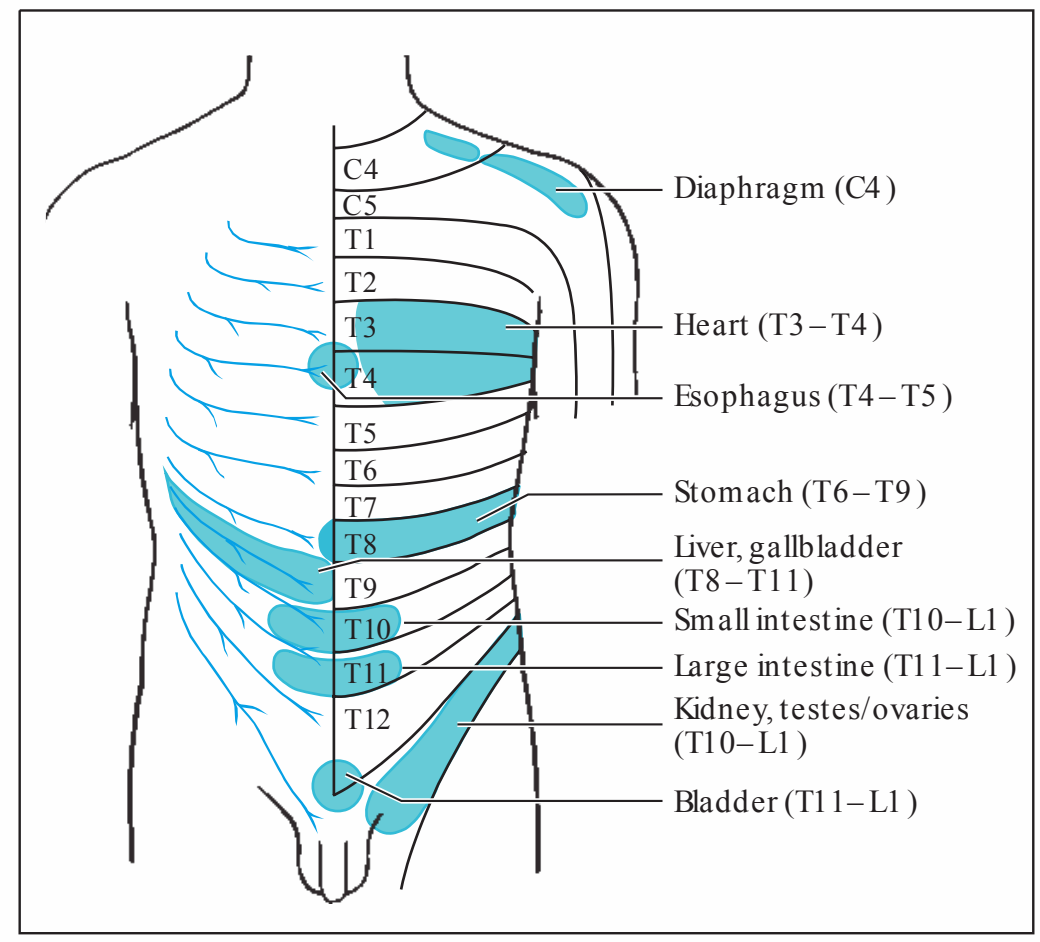

Fig. 6.**21** **The zones of Head**

Referred pain. The cell bodies of the afferent autonomic fibers, like those of the somatic afferent fibers, are located in the spinal ganglia. The autonomic fibers enter the spinal cord through the posterior root together with the somatic afferent fibers from the myotome and dermatome of each segmental level. Thus, each individual segment of the posterior horn receives converging afferent input, both from the internal organs and from the related myotome and dermatome. Activation from either set of afferent fibers (visceral or somatic) is transmitted centrally by the same fibers of the lateral spinothalamic tract (Fig. 6.**22**). It is therefore understandable that pain arising in a particular viscus is sometimes felt elsewhere, namely, in the dermatome or myotome represented by the same spinal segment. This phenomenon is called referred pain. It may be accompanied by a certain degree of hypersensitivity to somatosensory stimulation in the dermatome to which pain is referred. The abdominal wall may also become rigid. The exact mechanism by which referred pain arises has not yet been conclusively explained, though there are a number of hypotheses.

Pain of cardiac origin, for example, is often referred elsewhere. The upper thoracic segments on the left side receive somatic afferent fibers from the left side of the chest and the left arm, as well as visceral afferent fibers from the heart. Cardiac disease, particularly ischemia, often produces pain in one of these dermatomes (angina pectoris). The particular zones to which pain is referred from the

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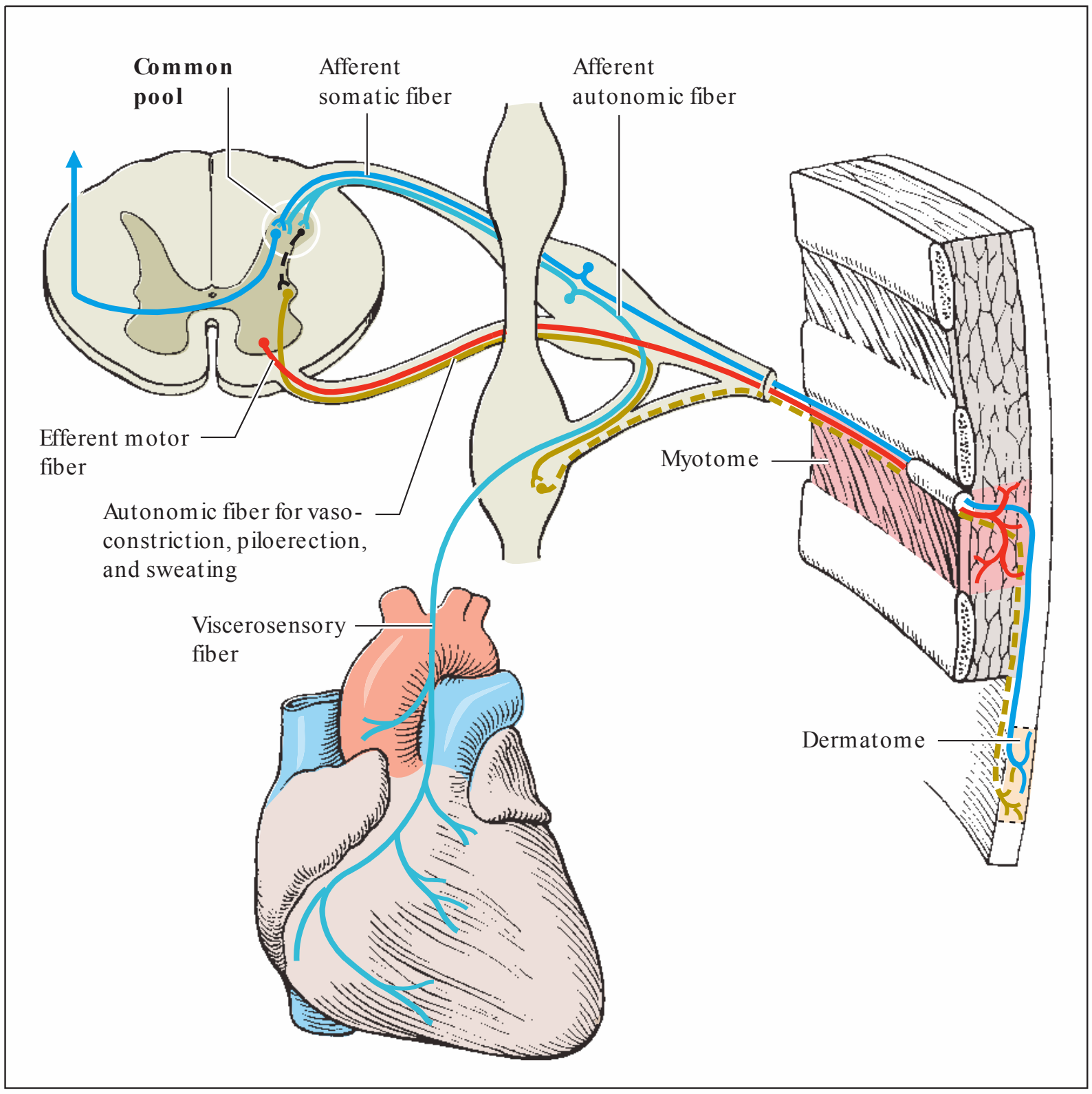

Fig. 6.**22** **The viscerocutaneous reflex arc** with myotome, dermatome, and enterotome. Viscerosensory and somatosensory impulses converge at the level of the posterior horn onto a common neuron, which transmits further impulses centrally along a single common pathway. Thus, afferent signals from the internal organs can be "misinterpreted" as having arisen in the corresponding cutaneous or muscular areas (dermatome or myotome). This is the mechanism of referred pain.

individual internal organs are very important in physical diagnosis and are called the zones of Head (Fig. 6.**21**). It is also the case, however, that impulses arising from the skin can be projected (referred) to the internal organs. Clearly, the somatic afferent fibers are interconnected with visceral reflex arcs within the spinal cord. This may explain how therapeutic measures at the body surface (such as the application of warmth or heat, compresses, rubbing, etc.) often relieve pain arising from the autonomically innervated viscera.

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