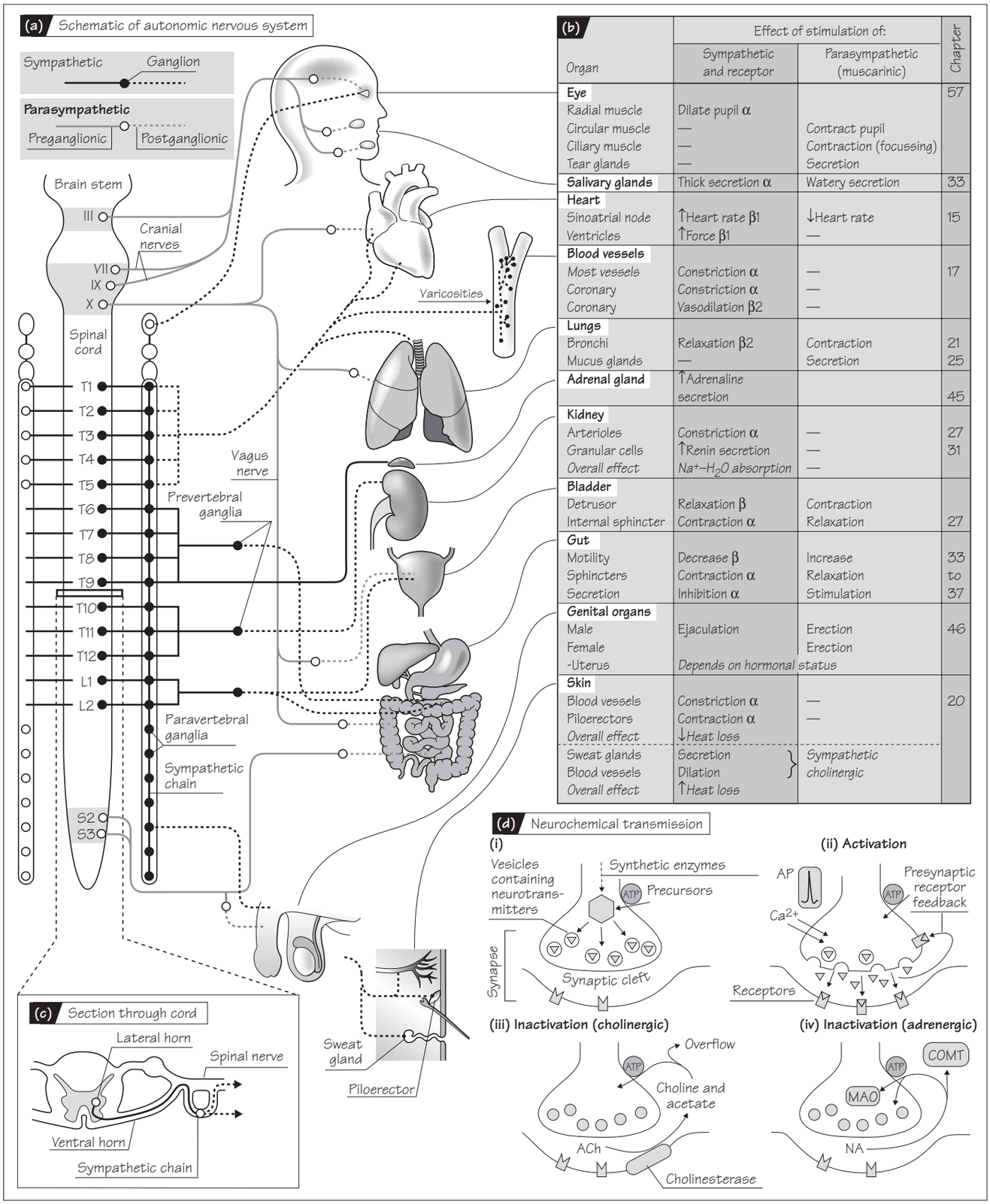
8 The autonomic nervous system



(b)

Organ	Effect of stimulation of: Sympathetic and receptor	Parasympathetic (muscarinic)	Chapter
Eye			57
Radial muscle	Dilate pupil α		
Circular muscle	—	Contract pupil	
Ciliary muscle	—	Contraction (focussing)	
Tear glands	—	Secretion	
Salivary glands	Thick secretion α	Watery secretion	33
Heart			
Sinoatrial node	↑Heart rate β1	↓Heart rate	15
Ventricles	↑Force β1	—	
Blood vessels			
Most vessels	Constriction α	—	17
Coronary	Constriction α	—	
Coronary	Vasodilation β2	—	
Lungs			
Bronchi	Relaxation β2	Contraction	21
Mucus glands	—	Secretion	25
Adrenal gland	↑Adrenaline secretion		45
Kidney			
Arterioles	Constriction α	—	27
Granular cells	↑Renin secretion	—	31
Overall effect	*Na^+–H_2O absorption*	—	
Bladder			
Detrusor	Relaxation β	Contraction	
Internal sphincter	Contraction α	Relaxation	27
Gut			
Motility	Decrease β	Increase	33
Sphincters	Contraction α	Relaxation	to
Secretion	Inhibition α	Stimulation	37
Genital organs			
Male	Ejaculation	Erection	46
Female		Erection	
-Uterus	*Depends on hormonal status*		
Skin			
Blood vessels	Constriction α	—	20
Piloerectors	Contraction α	—	
Overall effect	↓*Heat loss*		
Sweat glands	Secretion	*Sympathetic cholinergic*	
Blood vessels	Dilation		
Overall effect	↑*Heat loss*		

The **autonomic nervous system** (**ANS**) provides the **efferent** pathway for the **involuntary** control of most organs, excluding the motor control of skeletal muscle (Chapters 50 & 51). The ANS provides the effector arm for **homeostatic reflexes** (e.g. control of blood pressure), and allows the integration and modulation of function by central mechanisms in the brain in response to *environmental* and *emotional* stimuli (e.g. exercise, thermoregulation, 'fight or flight'). Figure 8a shows a simplified schematic diagram of the ANS, and Fig. 8b its actions on major organs.

The ANS is divided into **sympathetic** and **parasympathetic** systems. Both contain **preganglionic neurones** originating in the central nervous system that synapse with non-myelinated **postganglionic neurones** in the **peripheral ganglia**; postganglionic neurones innervate the target organ or tissue (Fig. 8a,b). Preganglionic neurones of both sympathetic and parasympathetic systems release **acetylcholine** in the synapse, which acts on **cholinergic nicotinic** receptors on the postganglionic fibre. The postganglionic neurotransmitters and receptors depend on the system and organ (see below). Parasympathetic peripheral ganglia are generally found close to or in the target organ, whereas sympathetic ganglia are largely located in two **sympathetic chains** either side of the vertebral column (*paravertebral ganglia*), or in diffuse *prevertebral ganglia* of the visceral plexuses of the abdomen and pelvis (Fig. 8a). Sympathetic postganglionic neurones are therefore generally long, whereas parasympathetic neurones are generally short. An exception is the sympathetic innervation of the **adrenal gland**, where preganglionic neurones directly innervate the adrenal medulla.

The sympathetic system is more pervasive than the parasympathetic; where an organ is innervated by both systems, they often act antagonistically (Fig. 8b). However, there is a high degree of central coordination, so that an increase in sympathetic activity to an organ is commonly accompanied by a decrease in parasympathetic activity. Sympathetic and parasympathetic activity may modulate different functions in the same organ (e.g. genital organs). In loose terms, the sympathetic system might be said to coordinate '*flight or fight*' responses, and the parasympathetic system '*rest and digest*' responses.

Sympathetic system

Sympathetic preganglionic neurones originate in the *lateral horn* of segments T1–L2 of the spinal cord, and exit the cord via the *ventral horn* (Fig. 8c) on their way to the paravertebral or prevertebral ganglia. Sympathetic postganglionic neurones terminate in the effector organs, where they release **noradrenaline** (**norepinephrine**). Noradrenaline and **adrenaline** (**epinephrine**), which is released by the adrenal medulla, are catecholamines, and activate **adrenergic** receptors, which are linked via G-proteins to cellular effector mechanisms. There are two main classes of adrenergic receptor, α and β, and these are further subdivided into several subtypes (e.g. α_1, α_2, β_1, β_2). Noradrenaline and adrenaline are equally potent on α_1-receptors, which are linked to G_q-proteins and are commonly associated with smooth muscle contraction (e.g. blood vessels). The α_2-receptors are $G_{i/o}$-protein linked and are often inhibitory. All β-receptors are linked to G_s-protein and activate adenylyl cyclase to make cyclic adenosine monophosphate (cAMP). Noradrenaline is more potent at β_1-receptors and adrenaline is more potent at β_2-receptors. The activation of β-receptors is associated with the relaxation of smooth muscle (e.g. blood vessels, airways), but causes increased heart rate and force (Fig. 8b).

A few sympathetic neurones release acetylcholine at the effector (e.g. sweat glands), and are thus known as **sympathetic cholinergic** neurones.

Parasympathetic system

Parasympathetic preganglionic neurones originate in the brain stem, from which they run in the IIIrd, VIIth, IXth and Xth (**vagus**) cranial nerves, and also from the second and third sacral segments of the spinal cord (Fig. 8a). Parasympathetic postganglionic neurones release acetylcholine, which acts on **cholinergic muscarinic** receptors. Parasympathetic activation causes secretion in many glands (e.g. bronchial mucous glands), and either contraction (e.g. bladder detrusor) or relaxation (e.g. bladder internal sphincter) of smooth muscle, although it has little effect on blood vessels. Notable exceptions, however, include vasodilatation in the penis and clitoris with subsequent erection (Chapter 45).

Neurochemical transmission

Action potentials (APs) in incoming neurones are transmitted by the release of neurotransmitters that bind to receptors on the postganglionic neurone or effector tissue. Between neurones (e.g. in ganglia), this occurs within a classical **synapse**, where the axon terminates in a bulbous swelling or **bouton** separated from the target by a narrow (10–20 nm) synaptic cleft (Fig. 8d). Postganglionic neurones branch repeatedly and have numerous boutons along their length, forming **varicosities** (e.g. see blood vessel in Fig. 8a). The boutons may either be close (~20 nm) to the effector membrane, allowing fast and specific delivery of the signal, or at some distance (100–200 nm), allowing a more distributed but slower effect. The mechanisms of neurochemical transmission are similar, and although the text below and Fig. 8di–iv refer to synapses, the same principles apply.

Synthetic enzymes are transported down the axon into the bouton, where they synthesize neurotransmitter (acetylcholine, noradrenaline) from precursors transported into the bouton. The neurotransmitter is stored in 50 nm **vesicles** (Fig. 8di). The arrival of an AP at the nerve ending causes an influx of Ca^{2+}, the fusion of vesicles with the membrane and the release of neurotransmitter; this binds to postsynaptic receptors and activates the response. Neurotransmitter release can be suppressed by feedback onto **presynaptic inhibitory receptors** (α_2-*receptors* for adrenergic synapses) (Fig. 8dii). Neurotransmitters must be removed at the end of activation. In *cholinergic* synapses, **cholinesterase** rapidly breaks down acetylcholine into *choline* and *acetate*, which are recycled; some may escape into interstitial fluid (*overflow*) (Fig. 8diii). In adrenergic synapses, most noradrenaline is rapidly taken up again by the nerve ending via an adenosine triphosphate (ATP)-dependent transporter called **uptake-1**; recovered noradrenaline is recycled. Some facilitated diffusion (**uptake-2**) also occurs into smooth muscle. Excess noradrenaline and sympathomimetic amines, such as tyramine (found in some foodstuffs), are metabolized in the neurone by mitochondrial **mono-amine oxidase** (**MAO**). Noradrenaline and other catecholamines that enter the circulation are metabolized sequentially by **catechol-O-methyl transferase** (**COMT**) and MAO (Fig. 8div).