a predator). The monoaminergic systems include important descending projections to the dorsal horn of the spinal cord that modulate pain perception (Chapter 20).

The noradrenergic inputs to the spinal cord originate from the pontine cell groups A5–A7, with the locus ceruleus (A6) providing most of the input to the dorsal horn. Similarly, the serotonergic raphe nuclei in the medulla, particularly the nucleus raphe magnus, project to the dorsal horn where they modulate the processing of information about noxious stimuli. Direct application of serotonin to dorsal horn neurons inhibits their response to noxious stimuli, and intrathecal administration of serotonin attenuates the defensive withdrawal of the paw evoked by noxious stimuli. In addition, intrathecal administration of antagonists of serotonin receptors blocks the pain inhibition evoked by stimulation of the raphe nuclei.

Insight into the role of serotonin in pain processing has been used in treating migraine headaches. In particular, the triptan agonists of 5-HT_{1D} receptors have been found to be therapeutically effective. One of the possible mechanisms of action of this family of tryptamine-based drugs includes presynaptic inhibition of pain afferents from the meninges, preventing sensitization of central neurons. Drugs that block monoamine reuptake, including both traditional antidepressants and selective serotonin reuptake inhibitors, are effective in limiting pain in patients with chronic pain and migraine headaches.

Motor Activity Is Facilitated by Monoaminergic Pathways

The dopaminergic system is critical for normal motor performance. A massive projection ascends from the substantia nigra pars compacta to the striatum, where dopaminergic fibers act on striatal neuron receptors to release inhibition of motor responses (Chapter 38).

Patients with Parkinson disease in whom midbrain dopaminergic neurons have degenerated have trouble initiating movement and difficulty sustaining movements. Such patients speak softly, write with small letters, and take small steps. Conversely, drugs that facilitate dopaminergic transmission in the striatum can result in unintended behaviors, ranging from motor tics (small muscle twitches), to chorea (large-scale, jerky limb movements), to complex cognitive behaviors (such as compulsive gambling or sexual activity).

As first shown by Sten Grillner, serotonergic neurons play an important role in modulating motor programs. Drugs that activate serotonin receptors can induce hyperactivity, myoclonus, tremor, and rigidity, all of which are part of the "serotonin syndrome." Increases in the firing of raphe neurons have been observed in animals during repetitive motor activities such as feeding, grooming, locomotion, and deep breathing. Conversely, the firing of both serotonergic raphe and noradrenergic locus ceruleus neurons practically ceases during the atonia and lack of movement that occur during rapid eye movement (REM) sleep.

Noradrenergic cell groups in the pons also send extensive projections to motor cell groups. This modulatory input acts on presynaptic β- and α_1-adrenergic receptors to facilitate excitatory inputs to motor neurons (Chapter 31). The sum of these effects is to facilitate motor neuron responses in stereotypic and repetitive behaviors such as rhythmic chewing, swimming, or locomotion. Conversely, increased β-adrenergic activation during stress can exaggerate motor responses and produce tremor. Drugs that block β-adrenergic receptors are used clinically to reduce certain types of tremor and are often taken by musicians prior to performances to minimize tremulousness.

Ascending Monoaminergic Projections Modulate Forebrain Systems for Motivation and Reward

The forebrain is continuously bombarded with sensory information and must determine which stimuli deserve attention. It must also decide which of many available behaviors should receive priority, based in part on experience—which behaviors have achieved rewarding outcomes in the past. The ascending monoaminergic systems play key roles in modulating all of these choices.

As noted earlier, dopaminergic inputs to the striatum adjust the likelihood that a specific motor pattern or even a cognitive pattern will be expressed. Low dopamine levels reduce output from the direct pathway striatal neurons (which release behaviors) and increase activity of indirect pathway striatal neurons (which inhibit behavior). Dopamine also has been linked to reward-based learning. Rewards are objects or events for which an animal will work (Chapter 42) and are useful in positively reinforcing behavior. Activity of dopaminergic neurons increases when a reward (such as food or juice) is unexpectedly given. But after animals are trained to expect a reward following a conditioned stimulus, the activity of the neurons increases immediately after the conditioned stimulus rather than after the reward. This pattern of activity indicates that dopaminergic neurons provide a reward-prediction error signal, an important element in reinforcement learning. The importance of dopamine in learning is also supported by observations that lesions of dopaminergic systems prevent reward-based learning.

The same dopaminergic pathways that are important for reward and learning are involved in addiction to many drugs of abuse (Chapter 43)

Noradrenergic neurons of the locus ceruleus play an important role in attention. These neurons have a low baseline level of activity in drowsy monkeys. In alert, attentive monkeys the cells have two firing patterns. In the *phasic mode*, the baseline activity of the neurons is low to moderate, but there are bursts of firing just before the monkey responds to stimuli to which it has been attentive. This pattern of activity is thought to facilitate selective attention to a stimulus that is about to initiate a behavior. In contrast, in the *tonic mode*, the baseline level of activity is elevated and does not change in response to external stimuli. This mode of firing may promote the search for a new behavioral and attentional goal when the current task is no longer rewarding (Figure 40–14).

Many monoaminergic neurons also participate in regulating overall arousal (Figure 40–15). The noradrenergic locus ceruleus, serotonergic dorsal and median raphe nuclei, dopaminergic A10 neurons, and histaminergic tuberomammillary neurons innervate the thalamus, hypothalamus, basal forebrain, and cerebral cortex. All of these systems have the property of firing fastest during wakefulness, slowing down during slow wave (or non-REM) sleep, and grinding to a halt during REM sleep.

Stimulation of noradrenergic neurons in the locus ceruleus or histaminergic cells in the tuberomammillary nucleus increases electroencephalogram (EEG) arousal, indicating that these systems play an important role in cortical and behavioral arousal. However, lesions restricted to one or even a combination of monoaminergic cell groups do not cause profound loss of wakefulness, suggesting that the various cell groups

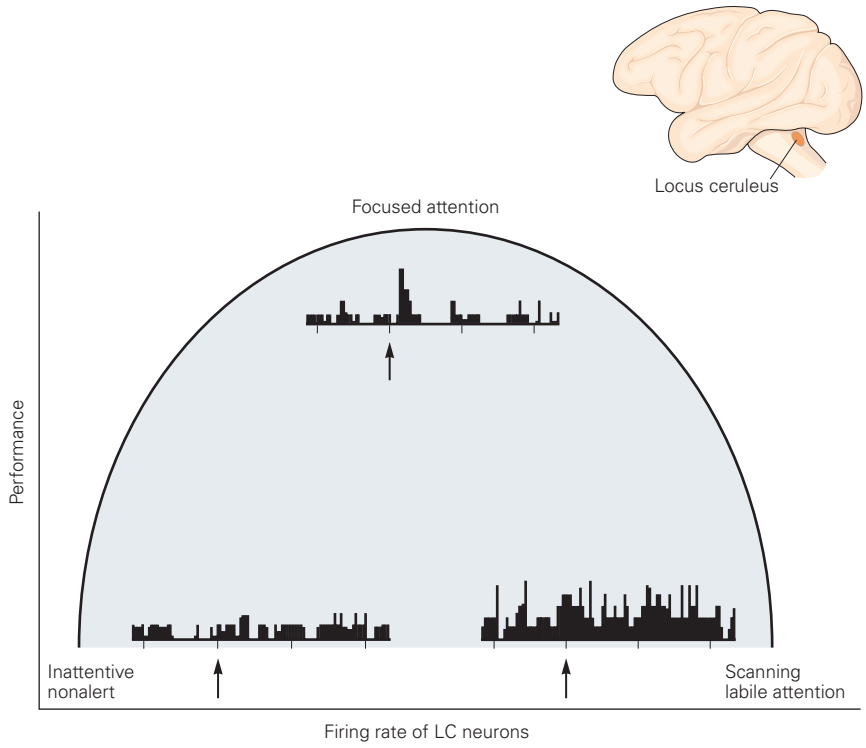

Figure 40–14 Locus ceruleus (LC) neurons exhibit different patterns of activity with different levels of attentiveness and task performance. The inverted U curve shows the relationship between a monkey's performance on a target detection task and the level of locus ceruleus activity. Histograms show the responses of LC neurons to presentation of the target during different levels of task performance. Performance is poor at low levels of LC activity because the animals are not alert. Performance is optimal when baseline activity is moderate and phasic activation follows presentation of the target. Performance is also poor when baseline activity is high because the higher baseline is incompatible with focusing on the assigned task. The tonic mode (with high baseline activity) might be optimal for tasks (or contexts) that require behavioral flexibility instead of focused attention. If so, the LC could regulate the balance between focused and flexible behavior. (Adapted, with permission, from Aston-Jones, Rajkowski, and Cohen 1999. Copyright © 1999 Society of Biological Psychiatry. Published by Elsevier Inc.)

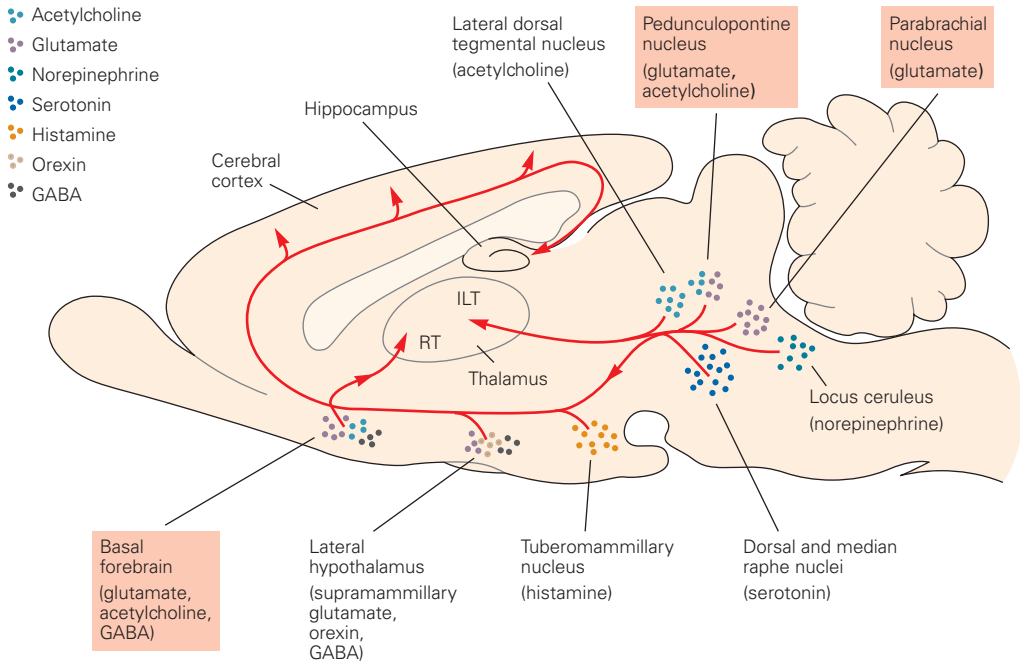

Figure 40–15 Major cell groups in the ascending arousal system. Neurons using the neurotransmitters norepinephrine, serotonin, dopamine, histamine, and acetylcholine have widespread forebrain projections. Although they all contribute to arousal by modulating various brain functions, ablation of any one of these cell groups has little effect on the waking state, suggesting that none of them are essential for maintaining a waking state. On the other hand, extensive damage to glutamatergic neurons in the parabrachial and pedunculopontine nuclei or to the GABAergic, glutamatergic, and cholinergic neurons in the basal forebrain (**orange boxes**) can cause a profound and prolonged coma. Thus, the parabrachial–pedunculopontine–basal forebrain–cortical pathway appears to be the only one that is essential to maintaining a waking state. (Abbreviations: **GABA**, γ-aminobutyric acid; **ILT**, intralaminar thalamic nuclei; **LC**, locus ceruleus; **RT**, reticular nucleus of the thalamus.)

probably have overlapping and at least partly redundant roles in sleep/wake regulation. The monoaminergic pathways modulate specific cellular properties of postsynaptic neurons in the thalamus and cerebral cortex, enhancing alertness and interaction with environmental stimuli.

Monoaminergic and Cholinergic Neurons Maintain Arousal by Modulating Forebrain Neurons

The monoaminergic and cholinergic neurons induce arousal by activating cortical neurons both directly and indirectly. They do this in part by modulating the activity of neurons in the brain stem, hypothalamus, basal forebrain, and thalamus that activate the cerebral cortex.

Both noradrenergic and serotonergic neurons innervate the parabrachial complex, a glutamatergic cell group that is critical for maintaining a waking forebrain. Noradrenergic inputs also activate histaminergic and orexin neurons in the lateral hypothalamus as well as cholinergic and GABAergic neurons in the basal forebrain, all of which project directly to the cerebral cortex. The parabrachial, histaminergic, orexin, and cholinergic basal forebrain neurons all excite cortical pyramidal cells, whereas the GABAergic basal forebrain neurons inhibit cortical inhibitory interneurons, thus disinhibiting the cortical pyramidal cells. The net effect of these inputs is to make the cortical pyramidal neurons more responsive to incoming sensory and cognitive inputs.

Parabrachial, noradrenergic, serotonergic, histaminergic, and cholinergic inputs also innervate the thalamus and modulate its ability to transmit sensory information to the cerebral cortex. Thalamic relay neurons fire in rhythmic bursts during sleep (Chapter 44) but fire single spikes related to incoming sensory stimuli during wakefulness. The firing pattern of thalamic and cortical neurons changes from burst mode to single-spike mode when the cells are depolarized following application of acetylcholine, norepinephrine,

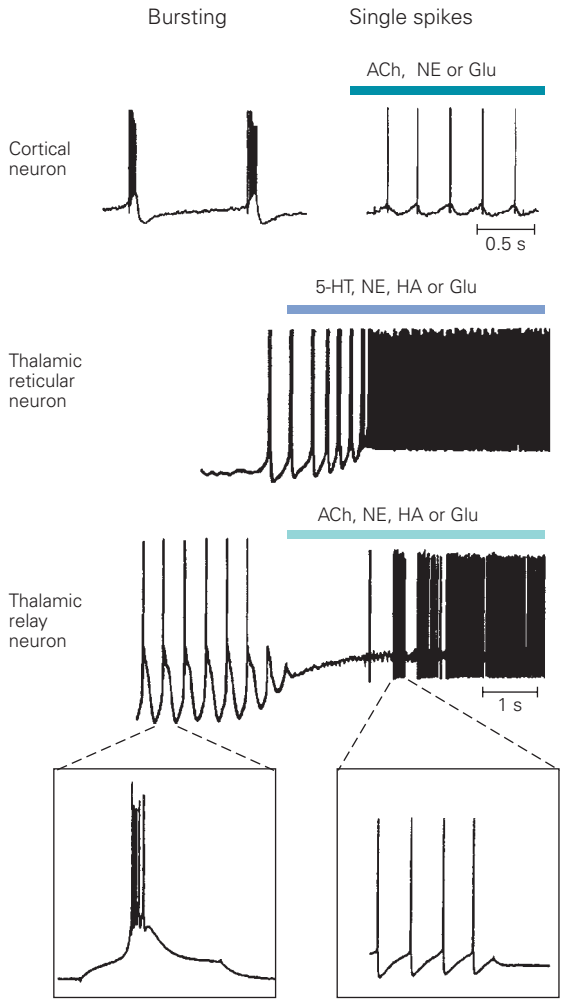

Figure 40–16 Monoaminergic and cholinergic systems modulate the activity of thalamic and cortical neurons to maintain arousal. The firing patterns of cortical and thalamic neurons are converted from burst mode to single-spike mode by the action of acetylcholine or monoamines. Recordings are from neurons in brain slices. Thalamic and cortical neurons have limited ability to convey information when firing in rhythmic bursts. However, when in single-spike mode, their firing activity reflects the inputs they receive. Therefore, the monoaminergic and cholinergic arousal systems keep open the lines of communication necessary for cortical information processing. (Reproduced, with permission, from Steriade, McCormick, and Sejnowski 1993. Copyright © 1993 AAAS.)

serotonin, or histamine (Figure 40–16). Thus, the monoaminergic neurons that participate in the ascending arousal system regulate cortical activity in part by altering the firing of thalamic neurons.

Many pharmacological agents that target monoaminergic and cholinergic systems influence arousal. For example, antihistamines cause drowsiness, serotonin reuptake blockers decrease the amount of REM sleep, and nicotine is a powerful stimulant. In addition, arousal is induced by amphetamines, cocaine, and other drugs that block dopamine reuptake; mice lacking the dopamine transporter are insensitive to such drugs.

Patients with Parkinson disease, who lose dopaminergic neurons in the substantia nigra, also lose noradrenergic neurons in the locus ceruleus and tend to be abnormally sleepy during the day. Some drugs used to treat Parkinson disease activate the D_2 dopamine receptor on presynaptic terminals of the remaining dopaminergic arousal neurons, which results in presynaptic inhibition, thus reducing dopamine release. As a result, although these drugs may make the movement disorder better (through their effects on postsynaptic D_2 receptors on neurons in the striatum), the inhibitory effect on remaining dopaminergic cells in the arousal system may exacerbate daytime sleepiness.

Highlights

1. The plan for the brain stem and the cranial nerves unfolds early in development, as neurons assemble into clusters that come, in time, to assume their functional organization. Building on the basic plan of the spinal cord, motor and sensory neurons concerned with the face, head, neck, and internal viscera form into discrete nuclei with specific functions and territories of innervation.
2. Neurons in the reticular formation surrounding these cranial nerve nuclei develop into ensembles of neurons that can generate patterns of autonomic and motor responses that subserve simple, stereotyped, coordinated functions, ranging from facial expression to feeding and breathing. These behavior patterns are sufficiently complex and flexible to represent the entire behavioral repertory of a newborn baby.
3. As the forebrain develops and exerts its control over these brain stem pattern generators, a variety of more complex responses and ultimately volitional control of behavior evolve.
4. Even a skilled actor, however, finds it difficult to produce the facial expressions associated with specific emotions unless he recreates the emotional states internally, thereby triggering the prepatterned facial expressions associated with those feeling states. Thus, some of the most complex human emotions and behaviors are played out unconsciously by means of stereotypic patterns of motor and autonomic responses in the brain stem.

5. The brain stem also contains a series of cell groups that have long-ranging and diffuse projections. Their targets range from the cognitive and behavioral systems in the cerebral cortex, to hypothalamic and brain stem autonomic control areas, to sensory and motor control systems in the spinal cord. Many of the neurons that participate in these modulatory systems, which set the tone for more specific sensory, motor, behavioral, and autonomic outputs, use monoamines as neuromodulators.
6. As a result of the diffuseness of these modulatory pathways and the multiplicity of receptors that they employ, a large portion of all central nervous system–active drugs act on these pathways. Unfortunately, many of the off-target effects of these drugs are due to the diffuseness of these pathways and their use of the same neurotransmitters and receptors at multiple locations. A challenge for the future of central nervous system pharmacology will be to develop drugs more highly selective for the targeted functions that require modulation.

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Selected Reading

Feldman JL, Del Negro CA, Gray PA. 2013. Understanding the rhythm of breathing: so near and yet so far. Ann Rev Physiol 75:423–452.

Gautron L, Elmquist JK, Williams KW. 2015. Neural control of energy balance: translating circuits to therapies. Cell 161:133–145.

Guyenet PG, Bayliss DA. 2015. Control of breathing and CO_2 homeostasis. Neuron 87:94–961.

Hodges MR, Richerson GB. 2010. Medullary serotonin neurons and their roles in central respiratory chemoreception. Respir Physiol Neurobiol 173:256–263.

Llorca-Torralba M, Borges G, Neto F, Mico JA, Berrocoso E. 2016. Noradrenergic locus coeruleus pathways in pain modulation. Neuroscience 338:93–113.

Plum F, Posner JB, Saper CB, Schiff ND. 2007. *Plum and Posner's Diagnosis of Stupor and Coma*, 4th ed. Philadelphia: Davis.

Saper CB. 2002. The central autonomic nervous system: conscious visceral perception and autonomic pattern generation. Annu Rev Neurosci 25:433–469.

Saper CB, Stornetta RL. 2014. Central autonomic system. In: G Paxinos (ed). *The Rat Nervous System*, 4th ed., pp. 627–671. San Diego: Elsevier.

Schultz W. 2016. Dopamine reward prediction-error signalling: a two-component response. Nat Rev Neurosci 17:183–195.

Sohn JW, Elmquist JK, Williams KW. 2013. Neuronal circuits that regulate feeding behaviour and metabolism. Trends Neurosci 36:504–512.

References

Aston-Jones G, Cohen JD. 2005. An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. Annu Rev Neurosci 28:403–450.

Aston-Jones G, Rajkowski J, Cohen J. 1999. Role of locus coeruleus in attention and behavioral flexibility. Biol Psychiatry 46:1309–1320.

Aston-Jones G, Bloom FE. 1981. Activity of norepinephrine-containing locus ceruleus neurons in behaving rats anticipates fluctuations in the sleep-wake cycle. J Neurosci 1:876–886.

Bieger D, Hopkins DA. 1987. Viscerotropic representation of the upper alimentary tract in the medulla oblongata in the rat: the nucleus ambiguus. J Comp Neurol 262:546–562.

Blessing WW, Li Y-W. 1989. Inhibitory vasomotor neurons in the caudal ventrolateral region of the medulla oblongata. Prog Brain Res 81:83–97.

Bouret S, Richmond BJ. 2015. Sensitivity of locus coeruleus neurons to reward value for goal-directed attention. J Neurosci 35:4005–4014.

Bradley SR, Pieribone VA, Wang W, Severson CA, Jacobs RA, Richerson GB. 2002. Chemosensitive serotonergic neurons are closely associated with large medullary arteries. Nat Neurosci 5:401–402.

Bruinstroop E, Cano G, Vanderhorst VG, et al. 2012. Spinal projections of the A5, A6 (locus coeruleus), and A7 noradrenergic cell groups in rats. J Comp Neurol 520:1985–2001.

Chang RB, Strochlic DE, Williams EK, Umans BD, Liberles SD. 2015. Vagal sensory neuron subtypes that differentially control breathing. Cell 161:622–633.

Filiano JJ, Kinney HC. 1994. A perspective on neuropathologic findings in victims of the sudden infant death syndrome: the triple-risk model. Biol Neonate 65:194–197.

Gray PA, Janczewski WA, Mellen N, McCrimmon DR, Feldman JL. 2001. Normal breathing requires pre-Bötzinger complex neurokinin-1 receptor-expressing neurons. Nat Neurosci 4:927–930.

Grunstein RR, Sullivan CE. 1990. Neural control of respiration during sleep. In: MJ Thorpy (ed). *Handbook of Sleep Disorders*. New York: Marcel Dekker.

Jenny AB, Saper CB. 1987. Organization of the facial nucleus and cortico-facial projection in the monkey: a reconsideration of the upper motor neuron facial palsy. Neurol 37:930–939.

Lahiri S, Maret K, Sherpa M, Peters R Jr. 1984. Sleep and periodic breathing at high altitude: Sherpa natives vs. sojourners. In: J West, S lahiri (eds). *High Altitude and Man*, pp. 73–90. Bethesda: American Physiological Society.

Morecraft RJ, Louie JL, Herrick JL, Stilwell-Morecraft KS. 2001. Cortical innervation of the facial nucleus in the non-human primate: a new interpretation of the effects of

stroke and related subtotal brain trauma on the muscles of facial expression. Brain 124(Pt 1):176–208.

Mulkey DK, Stornetta RL, Weston MC, et al. 2004. Respiratory control by ventral surface chemoreceptor neurons in rats. Nat Neurosci 7:1360–1369.

Nielson M, Smith H. 1952. Studies on the regulation of respiration in acute hypoxia; with an appendix on respiratory control during prolonged hypoxia. Acta Physiol Scan 24:293–313.

Richerson GB. 2004. Serotonergic neurons as carbon dioxide sensors that maintain pH homeostasis. Nat Rev Neurosci 5:449–461.

Richerson GB, Getting PA. 1987. Maintenance of complex neural function during perfusion of the mammalian brain. Brain Res 409:128–132.

Rinaman L, Card JP, Schwaber JS, Miselis RR. 1989. Ultrastructural demonstration of a gastric monosynaptic vagal circuit in the nucleus of the solitary tract in rat. J Neurosci 9:1985–1996.

Smith JC, Ellenberger HH, Ballanyi K, Richter DW, Feldman JL. 1991. Pre-Bötzinger complex: a brain stem region that may generate respiratory rhythm in mammals. Science 254:726–729.

Steriade M, McCormick DA, Sejnowski TJ. 1993. Thalamocortical oscillations in the sleeping and aroused brain. Science 262:679–685.

Wang W, Bradley SR, Richerson GB. 2002. Quantification of the response of rat medullary raphe neurons to independent change in pH and PCO_2. J Physiol 540:951–970.

Williams EK, Chang RB, Strochlic DE, Umans BE, Lowell BB, Liberles SD. 2016. Sensory neurons that detect stretch and nutrients in the digestive system. Cell 166:209–221.

41

The Hypothalamus: Autonomic, Hormonal, and Behavioral Control of Survival

THE SURVIVAL OF AN INDIVIDUAL requires tight control of body temperature, water balance, and blood pressure, together with sufficient food intake and appropriate regulation of sleep/wakefulness

cycles. Survival of a species requires that individuals be fertile, mate, and nurture their offspring, and that aggression toward others be appropriate and adaptive. Neurons in the hypothalamus control all of these key survival activities.

As we shall learn in this chapter, the hypothalamus together with interconnected areas of the brain responds to bodily and emotional challenges by recruiting appropriate behavioral and physiological responses. Coordination of these activities ensures constancy of the internal environment, a process known as homeostasis. The hypothalamus acts on three major systems: the autonomic motor system, the neuroendocrine system, and neural pathways that mediate motivated behavior.

The autonomic motor system is distinct from the somatic motor system, which controls skeletal muscle. Whereas somatic motor neurons regulate contractions of striated muscles (Chapter 31), autonomic motor neurons regulate blood vessels, the heart, the skin, and visceral organs through synapses upon smooth and cardiac muscle cells, upon glands cells that serve endocrine and exocrine functions, and upon metabolic targets such as adipocytes. The neuroendocrine system works differently, by secreting several peptide hormones from the pituitary, the "master gland," located just beneath the hypothalamus. These pituitary hormones control water retention by the kidney, parturition, lactation, somatic growth, gamete development, and also the release of nonpeptide hormones from three downstream glands—the gonads, adrenal cortex, and thyroid.

Although largely involuntary, autonomic and neuroendocrine responses are tightly integrated with voluntary behavior executed by the somatic motor system. Running, climbing, and lifting exemplify voluntary actions that have metabolic, cardiovascular, and thermoregulatory consequences. These needs are automatically met by the autonomic and neuroendocrine systems through changes in cardiorespiratory drive, cardiac output, regional blood flow, heat dissipation, and fuel mobilization. Such compensatory changes are implemented primarily by feedforward central commands, supplemented by reflexes activated by sensory feedback. Similarly, emotional states evoke autonomic and neuroendocrine responses. Feelings of fear, anger, happiness, and sadness have characteristic autonomic and hormonal manifestations.

In this chapter, we first explore the concept of homeostasis and the general means by which it is achieved. We then discuss the anatomical and functional organization of the hypothalamus and its two "involuntary" motor arms—the autonomic and neuroendocrine systems. After that, we focus in depth on three classic examples of hypothalamic homeostatic control—regulation of body temperature, of water balance and its related deficiency drive, thirst, and of energy balance and its drive, hunger. We conclude by examining sexually dimorphic regions of the hypothalamus and their role in regulating sexual behavior, aggression, and parenting. Additional discussion of sleep cycles and regulation of circadian rhythms can be found in Chapter 44.

Homeostasis Keeps Physiological Parameters Within a Narrow Range and Is Essential for Survival

In the mid-19th century, the French physiologist and founder of experimental medicine Claude Bernard drew attention to the stability of the body's internal environment over a broad range of behavioral states and external conditions. "The internal environment (*le milieu interior*)," he wrote, "is a necessary condition for a free life." Building on this idea, in the 1930s, the American physiologist Walter B. Cannon introduced the concept of homeostasis to describe the mechanisms that maintain the constancy of composition of the bodily fluids, body temperature, blood pressure, and other physiological variables—all of which are necessary for survival.

Homeostatic mechanisms are highly adaptive because they greatly extend the range of conditions that can be tolerated. For example, during exercise, many parameters can increase dramatically—cardiac output by 4- to 5-fold, oxygen and fuel consumption by 5- to 10-fold, and heat production to a similar degree. In the absence of compensatory responses, blood pressure would increase in proportion to cardiac output, rupturing blood vessels; circulating fuels would fall to critically low levels, starving cells of energy; and hyperthermia would denature cell proteins. Indeed, the capacity of homeostasis is remarkable, making it possible for animals to survive at high latitudes where seasonal temperatures can fluctuate by 70°C and for humans to run 251 km in the sands of the extremely hot Sahara Desert (Marathon des Sables). Homeostatic mechanisms greatly extend the range of habitats, activities, and traumas that can be survived.

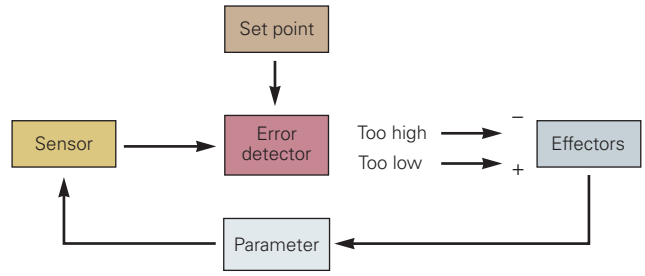
Homeostasis requires negative sensory feedback from the body. The concept of feedback loops evolved from the discovery of sensors that detect critical physiological variables and then couple them with behavioral, autonomic, and neuroendocrine motor outputs. Drawing upon the engineering principle of negative feedback control, this led to the concept that

physiological "set points" help control key parameters like body temperature, blood osmolarity, blood pressure, and body fat content.

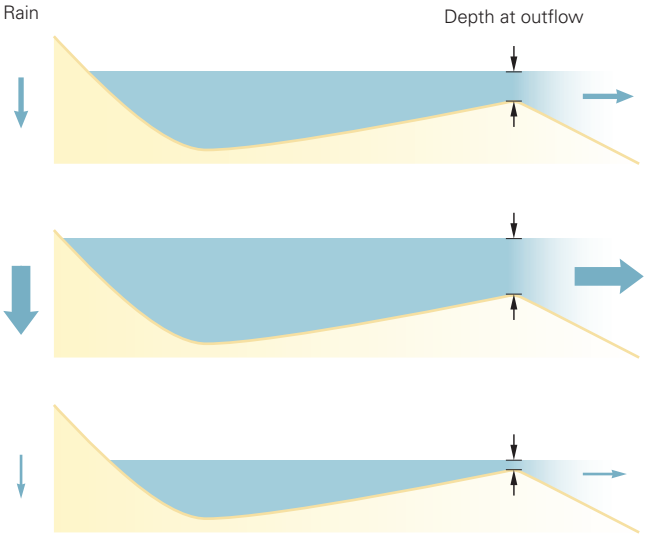
Set point models are appealing because thermostats are so effective in maintaining room temperature at a targeted set point and, by analogy, physiological variables like body temperature are likewise tightly controlled. In such models, a "set point" exists for a parameter, 37°C in the case of body temperature, and at any given moment, the real level of the parameter is assessed and compared with the targeted set point through feedback and error detection (Figure 41–1A). Any deviation above or below triggers counteracting corrective responses—if too hot, cutaneous vasodilatation, sweating, and a dip in the pool; if too cold, vasoconstriction, thermogenesis, shivering, and the donning of a sweater. For regulation of body temperature, the set point and detection of error were historically seen as emergent properties of neurons in the preoptic area of the hypothalamus (POA).

Over time, the set point model required revision because intensive investigation failed to uncover any molecular or neuronal bases for encoding set points and performing error detection. In addition, "set point–like" regulation can, in principle, be achieved without a set point, feedback, or error detection—the so-called "settling point" model (Figure 41–1B). Consider the changing level of a lake. When rainfall is excessive, its level rises; the rivers draining the lake rise and their flow increases. The converse is true when rainfall is low. The changing flow of the rivers draining the lake thus maintains its level near a settling point without requiring an idealized set point, feedback, or error detection. While aspects of the settling point model have appeal, it too is incomplete because homeostatic processes clearly receive important feedback

A Set point model



B Settling point model



C Combined model: settling point of multiple afferent/efferent loops

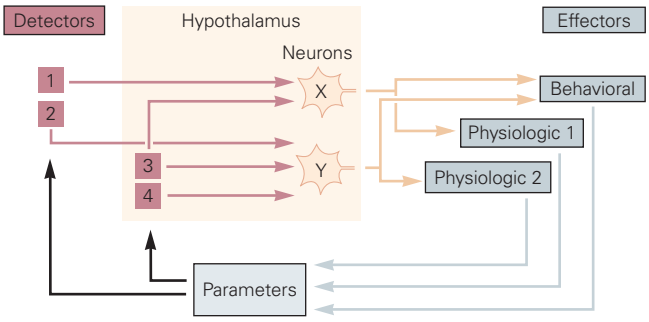


Figure 41–1 (Left) Set points, settling points, and homeostasis.

A. The set point view was inspired by engineering principles. As with a thermostat, constancy is achieved by providing feedback on the existing level of a parameter, determining how it compares to an idealized set point, and then instituting corrective measures to return the parameter to the set point. While popular for many years, it has fallen out of favor as years of research have failed to uncover molecular and neural bases for encoding set points and performing error detection.

B. The settling point model was inspired by observations that many systems achieve constancy in the absence of any feedback or error detection. In this example, the level of outflow of water from a lake is proportional to the depth of the lake. When it rains, the increase or decrease in the level of the lake causes more or less water to flow out of the lake. The level of the lake remains fairly constant without a set point or error detection. A related example is regulation of body weight. Increased food intake leads to increased body weight. As body weight increases, the energy cost of carrying and sustaining that increased weight goes up. Because of this, body weight too should have its settling point. (Reproduced, with permission, from Speakman et al. 2011.)

C. In this model the concepts of feedback in part **A** and settling point in part **B** are combined. The apparent set point is in fact the settling point, an emergent property of multiple feedback-informed afferent/efferent loops.