Chemical Control of the Brain and Behavior

Introduction

Most of the connections of the nervous system are precise and specific. Think about the precise organization of the sensory and motor systems. At the points of connection of those neurons chemical communication is usually restricted to individual synapses. However, some neurons are able to communicate with a remarkably large number of widespread neurons. These include:

- The secretory hypothalamus
- The autonomic nervous system
- The diffuse modulatory systems of the brain

The Secretory Hypothalamus

The hypothalamus and dorsal thalamus are adjacent to one another. The dorsal thalamus is in the path of the point-to-point sensory and motor connections with the neocortex. In contrast the hypothalamus integrates somatic and visceral responses in accordance with the needs of the brain and body.

Structure and Connections of the Hypothalamus

- The hypothalamus has three functional zones: lateral, medial and periventricular.
- The periventricular zone lies right next to the third ventricle.
    - One group of cells, the suprachiasmatic nucleus, receives signals from optic tract and synchronizes circadian rhythms with the light-dark cycle.
    - A second group of cells control the sympathetic and parasympathetic innervation of the visceral organs.
    - A third group of cells, neurosecretory cells, extend their axons down toward the pituitary gland

Pathways to the Pituitary

- The pituitary is held in the sphenoid bone at the base of the skull.
- The pituitary provides a major avenue for the hypothalamus to communicate with the body.
- The pituitary is separated into two lobes, each controlled in different ways.

Hypothalamic Control of the Posterior Pituitary

- The posterior lobe of the pituitary is really part of the brain.
- Magnocellular neurosecretory cells of the hypothalamus extend axons down the stalk of the pituitary and into the posterior lobe.

- These neurons secrete chemical messengers into blood capillaries of the posterior lobe.
- The Magnocellular neurons secrete two hormones into the blood: oxytocin and vasopressin.
    - Oxytocin stimulates uterine contraction and milk ejection.
    - Vasopressin stimulates water retention by the kidney and constriction of blood vessels.

Hypothalamic Control of the Anterior Pituitary

- The anterior lobe of the pituitary is an actual gland and <u>not</u> part of the brain.
- The cells of the anterior lobe synthesize and secrete a wide range of hormones that in turn regulate the secretions of other endocrine glands.
- Parvocellular neurosecretory cells of the hypothalamus extend axons only into the <u>upper part</u> of the stalk of the pituitary.
    - A specialized capillary bed is located at the floor of the third ventricle.
    - Tiny blood vessels run from these capillaries down the pituitary stalk and into the anterior lobe.
    - This network of blood vessels is called the pituitary portal circulation.
- The Parvocellular neurons secrete about seven different hormones into the pituitary portal circulation.
    - These hormones are collectively called hypophysiotropic hormones (or hypothalamic regulatory hormones).
- Cells in the anterior lobe respond to the hypophysiotropic hormones which controls the production of about six different anterior pituitary hormones.

The Stress Response

- The stress response of the adrenal gland is a good illustration of how the hypothalamus and anterior pituitary work.
    - A physical or psychological stress excites hypothalamic parvocellular neurons that secrete corticotropin releasing hormone (CRH) into the pituitary portal circulation.
    - In the anterior lobe the CRH stimulates the release of corticotropin (aka adrenocorticotropic hormone (ACTH)) into the circulation.
    - In the adrenal gland corticotropin stimulates the release of cortisol (aka hydrocortisone).
    - Cortisol acts on numerous cells in the brain and body.
        - In the hypothalamus cortisol dampens production of CRH.
        - In hippocampus cortisol induces degeneration.
        - In the body cortisol modifies cellular metabolism (decreases glucose uptake and increases lipolysis) and suppresses the immune system.

The Autonomic Nervous System

The autonomic nervous system (ANS) is a widespread interconnected network of neurons that control our internal organs. Sometimes the ANS is called the visceral nervous system.

ANS Circuits

- The somatic motor system innervates and controls skeletal muscle cells.
    - Innervation involves a monosynaptic pathway
    - The cell body of a somatic motor neuron is in the CNS and the axon of that neuron innervates the muscle cell
- The visceral nervous system innervates and controls every other tissue and organ in the body; especially cardiac muscle cells, smooth muscle cells, and glands.
    - Innervation involves a disynaptic pathway
    - The cell body of one neuron is in the CNS (Preganglionic neuron) and the cell body of a second neuron is outside of the CNS (Postganglionic neuron)
    - The axon of the preganglionic neuron innervates the postganglionic neuron whose cell body is in an autonomic ganglion in the peripheral nervous system.
    - The axon of the postganglionic neuron innervates the muscle cell.

Sympathetic and Parasympathetic Divisions

- Sympathetic preganglionic axons emerge mainly from thoracic and some lumbar spinal cord.
    - The sympathetic division mainly controls responses of organs needed during physical activity.
- Parasympathetic preganglionic axons emerge mainly from the brain stem and from sacral spinal cord.
    - The parasympathetic division mainly controls responses of organs needed during resting and eating.
- Visceral innervation
    - Secretory glands
    - Heart and blood vessels
    - Bronchi of lungs
    - Gastrointestinal tract
    - Kidney and bladder
    - Reproductive organs

The Enteric Divisions

- Networks of sensory neurons, interneurons, and motor neurons imbedded in the walls of the gastrointestinal tract and related organs.
- Control many of the physiological processes involved in transport and digestion of food.
- Controlled by the parasympathetic and sympathetic divsions.

Central Control of the ANS

- The hypothalamus and various brain stem structures connect to sympathetic and parasympathetic preganglionic neurons.
- The hypothalamus and various brain stem structures receive visceral sensory information from the nucleus of the solitary tract in the medulla.

Neurotransmitters and Pharmacology of Autonomic Function

Preganglionic Neurotransmitters

- Sympathetic preganglionic axons secrete acetylcholine that acts on nicotinic receptors of the postganglionic dendrites.
- Parasympathetic preganglionic axons secrete acetylcholine that acts on nicotinic receptors of the postganglionic dendrites.

Postganglionic Neurotransmitters

- Sympathetic postganglionic axons secrete norepinephrine that acts on adrenergic alpha or beta receptors of the target organs.
- Parasympathetic postganglionic axons secrete acetylcholine that acts on muscarinic receptors of the target organs.

The Diffuse Modulatory System of the Brain

The diffuse modulatory systems provide messages that must be received by broad regions of the brain. The cells in these systems perform regulatory functions; modulating vast assemblies of postsynaptic neurons especially in the cerebral cortex, thalamus and spinal cord, making them more or less excitable. Different systems seem to be essential for aspects of motor control, memory, mood, motivation, and metabolic rate.

Anatomy and Functions of the Diffuse Modulatory Systems

- Each system has a small set of neurons.
- Neurons of the diffuse systems arise from the central core of the brain, especially the brain stem.
- Each neuron can influence many other neurons; each axon can synapse with 10,000 or more neurons.
- The synapses made by many of these neurons release their neurotransmitters into the extracellular fluid as well as into synaptic clefts.

The Noradrenergic Locus Coeruleus

- The noradrenergic locus coeruleus consist of two nuclei near the anterior edges of the fourth ventricle. There are about 12,000 cells in each nucleus.
- Axons innervate just about every part of the brain: all of the cerebral cortex, the thalamus and hypothalamus, the olfactory bulb, the cerebellum, the midbrain, and the spinal cord.
- A single neuron can make more than 250,000 synapses.

- Neurons of the locus coeruleus seem to be involved in the regulation of attention, arousal, sleep wake cycles, learning and memory, anxiety and pain, mood, and brain metabolism.
- Neurons of the locus coeruleus are best activated by new, unexpected, non-painful sensory stimuli.
- The locus coeruleus may function to increase brain responsiveness, speeding information processing by the sensory and motor systems.

The Serotonergic Raphe Nuclei

- The serotoninergic raphe nuclei are located in several areas of the midline of the brain stem.
- Those more caudal innervate the spinal cord where they modulate pain related sensory signals.
- Those more rostral innervate most of the brain in much the same diffuse way as do the locus coeruleus neurons.
- Neurons of the raphe nuclei are most active during behavioral arousal and activity; and most quiet during sleep.
- The raphe nuclei may be involved in sleep-wake cycles, and in mood and certain emotional behaviors.

The Dopaminergic Substantia Nigra and Ventral Tegmental Area

- The dopamine neurons in the substantia nigra of the midbrain synapse with neurons in the caudate nucleus and putamen and facilitate the initiation of voluntary movement.
- Degeneration of these neurons produces Parkinson’s disease.
- The dopamine neurons in the ventral tegmental area of the midbrain synapse with a circumscribed area of the frontal cortex and parts of the limbic system (mesolimbic dopamine system).
- These later neurons are implicated in a “reward” system that somehow assigns value to, or reinforces, certain behaviors

The Cholinergic Basal Forebrain and Brain Stem Complexes

- The cholinergic neurons in the basal forebrain complex include the medial septal nuclei which innervate the hippocampus; and the basal nucleus of Meynert which innervates the neocortex.
- Neurons in the basal forebrain complex are the first to die in Alzheimer’s disease.
- These neurons are implicated in regulating general excitability during arousal and sleep-wake cycles, and may play a special role in learning and memory formation.
- The cholinergic neurons in the pontomesencephalotegmental complex act mainly on the dorsal thalamus, where, together with the noradrenergic and serotonergic systems, regulate the excitability of the sensory relay nuclei.

Drugs and the Diffuse Modulatory Systems

Hallucinogens

- LSD is a potent agonist at serotonin receptors on the presynaptic terminals of neurons in the raphe nuclei.
- (LSD reduces the outflow of the serotonergic diffuse modulatory system.)

Stimulants

- Cocaine and amphetamine exert their effects at synapses of dopaminergic and adrenergic systems.
- Cocaine and amphetamine inhibit reuptake of dopamine and norepinephrine.