

See topic and resource outline for required reading etc. Additional information for this unit is taken from:

Donatelle, R.J. Access to Health 8/e. 2004, Benjamin Cummings  
The American Academy of Neurology, Practice Parameters: Assessment and Management of Patients in the Persistent Vegetative State  
([http://www.aan.com/professionals/practice/pdfs/pdf\\_1995\\_thru\\_1998/1995.45.1015.pdf](http://www.aan.com/professionals/practice/pdfs/pdf_1995_thru_1998/1995.45.1015.pdf)) and  
Certain Aspects of the Care and Management of the Persistent Vegetative State Patient (<http://www.aan.com/about/ethics/109556.pdf>)

- I. The nervous system is ultimately responsible for keeping us alive by coordinating all of our physiological processes and maintaining homeostasis. For many, the brain is the seat of our humanity – it generates our thoughts, emotions, motivations, and behaviors. In this unit we'll introduce the nervous system by examining the following topics:
  - A. Essential anatomy and physiology I: structure/function at the cellular level
  - B. Application I: neurotoxins
  - C. Essential anatomy and physiology II: Hierarchical organization and homeostasis
  - D. Essential anatomy and physiology III: Brain structure and function
  - E. Application II:
    1. Persistent vegetative state
    2. Drugs of abuse
    3. Other brain disorders
  - F. Application II: drugs and brain disorders
- II. The nervous system processes information
  - A. Information processing relies on 3 interrelated tasks/functions:
    1. **Sensory input**
      - a. receive information from internal/external environment via sensory systems
      - b. conduct sensory input to processing center
    2. **Integration**
      - a. combine information from all sensory systems

- b. interpret using existing information + information from experience
  - c. formulate response
  - 3. **Motor output**
    - a. conduct response to effectors = muscles, glands that perform the response
  - 4. To function properly as whole organisms, we rely on our nervous systems to maintain all 3 activities continuously, with constant feedback to monitor, fine-tune our activities (conscious & unconscious)
- B. Essential vocabulary for understanding the structure/function of the nervous system:
- 1. The two major divisions of the nervous system (we'll discuss subdivisions of each later) are
    - a. the **central nervous system = CNS**
      - (1) anatomically = brain, spinal cord
      - (2) functionally = integration centers (mostly) = where sensory information is processed and responses "decided"
    - b. the **peripheral nervous system = PNS**
      - (1) anatomically = nerves connecting CNS to muscles, glands, and sensory organs
      - (2) functionally = carry information to/from CNS:
        - (a) carry information/signals from sensory systems to CNS
        - (b) carry motor responses from CNS to muscles/glands
  - 2. Three types of information-carrying cells correspond to the three basic tasks/functions of the nervous system:
    - a. individual information-carrying cell = **neuron**
    - b. 3 basic types
      - (1) **sensory neurons** carry information from sensory organs to CNS (part of PNS)

- (2) **motor neurons** carry information from CNS to muscles/glands (part of PNS)
  - (3) **interneurons** integrate information, relay appropriate responses (part of CNS)
  - c. 3 types of neurons are organized to create a one-way flow of information: stimulus = information from the environment -> sensory receptor -> **sensory neuron** -> **interneuron** (in “decision-making center”) -> **motor neuron** -> effector (muscle or gland)
3. **Nerves** = bundles of neurons wrapped in connective tissue
- a. individual nerves contain both sensory and motor neurons
  - b. branch out through the body ~ like blood vessels: large where they exit/enter the spinal cord/brain, then branching into smaller & smaller bundles as they penetrate body tissues
  - c. result =
    - (1) complex network of sensory neurons constantly monitoring internal, external environment
    - (2) responses of muscles/glands can be very precisely controlled – note that this is important for both
      - (a) maintaining homeostasis
      - (b) performing other critical “life tasks” (finding food, mating, escaping predators, etc.)
- III. Neurons are the functional units of the nervous system – understanding their basic structure/function helps us understand how the whole system works
- A. Essential anatomy: neurons vary in size, shape, but all share same basic structural plan:
- 1. large **cell body** houses nucleus, other critical cellular organelles; this is usually found at one end of the neuron
  - 2. **dendrites**

- a. = numerous, branching fiber-like extensions of the cell branching off the cell body
  - b. function = receive information (from sensory cell, interneuron)
3. **axon**
- a. single long extension of the cell
  - b. function = conduct information to interneuron, effector (muscle/gland)
  - c. many axons are wrapped in fatty “insulating” material called **myelin**, but not continuously – gaps are important for conducting nerve signals
4. axons end in a cluster of branches, each ending in a **synaptic knob**;  
function = transmit information to another neuron or to an effector
- B. Neurons conduct information using a combination of electrical & chemical signals
1. Electrical signals called **action potentials** (AP’s) transmit information along the neuron
    - a. flow of information is always one way: dendrite -> axon -> synaptic knob
    - b. AP’s are generated, propagated, via carefully regulated movement of charged atoms (ions) across the neuron cell membrane.
      - (1) The critical ions are **sodium, calcium, potassium, and chloride**; these are also called **electrolytes**
      - (2) Muscle cells also use AP’s – but they use them to initiate contraction
      - (3) This is why electrolyte imbalance (following, e.g., dehydration) is potentially deadly – we need proper balance for our nerves and muscles to work properly
      - (4) restoration of electrolytes was reason behind “invention” of Gatorade!
    - c. Fatty insulation allows AP’s to be propagated very quickly. In humans, AP’s can travel

- (1) 150 m/sec = 330 mi/hr with insulation: signal from brain to finger in few milliseconds
- (2) 5 m/sec without insulation = much slower response time!
- d. Neurons can generate electrical signals of different intensity by varying AP frequency
  - (1) “strong” signal = high AP frequency; “weak” signal = low AP frequency
  - (2) This is very important for precise, flexible information processing – it means we can “recognize” sensory input of different intensity & can generate different intensities of response as appropriate
2. Chemical signals transmit information from neuron to neuron (and often from neuron to effector – e.g., motor neuron to muscle cell)
  - a. Neurons “connect” at junctions called **synapses**
  - b. Structurally, the synapse consists of
    - (1) a **synaptic knob** of the “sending” neuron
    - (2) a physical, fluid-filled gap called the **synaptic cleft**
    - (3) a portion of membrane along a dendrite of the “receiving” neuron called the **post-synaptic membrane**
  - c. Signals are conducted across the synaptic cleft via specialized molecules called **neurotransmitters**
    - (1) some familiar ones might be norepinephrine, serotonin, dopamine
    - (2) neurotransmitters (mostly proteins) are stored in vesicles in the synaptic knob (question: where in the cell are these made and how do they get into the vesicles?)
  - d. Process of transmission:
    - (1) AP reaches synaptic knob
    - (2) AP’s trigger a complex series of chemical responses that result in vesicles dumping their neurotransmitter into the synaptic cleft (the

- stronger the signal, the more vesicles dump neurotransmitter)
- (3) Neurotransmitters migrate across the synaptic cleft and bind with specialized protein **receptors** on the membrane of the receiving neuron
    - (a) note: receptors are shape-specific: they only respond when a chemical of the right shape binds to them
  - (4) Once a neurotransmitter binds to its receptor, the receptor changes its shape, allowing ions to move across the cell membrane
    - (a) which ions, and which way they move, vary from synapse to synapse
  - (5) The movement of ions across the dendrite membrane will have one of two effects, depending on which ions are involved.
    - (a) **Excitation**: the “receiving” neuron will generate AP’s
    - (b) **Inhibition**: the “receiving” neuron will be prevented from generating AP’s
  - (6) The activity of the neurotransmitters is limited – one of two mechanisms will remove them and stop their effects
    - (a) specific enzymes break the neurotransmitters down
    - (b) specific carrier molecules grab the neurotransmitters and transport them back into the synaptic knob
3. Chemical synapses are structurally and functionally complex, which allows complex information processing
- a. “Receiving” neurons may synapse with hundreds of different neurons via thousands of synaptic knobs
  - b. Each of those “sending” neurons may be sending different kinds of signals
    - (1) some excitatory, some inhibitory
    - (2) some strong, some weak (in both categories)

- c. Ultimately, the signal the “receiving” neuron transmits represents a response to the summation or “average” of all the signals it receives
- C. **Application I: Neurotoxins** work by interfering with either the electrical or chemical signals of the nervous system – a few examples
1. Japanese pufferfish (fugu) venom
    - a. strongly blocks sodium movement across axon membranes, preventing AP’s from being propagated – paralyzes nerves, muscles
    - b. actually synthesized by mutualistic bacterium
    - c. Fugu is immune
  2. Paralytic shellfish poisoning is caused by a neurotoxin that acts in the same way, but not as strong
    - a. manufactured by bacterial mutualist of marine phytoplankton (“red tide” organism)
    - b. shellfish eat phytoplankton during “red tides”, accumulate toxin in own tissues
    - c. humans affected when we eat the shellfish
  3. Black widow spider venom
    - a. causes massive release of excitatory neurotransmitters from motor neurons to muscles – tetanic paralysis
    - b. fortunately, although toxin is extremely potent, a single bite delivers very little of it!
  4. Mojave rattlesnake venom does the opposite
    - a. prevents the release of excitatory neurotransmitters from motor neurons to muscles – flaccid paralysis
    - b. canebrake rattlesnakes may have similar venom
    - c. fortunately, rattlesnakes are usually pretty timid & give plenty of warning!
  5. Military nerve gas prevents the breakdown of the neurotransmitter that stimulates skeletal muscle & the smooth muscle of many of the body’s organs – so the neurotransmitter remains in the synaptic cleft & bound to

receptors

- a. symptoms include convulsions as well as constricted pupils, uncontrollable salivation, urination, defecation
- b. treated with atropine, which binds to the same receptors and prevents them from being stimulated (of course, this is also a problem because it keeps the neurotransmitter from doing its normal job!)

IV. The nervous system as a whole is hierarchically organized, which allows complex integration & regulation. Structurally and functionally, the system is divided into these components:

A. The **CNS** = brain + spinal cord: integrates information & generates responses

B. The **PNS** receives information from the internal & external environment, sends it to the CNS, and transmits responses to muscles & glands. It has two subdivisions:

1. **somatic**: nerves carry signals to/from **skeletal muscles, tendons, & skin** (these are mostly under voluntary control, but not entirely)
2. **autonomic**: nerves carry signals to/from the **smooth muscles & glands of internal organs** (e.g., gut, heart, adrenal glands, etc.) – these are mostly under involuntary control, but not entirely. The autonomic system is further divided into “opposing” elements that tend to balance one another:
  - a. **parasympathetic nerves** generate “**rest & digest**” signals: they stimulate the digestive organs & glands associated with them, while inhibiting activities associated with exercise – goal is conservation of energy
  - b. **sympathetic nerves** generate “**fight or flight**” responses: they stimulate the heart, lungs, and muscles to get them ready for rapid movement; at the same time, they inhibit the digestive organs & glands

C. Note that much of maintaining homeostasis involves balancing sympathetic & parasympathetic input to various body organs

1. Most organs receive input from both units

2. Opposing signals adjust activity to appropriate levels
  3. Changing stimuli changes the balance of inputs, leading to changes in activity levels
  4. Even our thoughts can be stimuli:
    - a. Thinking of favorite food increases parasympathetic activity, leading to increase in salivation & stomach contraction.
    - b. Thinking of an important test or performance increases sympathetic activity, leading to an increase in heart, breathing rate
- V. The brain is the supercomputer that controls everything
- A. The brain is protected physically and chemically
1. housed in bony box = **skull**
  2. further protected by tough layers of tissues collectively called the **meninges** (literally, “membranes”; these also surround the spinal cord; **meningitis** = inflammation of these tissues)
  3. floats on & is surrounded by a cushion of fluid = **cerebrospinal fluid**
    - a. floats on fluid in internal chambers called ventricles
    - b. another layer of the fluid creates a cushion between two layers of the meninges
  4. The **blood-brain barrier** keeps microbes & toxins from leaving the plasma and entering the interstitial fluid of the brain
    - a. The term “blood-brain barrier” refers to the fact that the capillary beds supplying the brain with oxygen and nutrients restrict the movement of dissolved materials into the brain tissue much more tightly than they do in other parts of the body
    - b. two related mechanisms create the barrier:
      - (1) cells making up capillary walls are very tightly joined together, so nothing leaks between them –
        - (a) the only way out is across the cell membranes

- (b) cell membranes have mechanisms that allow them to screen molecules and to be very selective about what moves across them
  - (2) specialized nervous tissue cells have “feet” that wrap around the capillaries, helping to restrict the movement of materials out of the plasma into the interstitial fluid of the brain
  - c. the “weak spot” in the blood-brain barrier is the fact that small, lipid-soluble chemicals – like alcohol and the active ingredients of psychoactive drugs, e.g., can freely cross the capillary cell membranes into the brain
- B. Regions of the brain work together to receive & process information
1. The **brainstem** begins where the spinal cord enters the skull; its main functions are to
    - a. filter sensory information (decides what gets sent to “higher” brain centers)
    - b. regulate sleep & arousal
    - c. control critical functions of breathing, circulation, swallowing, digestion
    - d. the brainstem remains functional (in whole or in part) in individuals in a persistent vegetative state (PVS - more on this later)
  2. The **cerebellum** coordinates body movements & is involved in learning & remembering motor skills
  3. The **thalamus** sorts and organizes information going to higher brain centers; responses from the higher brain centers travel through here as well.
  4. The **hypothalamus** has many important roles; they include:
    - a. it is the homeostatic control center (body temperature, blood pressure, etc.)
    - b. related to that, it is the source of major “survival” drives – hunger, thirst,

- sexual arousal
  - c. it functions as our biological clock – maintaining daily rhythms of sleep, hunger, etc.
  - d. the hypothalamus remains completely or partially functional in persons in PVS as well
  - e. plays an important role in feelings of pleasure and punishment, and linking those feelings to specific actions – more on this in a bit . . .
5. The **cerebrum** is the largest & most sophisticated part of the brain; it is responsible for higher-order brain activity (sensory perception, thinking) as well as some important motor functions (voluntary movement).
- a. physically, the cerebrum is divided into right and left hemispheres, connected by a band of nerve tissue
    - (1) The left hemisphere receives information & controls movement on the right side of the body, and vice-versa
    - (2) Both hemispheres contain the same general functional areas, but in most people, each hemisphere tends to use those areas for a different set of tasks – usually
      - (a) left hemisphere most adept at language, logic, mathematics, detailed skeletal motor control, fine visual/auditory detail
      - (b) right hemisphere most adept at spatial relations, pattern/facial recognition, musical ability, emotional processing
  - b. Most of the cerebrum consists of the highly folded **cerebral cortex**. On each side, the cerebral cortex has 4 lobes, each responsible for sensory input, integration/association, and motor responses for one general set of functions – in very general terms, they are:
    - (1) frontal lobe = planning, evaluating consequences, inhibiting inappropriate behavior
    - (2) parietal lobe = body sensations

- (3) occipital lobe = vision
  - (4) temporal lobe = hearing
  - c. complex brain functions often involve components of more than one lobe – e.g., speech/language involves portions of the parietal, frontal, and temporal lobes
- C. The **limbic system** is a particularly interesting functional unit of the brain because of its role in memory, learning, emotional behavior (anger, love, sorrow, fear), and motivational drives. It does these things through the interactions among its major components – e.g.:
1. “Emotional scent memories” – certain smells can bring up very strong feelings
    - a. process seems to be something like this:
      - (1) the olfactory bulbs bring sensory input from the nose to the limbic system, eventually to the amygdala & hippocampus
      - (2) the hippocampus stores & retrieves new long-term memories
      - (3) the amygdala links emotions with specific memories
      - (4) So, put it all together: smell is linked to memory, which is linked to a specific emotion
    - b. may have originated evolutionarily as physiological mechanism that promotes social bonding (especially infants to mothers & vice-versa)
  2. The limbic system generates “motivation” by linking emotions to “drives”
    - a. the hypothalamus contains centers for basic drives (hunger, thirst, sexual arousal)
    - b. the hypothalamus and amygdala are both involved with pain, pleasure, and strong emotion (fear, e.g.)
    - c. linking specific strong emotions to acting on basic drives creates motivation for those behaviors – in simple terms, the hypothalamus alone says “I’m hungry”; the limbic system turns that into “I want to eat”

and “That was an enjoyable meal.”

3. The thalamus connects the limbic system to the cerebrum, allowing our conscious thoughts to assess and modify the responses generated by the limbic system – e.g., a strong desire to eat can be prevented from turning into actual feeding by the recognition that we have to finish class and that food isn’t allowed in the classroom.
  4. Ongoing interactions between the limbic system and the prefrontal cortex (also part of the cerebrum, involved in complex learning, reasoning, and personality) generate connections between our feelings and our thoughts.
- VI. Death, brain death, and PVS: harder distinctions – and much harder decisions – to make with advances in medical technology

**A. Death**

1. can be defined as “the final cessation of the vital functions” – what are those? Most critical are
  - a. circulation
  - b. respiration
2. Medical intervention allows us to keep patients alive on respirators (Christopher Reeve, e.g.) when injury or disease would otherwise kill them.
3. Legal and ethical issues related to death and dying led to the development of the 1981 Uniform Determination of Death Act
  - a. endorsed by the American Medical Association and American Bar Association
  - b. recommended for adoption by all states (and in fact adopted by most by 1985 – including Virginia)
  - c. states that “An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. A determination of death must be made in accordance with

accepted medical standards.”

- B. In part because we have ways of maintaining circulatory and respiratory function artificially, the concept of **brain death** has become increasingly used when trying to determine a course of treatment/action.
1. Definition = irreversible cessation of all functions of the brainstem
  2. How do we know it's happened? Criteria (first established by the Harvard Medical School in 1968, then expanded) include the following - think about how they relate to brainstem function:
    - a. unreceptivity and unresponsiveness – i.e., no response even to painful stimuli
    - b. no movement for a continuous hour after observation by a physician
    - c. no breathing after 3 minutes off a respirator
    - d. no reflexes, including brain stem reflexes (fixed and dilated pupils are one sign of this)
    - e. “flat” EEG for at least 10 minutes
    - f. all tests repeated at least 24 hours later with no change
  3. New brain imaging techniques mean we can add a variety of tests to look at circulatory and electrical activity in the brain in more detail as well.
- C. **Persistent vegetative state** (PVS) is an “in-between” condition. According to the American Academy of Neurology:
1. Definition = irreversible (that's important!) “condition of complete unawareness of the self and the environment accompanied by sleep-wake cycles with either complete or partial preservation of the hypothalamic and brainstem autonomic functions”; also referred to as “a form of eyes-open permanent unconsciousness”
    - a. Conditions of unawareness may be reversible, in which case the condition is simply a vegetative state
    - b. Cerebral cortex is completely inactive

- c. Patients may still be able to
  - (1) breathe spontaneously
  - (2) digest food, but not chew and swallow
- 2. The criteria for diagnosis include
  - a. No evidence of awareness of self or environment; inability to interact with others
  - b. No evidence of sustained, reproducible, purposeful or voluntary behavioral responses to any stimuli, including pain
    - (1) i.e., patients do not have the capacity to experience pain or suffering
  - c. No evidence of language comprehension or expression
  - d. Intermittent wakefulness; the presence of sleep-wake cycles
  - e. Sufficient autonomic functions to permit survival with medical/nursing care
  - f. Bowel and bladder incontinence
  - g. Variably preserved cranial nerve and spinal reflexes (e.g., pupils may still dilate)
- 3. Note the relationship of the definition to functions of cerebral cortex, brainstem and hypothalamus:
  - a. unawareness of self because no cerebral cortex activity
  - b. no voluntary responses to stimuli, language comprehension because cerebral cortex doesn't function
  - c. sleep-wake cycles may persist because the hypothalamus is partially functional
  - d. patients still breathe, pump blood, and digest food because of brainstem activity
  - e. can't chew because cerebral cortex doesn't work
- 4. The probability of recovering from PVS varies depending on the cause and its severity. According to the AAN, however,

- a. Recovery after 12 months in a PVS is extremely unlikely when the PVS was caused by a traumatic injury – so condition may be judged permanent after that point
  - b. Recovery after even 3 months in a PVS is extremely unlikely when the PVS was caused by a non-traumatic injury – so condition may be judged permanent after that point
5. When a patient is diagnosed as being in a PVS, current ethical guidelines permit the withdrawal of artificial nutrients and fluids (i.e., removal of feeding tubes) under the same guidelines as removal of artificial respirators – decision must be made in conjunction with the family and honoring the individual's wishes insofar as they are known.

VII. Drugs of abuse: why do recreational drugs make people “high”?

- A. To understand this, we need to first identify some of the major neurotransmitters of the brain (and especially of the limbic system):
1. **dopamine** is released in many areas of the brain; it is inhibitory in some, and excitatory in the pleasure centers of the limbic system
  2. **serotonin** is also released in many areas of the brain – including the limbic system – involved in attention and emotional state
  3. **norepinephrine** is found in both the brain and the autonomic nervous system, where it is excitatory (think of adrenaline)
  4. **substance P** transmits sensations of pain in the brain
  5. **endorphins** inhibit the release of substance P – they're the brain's “natural painkillers”
- B. Typical drugs of abuse produce their results by affecting these neurotransmitters in the limbic system. Most result in an increase in the amount of dopamine in the limbic system, which stimulates the pleasure centers more than usual.
1. **Nicotine** increases dopamine release, among its other effects

2. **Alcohol**
    - a. increases dopamine release
    - b. increases serotonin release
    - c. modifies serotonin's "receiving neurons" so that the serotonin present has a stronger effect than normal
  3. **Cocaine** blocks dopamine reuptake in the pleasure center – so although extra dopamine isn't produced, it stays present in the synapse longer; the result is still enhanced stimulation of the pleasure center
  4. **MDMA** ("ecstasy")
    - a. increases dopamine release
    - b. increases serotonin release
    - c. increases norepinephrine release
  5. **Opiates** (morphine, heroin, opium) act like endorphins in the brain, blocking substance P (this is why morphine is a good painkiller) – this probably contributes to the "high"
  6. **LSD** produces hallucinations by stimulating serotonin release in many parts of the brain, including the brain stem & limbic system
- C. The brain responds structurally and functionally to experience – long-term use of many of these drugs (cocaine, alcohol, etc.) leads to **tolerance**. In simple terms, this involves
1. brain "recognizing" that it has too much dopamine, serotonin present
  2. homeostatic mechanisms respond by reducing production by "sending" neurons and/or sensitivity in "receiving" neurons
  3. two consequences:
    - a. when the drugs aren't present, mood depressed
    - b. more and more of the drug is needed to produce the same "high"
  4. Note: drugs of abuse (legal or otherwise) have many more effects than those we've listed here!

VIII. Disorders of the brain

A. Many important brain disorders involve neurotransmitters. Just a few examples:

1. **Depression** is associated with reduced serotonin production. Common medications (Prozac, Zoloft, etc.) work by blocking the reuptake of serotonin, leaving it present in the synapses for longer.
2. **Parkinson's disease** results from the degeneration of specific dopamine-producing neurons in the brain
  - a. A group of cells called the basal ganglia provide communication between the cerebrum ("thinking") and the cerebellum ("moving") – they're an important part of controlling normal movement.
  - b. Neurons leaving the basal ganglia receive:
    - (1) excitatory input from cells producing the neurotransmitter Ach (acetylcholine)
    - (2) inhibitory input from cells producing dopamine
  - c. Normal motor function results from the proper balance of excitatory and inhibitory input
  - d. For reasons that aren't clear, something causes the dopamine-producing neurons to degenerate
    - (1) this means "receiving" cells communicating with the cerebellum are overstimulated
    - (2) overstimulation results in the increase in muscle tone (rigidity) and muscle tremors that characterize Parkinson's disease.
3. **Migraine headaches** involve complex interactions between nerves and blood vessels in the brain.
  - a. Although the exact pathways are still not fully understood, the major system involved seems to be the trigeminovascular system = network comprising
    - (1) the trigeminal nerve (which innervates much of the face and skull

- region)
- (2) the blood vessels it innervates, including those in the meninges
- b. A very simplified version of current thinking is that
- (1) Headache begins with trigger (varies among people, may include stress, caffeine, specific foods, withdrawal of estrogen, lack of sleep, etc.)
  - (2) Trigger somehow activates the trigeminal nerve, which releases several neurotransmitters
    - (a) all act to dilate (expand) the blood vessels the trigeminal nerve stimulates
    - (b) substance P, in addition to dilating blood vessels, sends pain signals back to trigeminal nerve
    - (c) neurotransmitters also cause other cells to release serotonin, which constricts some blood vessels (but not others)
      - i) this may cause the “aura” experienced by ~ 20% of migraine sufferers
      - ii) other effects of serotonin in migraines not clearly understood, but we know they’re involved somehow . . .
  - (3) Blood vessels in the meninges are surrounded by nerve fibers. When blood vessels expand, they activate the nerve fibers to send more pain signals back to the trigeminal nerve – so there’s a positive feedback loop of pain -> nerve activity -> blood vessel dilation -> pain etc.
  - (4) Other fibers of the trigeminal nerve carry pain impulses up through the thalamus to the cortex, leading to the sensation/experience of pain
- c. Triptans are a family of drugs currently used to treat migraines (Imitrex, Relpax, Amerge, Zomig, etc.)

- (1) drugs act as serotonin mimics, causing dilated blood vessels to constrict
  - (2) this relieves the pain and other symptoms of the migraine
- d. Other migraine notes:
- (1) As many as 28 million Americans may suffer from migraines, ~ 75% of them women.
  - (2) Migraines can develop (and disappear) spontaneously at any age.
  - (3) Migraines have a clear genetic component, probably related to neurotransmitter receptors (which affect how the brain responds to triggers etc.).
  - (4) The relationship of estrogen to migraines is complex and poorly understood: presence causes migraines in some; absence causes migraines in others.
  - (5) Migraines are highly variable; symptoms can be very different from person to person
    - (a) "auras" only occur in ~ 20% of migraine sufferers
    - (b) new findings demonstrate that what appear to be sinus headaches are migraines