

PL3232 Biological Psychology

Spring 2021

Section 3

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3.1. Pain.

3.1.1. Nociception.

- The brain converts noxious stimuli into a sensation of pain within the brain.
 - (1) Pain is a sensation which does not exist outside of our brain.
 - (2) Nociceptors detect noxious stimuli and send pain signals to the brain in a process called **transduction**.
 - Most pain axons are unmyelinated and slow at transmitting signals.
 - Some pain axons are myelinated, e.g. $A\delta$ fibers.
 - (3) Multiple types of nociceptors exist and have different characteristics.

3.1.2. Pain experience.

- Multiple brain regions are involved in processing pain.
 - (1) From the nociceptors, pain signals are sent through the spinal cord, into the thalamus and hypothalamus.
 - (2) The **thalamus** then projects to the somatosensory cortex and the amygdala, hippocampus, PFC, and ACC.
 - (3) The **somatosensory cortex** assesses the location and intensity of the painful stimulus.
 - (4) The **insular cortex** and **ACC** contribute to our subjective interpretation (i.e. affective experience) of pain.

3.1.3. Emotional pain.

- The mechanisms of emotional pain are similar to nociceptive pain in the brain.
 - (1) Even in the absence of noxious stimuli, similar brain activity is triggered by emotional pain.
 - (2) Just as with nociceptive pain, emotional pain is sensitive to painkillers.

3.1.4. Neuropathic pain.

- Neuropathic pain differs from nociceptive pain in its origins.
 - (1) Neuropathic pain comes from damage to the nervous system (e.g. autoimmune disorders, trauma, nerve compression), rather than from noxious stimuli.
 - (2) Neuropathic pain can also arise from sensitization of the nervous system, e.g.:
 - **Hyperalgesia:** increased sensitivity to pain.
 - **Allodynia:** painful sensation in response to normally non-painful stimuli.

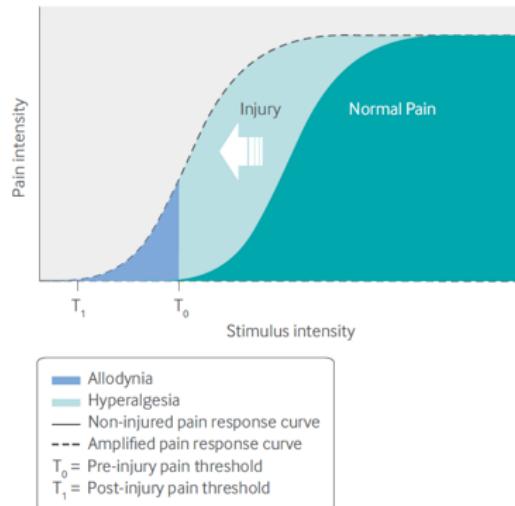


FIGURE 3.1. Allodynia vs hyperalgesia.

- Sensitization occurs when signals are sent more often.
 - (1) Sodium or potassium channels are being over- or under-expressed respectively.
 - Sodium is responsible for **depolarization**.
 - Potassium is responsible for **repolarizing** neurons.
 - Neurons fire at a rate higher than usual.
 - (2) Increased release of excitatory neurotransmitters.
 - (3) Increase in synaptic efficiency.
 - (4) LTP occurs in pain neurons.

3.1.5. Opioids.

- Opioids are a class of chemicals that reduce or inhibit the feeling of pain.
 - (1) Opioids work by producing an inhibitory signal for pain receptors.
 - They bind to opioid receptors found on neurons which transmit pain signals → produces inhibitory effects.
 - They also bind to receptors in reward-related areas of the brain such as the **ventral tegmental area** and the **midbrain** → trigger the release of dopamine + produce feelings of pleasure.
 - (2) The body generates its own opioid chemical, known as **endorphins**.

3.1.6. Placebos.

- Placebos are inert drugs which reduce the experience of pain in the absence of active ingredients.
 - (1) The effect of placebos are affected by our expectations.
 - (2) Placebos may exert their effect through increasing endorphin production, or reducing our response to painful stimuli.

3.2. Sleep.

3.2.1. Body rhythms.

- (1) Organisms generate their own **circadian rhythms** independent of external cues.
- These cycles are studied through **constant routine** protocols, where participants are kept in the lab under constant conditions for 24+ hours.
 - They persist even in the absence of external cues.

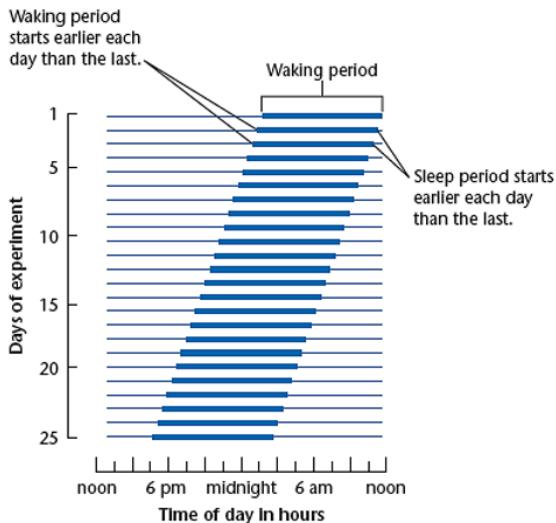


FIGURE 3.2. Results of Kletiman's cave experiment.

- (2) **Exogenous cues**, especially light, help to adjust our **endogenous rhythms**.
- **Phase delay** refers to us sleeping and waking later.
 - **Phase advance** refers to us sleeping and waking earlier.
 - We readjust our internal cycles *daily* to stay in-phase with the world, i.e. light is our primary **zeitgeber** (time-giver).
 - Without light cues, organisms default to endogenous cues, and circadian cycles drift.
 - However, sometimes external factors are not fast enough at changing our circadian rhythms, e.g. in the case of jet lag.
- (3) Humans vary in the phase of their circadian rhythms, which affects whether they have a **morning or evening preference**.
- This depends on both genetic and environmental factors.
 - However, evening types incur more health risks, because of circadian mismatch.
 - Circadian cycles change with age; as we get older, we generally become more morning people (depends primarily on genetics).

3.2.2. Neural mechanisms of body rhythms.

- (1) The **suprachiasmatic nucleus (SCN)** of the hypothalamus generates the body's circadian rhythms.
- It lies just above the optic chiasm.
 - SCN neurons that are maintained in tissue culture (outside of the human brain) continue to produce circadian rhythms for up to weeks (i.e. they generate rhythms by themselves).
 - Mutations can cause changes in the length of circadian rhythms.
 - Lesioning the SCN causes animals to lose circadian rhythms.

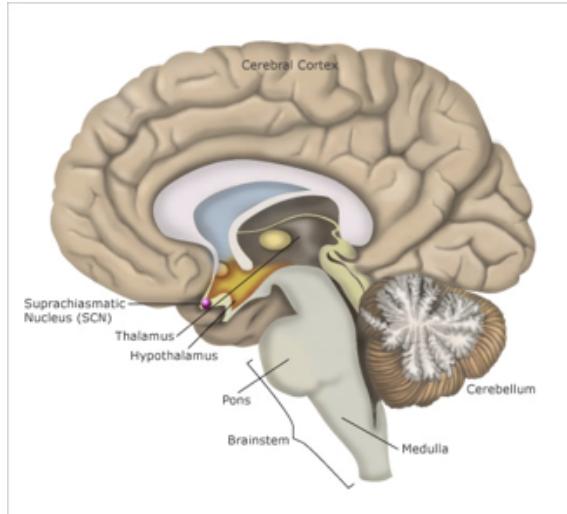


FIGURE 3.3. Location of the SCN.

- (2) **Melanopsin** responds directly to light, and is found in a third class of photoreceptors (**photoreceptive retinal ganglion cells (pRGCs)**) that project directly to the SCN.
 - These cells are more sensitive to short-wavelength (blue) light, thus people who use devices emitting these wavelengths in the evening have a harder time falling asleep.
 - Melanopsin is slower-acting than rhodopsin/iodopsin, and plays a large role in resetting the circadian rhythm.
- (3) The circadian rhythm is generated by a feedback cycle of **PER** and **TIM** proteins.
 - These proteins promote sleep, and inhibit genes that produce PER and TIM (*negative feedback*).
 - Light activates an enzyme that breaks down TIM, thus adjusting the cycle.
 - Mutations in these genes causes sleep problems and depression.
- (4) We sleep at night because of two interacting processes: the **circadian** (process C) and **homeostatic** (process S) processes.
 - **Melatonin** is a hormone primarily released by the pineal gland at night, and is associated with control of the sleep-wake cycle.
 - **Dim light melatonin onset** is a useful research tool for assessing circadian phase.

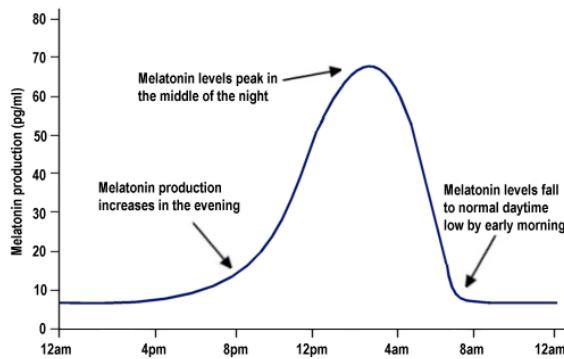


FIGURE 3.4. Melatonin production cycle.

- Process C is an endogenous circadian cycle that promotes arousal.
- Process S builds up our drive to sleep the longer we stay awake. **Adenosine** release from the basal forebrain is an important mediator of the sleep drive.

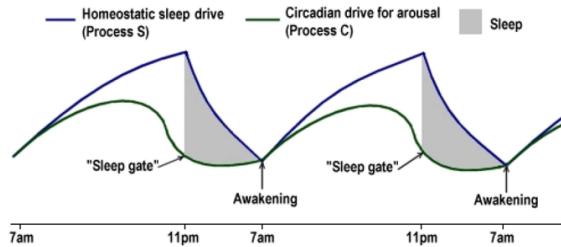


FIGURE 3.5. Borbely's two-process model of the circadian and homeostatic cycles.

3.2.3. Sleep.

- (1) Sleep is not a homogeneous process: stages 1, 2, 3, 4, and REM sleep all have different defining features.
 - A **polysomnograph (PSG)** can be used to measure sleep (i.e. measures a combination of EEG and eye-movement).
 - Sleep usually occurs with the lower EEG frequency bands: in α , θ , and δ .

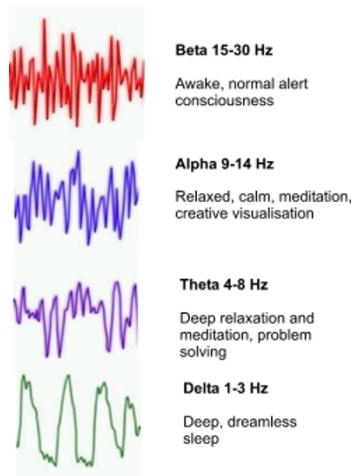


FIGURE 3.6. EEG frequency bands.

- PSG signals change over the course of sleep.

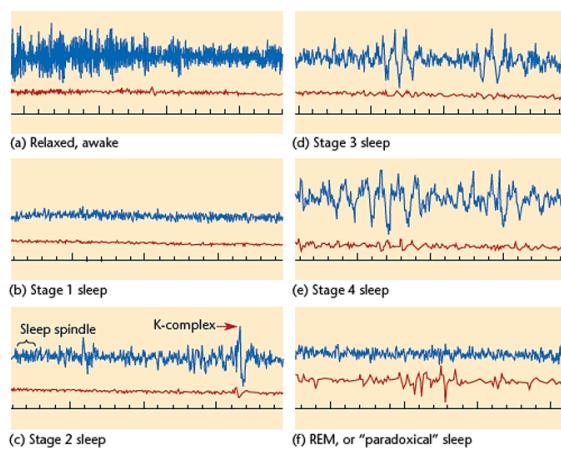


FIGURE 3.7. EEG frequency bands (blue) and eye movement (red).

- (a) When we are relaxed but awake, EEG signals are dominated by α waves. These waves are characteristic of relaxation, but not all of wakefulness (e.g. they are less prominent when an individual is engaged in cognitive activity).
- (b) As a person starts to drift into sleep, he/she enters stage 1 sleep, dominated by irregular low-voltage waves. People in this stage of sleep can still respond to environmental stimuli to a limited extent.
- (c) Stage 2 sleep is the first stage of *true sleep*, in which people are less responsive to the environment. It is defined by two unique features:
- **K-complexes:** sharp waves associated with temporary inhibition of neuronal firing.
 - **Sleep spindles:** bursts of activity in the 12-14 Hz range that lasts about 0.5-1.5 seconds.
- These are associated with the integration of new knowledge in the schema.
- (d) The deepest stages of sleep are stages 3 and 4 (collectively scored as “N3 sleep”) which are dominated by large-amplitude, low-frequency δ waves. Slow-wave sleep is important for restoring the body and the brain, as well as for memory formation.
- (e) REM sleep is a sleep state with similarities to the awake state. This state features low-voltage waves and rapid eye movements, which indicate increases in neuronal activity. Postural muscles are also more relaxed than in other sleep stages; body in a state of near-paralysis – which prevents people from “acting out their dreams”.
- (2) Sleep stages occur in cycles throughout the night.
- (a) Deep sleep (stages 3 and 4) dominate early in the night.
 - (b) REM sleep dominates towards the morning.
 - (c) Dreams are more common during REM (but also happen during non-REM).

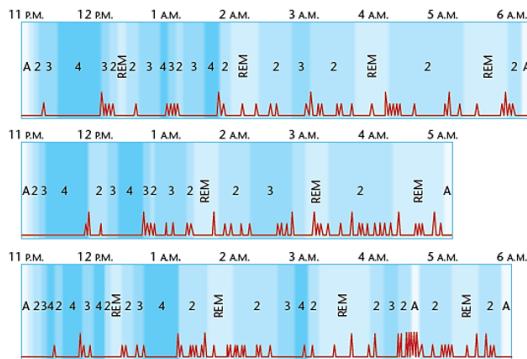


FIGURE 3.8. Stages of sleep.

- (3) The brain has multiple systems for arousal: the *pontomesencephalon*, *hypothalamus*, and *basal forebrain* contain neurons that promote wake and others that promote sleep.
- (a) **Reticular formation and pontomesencephalon:**
 - Release glutamate, acetylcholine, dopamine, and GABA.
 - Project to the hypothalamus, thalamus, and basal forebrain.
 - Maintain arousal during wakefulness.
 - (b) **Locus coeruleus and pons:**
 - Release norepinephrine throughout the cortex.
 - Increase wakefulness due to emotional arousal (dormant during sleep).
 - (c) **Hypothalamus:**
 - Releases histamine and **orexin** (an important peptide that promotes wakefulness).
 - Widespread excitatory effects (antihistamines – histamine antagonists – produce sleepiness).
 - Orexin/hypocretin keeps us awake.

- Narcolepsy (sudden overwhelming drowsiness during the day) is caused by lack of orexin.
- (d) **Basal forebrain:**
- Releases acetylcholine, which increases arousal, during wake and REM sleep.
 - Releases adenosine, which is important in regulating sleep homeostasis.
- (4) During sleep, GABA is released by the *basal forebrain* and *ventrolateral preoptic nucleus*
– results in weakening of connections throughout the brain and the loss of consciousness.

3.2.4. Functions of sleep.

- (1) Sleep has multiple functions, including saving energy and consolidating memories.
 - If we do not sleep, in the short-term, we would have:
 - Less attentional capacity, which leads to poor performance in school and more accidents.
 - Poor memory consolidation.
 - Increased reactivity to stress.
 - Low mood and well-being.
 - In the long-term, we may have:
 - Higher risk of developing physical illnesses.
 - Weight problems/obesity.
 - Increased risk of psychological illness.
 - Higher all-cause mortality.
 - We also sleep in order to save energy.
 - Sleep helps us to consolidate our memories. Sleeping after learning would enhance subsequent memories.
 - Animal studies have found when sleeping, our brain replays (more rapidly, and in both directions) the patterns which we have observed while we were awake.
 - During sleep, new dendritic branches formed that strengthened these memories.
 - However, this mechanism occurs during wakefulness as well, and is not exclusive to slow-wave sleep.
 - Sleep might also help to weaken/get rid of less successful synaptic connections (i.e. synaptic downscaling). This ensures that memories are maintained while brain connections are not saturated.

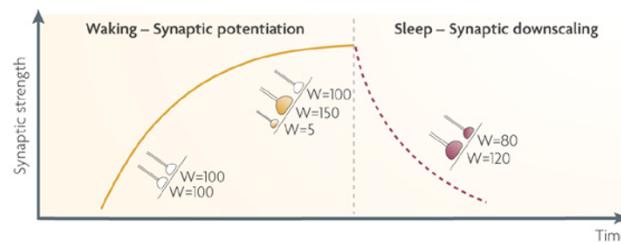


FIGURE 3.9. Process of synaptic homeostasis.

- Sleep might also benefit memories via metabolite clearance. During sleep, waste products are removed from the brain via the glymphatic system (which carries cerebrospinal fluid from the brain). Among these waste products is beta-amyloid (a peptide that can accumulate in the brain and contribute to Alzheimer's disease).
- (2) The function of REM sleep is not well understood.
- As daily total sleep decreases over the lifetime of a human, REM sleep changes significantly (i.e. the more total sleep, the higher the percentage of REM sleep), whereas non-REM sleep remains relatively stable.
 - Some experiments suggest that it is important for motor memory consolidation. However, people taking antidepressants (which significantly decreases REM sleep) have no memory problems.

3.3. Attention.

3.3.1. Sustained attention.

- (1) **Sustained attention** is the state of readiness to respond to stimuli in the environment over an extended period of time. It is typically measured using reaction time tests such as the *Psychomotor Vigilance Test*.
 - It is closely related to the concept of arousal.
 - It is a global state.
 - It is important in monotonous, lengthy tasks.
- (2) A network of brain regions (areas in the frontal and parietal cortex) is needed to maintain sustained attention.
 - These areas are responsible for *biasing* and *filtering* information.
 - Activity in these regions tend to decrease over time → we cannot sustain attention at a high level indefinitely.
- (3) Sustained attention is closely related to arousal, and fluctuates in a circadian manner (refer to the circadian cycle in figure 3.5).

3.3.2. Models of selective attention.

- (1) **Selective attention** is the ability to prioritize and attend to some things while ignoring others.
 - It is not a global state; it operates at any level of arousal.
 - This function is executed by *attentional control mechanisms* in the brain.
 - **Orienting** refers to us turning our selective attention towards something.
- It can be:
- **voluntary** (a.k.a. top-down, endogenous; i.e. conscious and goal-driven) or **reflexive** (a.k.a. bottom-up, exogenous; i.e. unconscious and driven by stimulus salience), and
 - **overt** (i.e. attending with fixation) or **covert** (i.e. attending without fixation).

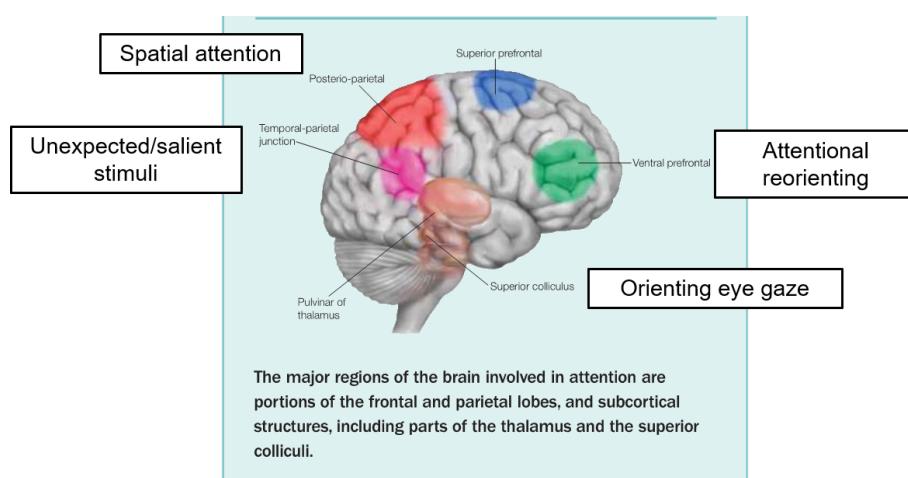


FIGURE 3.10. Anatomy of attention.

- (2) We can attend particular streams of information while selectively ignoring others (e.g. cocktail party effect).
 - In other words, voluntary attention affects what is processed (at the expense of irrelevant information).
 - *Information processing bottlenecks* occur at stages of perceptual analysis that have a limited capacity.
 - It is widely debated whether information is selected early in processing (via attention, before perceptual analysis) or late in processing (after perceptual processing).

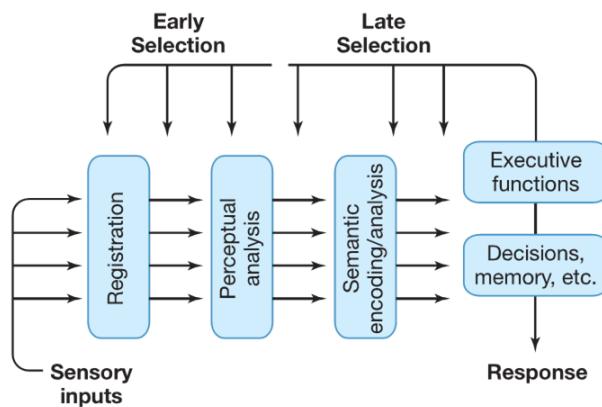


FIGURE 3.11. Early vs late processing.

- One problem with early processing models is that salient information from unattended streams are often consciously perceived.
- (3) *Cuing tasks* (e.g. the Posner cuing paradigm) are common paradigms used to study the effects of attention on information processing.
- In **endogenous cuing**, attention in space is consciously driven by the direction of an arrow.
 - **Fixation** refers to concentrating one's eyes on a target.
 - **Saccades** refer to the movement of eyes rapidly from one fixation point to another.

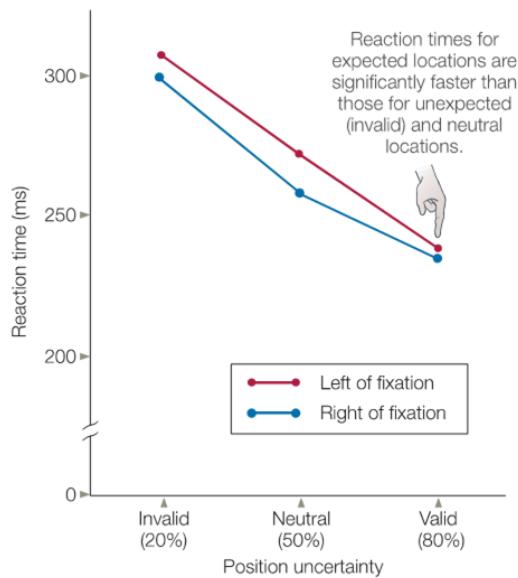


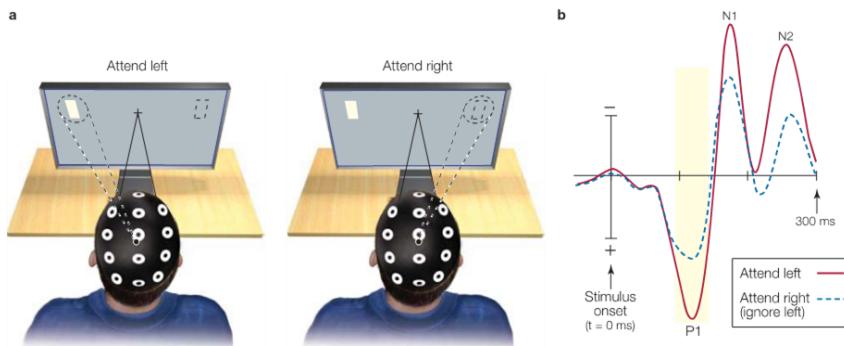
FIGURE 3.12. Results of the Posner cuing paradigm.

There is evidence from the cuing paradigm for early selection – perceptual processing is enhanced by covert attention to a location.

3.3.3. Neural mechanisms of selective attention.

- (1) Event-related potential (ERP) studies show that attention can modulate processing in early ERP components, supporting early processing models.

- ERPs are average EEG responses that are time-locked to a stimulus.
 - ERP waveforms have a letter and a number.
 - *N* refers to a negative deflection (plotted upwards), whereas *P* refers to a positive deflection (plotted downwards).
 - The number is the *latency* of the ERP, or the length of time from the stimulus to the peak of the waveform.
 - The *amplitude* of an ERP can also inform us about differences between experimental conditions.



- Paying (covert) attention to a location enhances ***P1*** responses to stimuli.
 - *P1* is generated by neural activity in the visual cortex (V1).
 - Similar effects can be observed in auditory experiments (e.g. dichotic listening tasks), with modulation of ***N1***.
- (2) Spatial attention influences visual processing, and this can be seen in multiple visual areas, including primary visual cortex, as well as the thalamus.
- Single-cell recordings show modulation in V4 when monkeys attend to the preferred stimulus of those cells.
 - In monkeys, the receptive fields of the visual cortex V1 respond more strongly in an attended part of the visual field. However, the organization of the receptive fields does not change.

The **biased competition model** has been proposed to explain these mechanisms.

- Objects presented simultaneously in the visual field compete for cell responses in the visual cortex.
- Objects that activate cells in the same area of the cortex will compete the most.
- These competitions can be biased in preference of one stimulus.
- Biasing during processing can be due to a stimuli possessing a specific, relevant feature, which may include color, texture, and shape.
- The prefrontal cortex plays a critical role in these biases.

Additionally, visual cortex neurons back-project to an area of the thalamus called the **thalamic reticular nucleus (TRN)**.

- Exciting the TRN neurons inhibits the LGN and vice versa.
- Thus, highly focused spatial attention can modulate activity even earlier than in the visual cortex.

- (3) Attention can be modulated to focus on particular features.

- Reflexive spatial attention:
 - Some stimuli attract our attention unconsciously, simply because they are conspicuous/salient.
 - 50-200 ms after a salient cue, responses to stimuli near the cue are *faster* (i.e. **exogenous cuing**).
 - After a longer interval (> 300 ms), this pattern is reversed (i.e. **inhibition of return**).

- * This is because we only need to momentarily shift our attention from a main task to something potentially life-threatening.
 - **Visual search** is a process where we search for an object of interest in a crowded scene.
 - It involves an interplay of voluntary and reflexive attention.
 - Items which are distinguished by a *single feature* will “pop-out” from the rest. This is in accordance to the **feature integration theory of attention**:
 - * Elementary features can be analyzed without attention, both early and in parallel.
 - * However, conjunction features (i.e. objects) require spatial attention, and must be analyzed serially.
 - Feature attention:
 - Objects are defined by their features, which can draw our attention (bottom-up), or be the target of our top-down attention.
 - Cuing the feature of a target (e.g. motion) enhances detection accuracy.
 - **Feature selection** occurs in visual (extrastriate) pathways specialized for processing those features. These effects occur very shortly after a stimulus appears, but are still slower than the effects of spatial attention.
- (4) Attention can be directed at entire objects.
- Object properties are the collection of elementary stimulus features that combine to yield an identifiable object or person.
 - Attention “spreads” within an object, leading to some enhancement and activity for uncued locations within the object.
 - Attention can affect the way objects are processed in the brain.

3.3.4. Attentional control networks.

- (1) Attentional control systems modulate our thoughts, actions, and sensory processes.
- (2) The **bilateral dorsal attentional network** controls goal-directed spatial attention.
 - They are active between the appearance of a spatial cue and a target, and not active during passive viewing of the cue.
 - Before targets appear, the effects of attentional control can already be seen in the visual cortex.

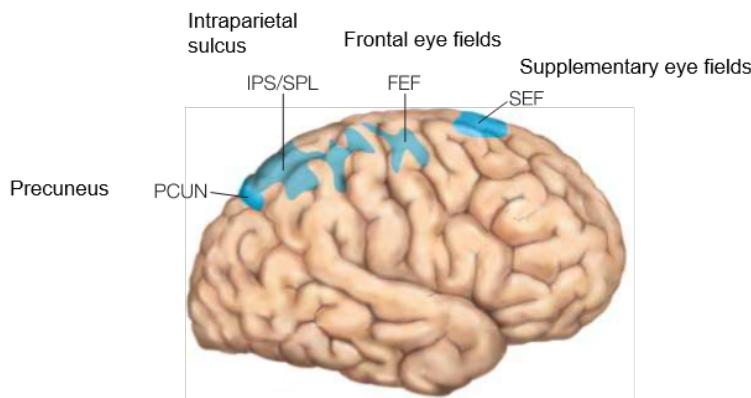


FIGURE 3.13. Dorsal frontoparietal regions involved in goal-directed control of spatial attention.

- The regions include:
 - **Frontal eye fields**
 - * Originally implicated in eye movements.
 - * Later hypothesized to be important in attentional control.
 - * Stimulation of the FEF in monkeys improves spatial attention in the area where their gaze would have been focused on.

- **Posterior parietal cortex**
 - * Shifts in spatial attention lead to increases in firing in posterior parietal neurons.
 - * Best attentional performance is seen when the target occurs in the location where the lateral intraparietal (LIP) activity is higher.
- (3) The **right-lateralized ventral network** is responsible for the non-spatial aspects of attention and alerting.
 - It is strongly right-lateralized, and is more important for stimulus-driven/reflexive attention.

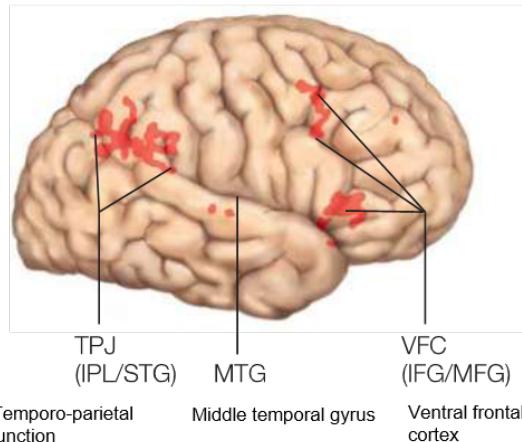


FIGURE 3.14. Ventral regions involved in control of non-spatial attention.

- It is not engaged in maintaining attention, but responds when stimuli appear in unexpected locations, especially during target detection tasks.
 - In particular, the right TPJ is known as the “circuit-breaker” – it responds to warning stimuli by interrupting the current focus of attention.
- (4) Subcortical areas such as the **superior colliculus** and **pulvinar nucleus** also play a role in controlling attention.
 - **Superior colliculi**
 - Located in the midbrain.
 - Receives retinal projections.
 - Responsible for eye movements (saccades).
 - Detect salient stimuli and guide eye movements toward them.
 - Activation requires attention to location of a stimulus, and preparation to shift its eyes to the target.
 - Important for *inhibition of return*.
 - **Pulvinar nucleus**
 - Located in the thalamus.
 - Contains neurons that respond to visual stimuli.
 - Important for covert spatial attention and filtering distractors.
 - Patients with pulvinar lesions have problems engaging attention at cued locations.

3.4. Interface Theory of Perception.

3.4.1. Monism vs dualism.

- (1) **Monism** (a.k.a. reductive physicalism) is the view that the mind is the brain, and that our mental states are a result of *physiological processes*.
 - Most of psychology research (e.g. biological psychology) assumes a monism/reductive physicalism stance.

- (2) **Dualism** is the view that mental states are separate from physical states/physiological processes.

3.4.2. Role of evolution.

- (1) Evolution works through natural selection, selecting for the fittest individual in a population based on the ecological niche.

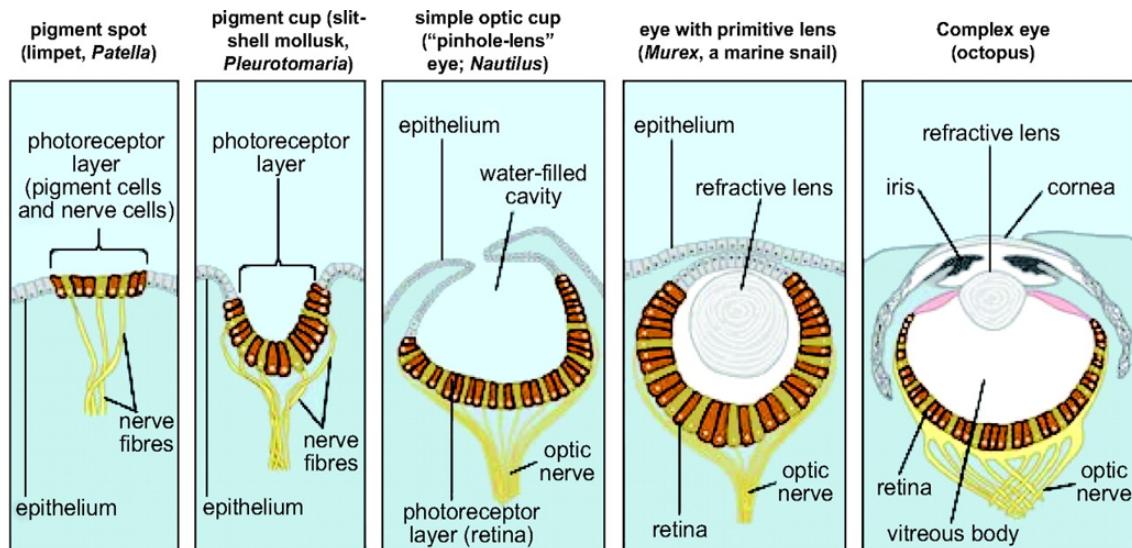


FIGURE 3.15. Role of evolution w.r.t. eye structures.

- Evolution doesn't select eyes and visual systems that see in *perfect acuity*.
 - Evolution selects perception and visual systems that see in terms of the *fitness needs of various species*.
 - It is perfectly fine for a species to have an "inferior" eye that fails to capture objective reality.
 - Perception is not always accurate.
- (2) Evolution has resulted/conditioned animals to devote an inordinate amount of attention to certain cues, resulting in biased perception of these cues.
- These cues are often of extreme importance to the organism (e.g. signs of potential mate, access to water or food, etc.)
 - Perception is biased to these cues as it is more advantageous to be cautious and have "false positives".
- (3) Fixed action patterns (FAP) are a series of (fixed) actions that arise in response to a stimulus, due to biased perception.

3.4.3. Interface theory of perception.

- (1) Organisms don't appear to see reality as it is; evolution has altered our perception to perceive reality in an altered state.
- (2) Reality is often simplified so that organisms can "see fitness" to undertake the necessary actions for maximum payoffs.
 - We have biological structures (e.g. fusiform gyrus) which evolved to be dedicated to specific stimuli (e.g. faces, body shapes/contours, and movement).
- (3) According to the theory, all of our perception is just a shared delusion among ourselves.
 - All that we perceive are optical illusions of our mind, and we don't (and can never) see reality as it is.

3.5. Learning and Memory.

3.5.1. Types of memory.

- (1) **Learning** is the activity or process of gaining knowledge or skill by studying, practicing, being taught, or experiencing something.
- (2) **Memory** can be classified into sensory memory, short-term/working memory, and long-term memory.

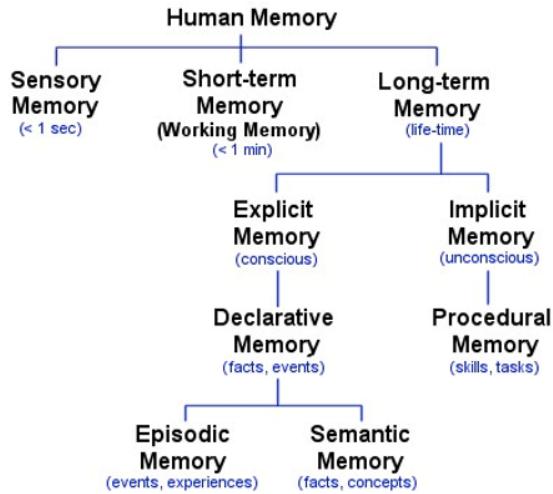


FIGURE 3.16. Types of human memory.

- (3) **Priming** is an implicit memory effect in which exposure to one stimulus (i.e. perceptual pattern) influences the response to another stimulus.

3.5.2. Conditioning.

- (1) **Operant (Instrumental) conditioning** involves strengthening/weakening behaviours by pairing them with a reward or punishment.
- (2) **Classical (Pavlovian) conditioning** is learning where a neutral signal is paired with an unconditioned reflex.

Classical conditioning	Operant conditioning
Involves placing a neutral signal <i>before</i> a reflex.	Involves applying a reward or punishment <i>after</i> a behaviour.
Focuses on involuntary, automatic behaviours (reflexes).	Focuses on strengthening or weakening voluntary behaviours.
First described by Ivan Pavlov.	First described by B. F. Skinner.

3.5.3. Brain areas involved in memory.

- (1) The **engram** is the theoretical unit of memory storage in the brain.
- (2) The **lateral interpositus nucleus (LIP)** in the cerebellum is essential for learning through classical conditioning (at least for the conditioning of eye blinks).
 - However, if the delay between the conditioned stimulus and unconditioned stimulus is longer than 2 seconds, the cerebellum recruits another structure for learning: the **basal ganglia**.
- (3) The **basal ganglia** are important in probabilistic learning.
 - People with Parkinson's disease (who have impairments of the basal ganglia) have no problem forming the initial rule in the weather prediction task (i.e. that triangles \Rightarrow rain), but they are unable to improve beyond that.

(4) The hippocampus is vital in:

- forming new long-term declarative memories.
- spatial navigation and context-dependent memories, as it contains:
 - **Place cells:** fire only a particular place field.
 - **Grid cells:** fire at regular intervals as an animal navigates an environment.
- Performance (in monkeys) were impaired on delayed matching-to-sample and delayed nonmatching-to-sample tasks following hippocampal damage.
- context dependent memory (e.g. learning list of words underwater → lists were best recalled underwater than on dry land).
 - The hippocampus coordinates contextual cues through widespread connections in the cortex.
 - Memories with a lot of contextual detail (e.g. recent memories) depend heavily on hippocampal activity, while older memories can be retrieved directly from the cortex.

(5) Other regions involved in memory include:

- **Parietal lobe:** damage can lead to the inability to link one memory to another.
- **Medial prefrontal lobe:** damage can lead to deficits in learning about reward and punishments.
- **Amygdala:** damage can lead to a deficit in fear memories.
- **Anterior temporal lobe:** damage can lead to *semantic dementia* (i.e. the selective forgetting of objects).

3.5.4. *Cellular mechanisms of memory formation.*(1) **Habituation** is a decrease in response to a repeated stimulus with no change in other stimuli.

- After a *mild* stimulus, a subsequent *mild* stimulus evokes a weaker reflex.

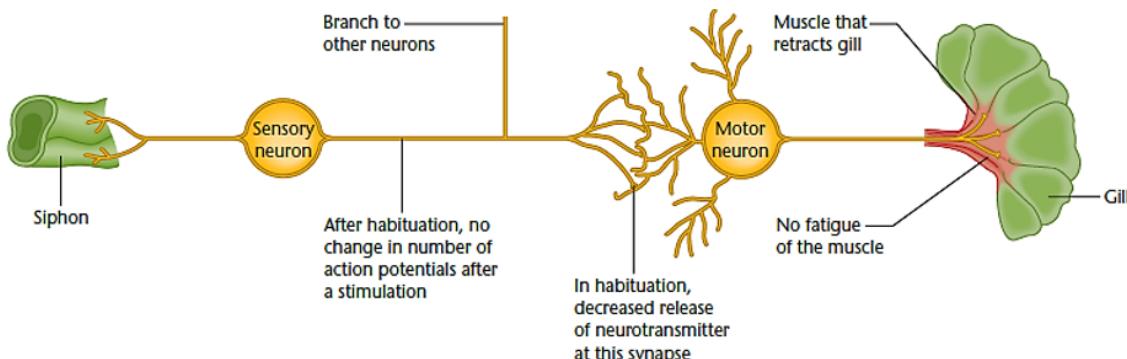


FIGURE 3.17. Habituation.

Sensitization is an increase in response to mild stimuli with exposure to stronger stimuli.

- (a) Serotonin blocks K^+ channels in the membranes of these neurons.
- (b) The membrane is slightly more depolarized.
- (c) The presynaptic neuron releases neurotransmitter for longer than usual.
- (d) Repeating this process leads to synthesis of new proteins that produce long-term sensitization.

Both of these processes are caused by synaptic changes.

(2) Synaptic plasticity consists of:

- **Long term potentiation (LTP):** an enhancement of response at synapses due to brief stimulation, typically from two or more input axons.
- **Long term depression (LTD):** a decrease in synaptic responsiveness due to slow rates of axonal input firing.

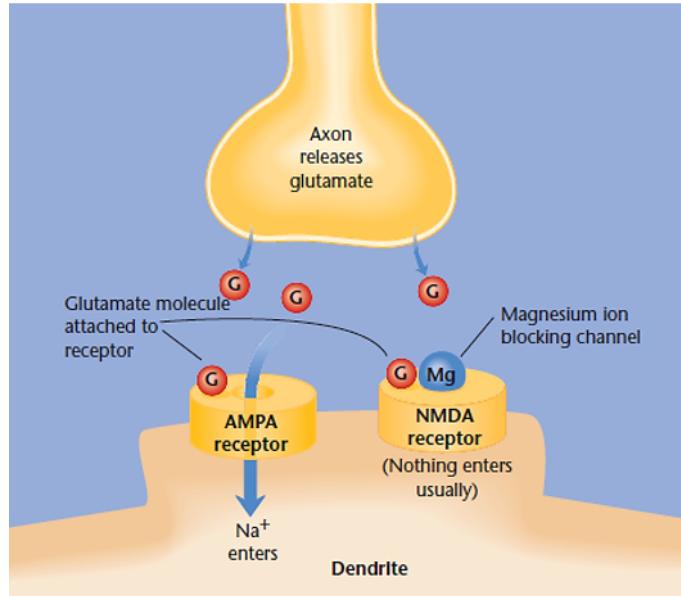
It is characterized by:

- **Specificity:** only active synapses become strengthened.

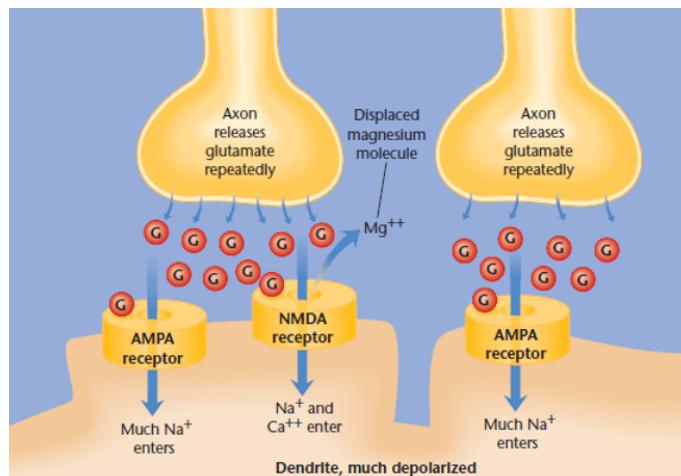
- **Cooperativity:** nearly simultaneous stimulation by two or more axons produces LTP more strongly than repeated stimulation by just one axon.
- **Associativity:** pairing a weak input to a strong input enhances later response to the weak input.

(3) Biochemical mechanism of LTP:

- LTP can increase synaptic strength by increasing receptors in the postsynaptic cell.

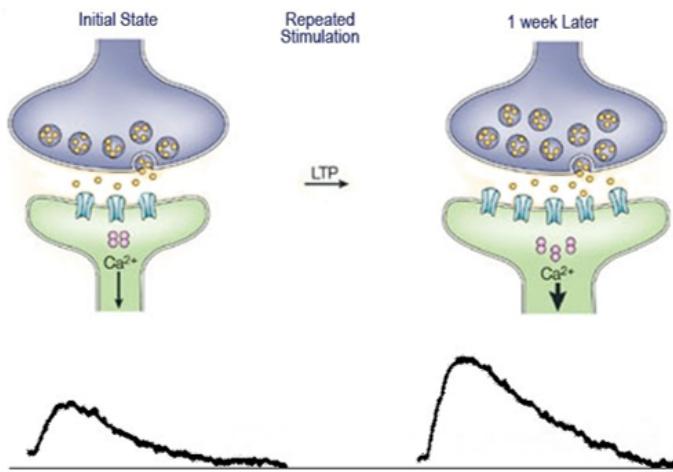


- (a) **AMPA** and **NMDA** are ionotropic glutamate receptors (i.e. they have an ion channel that allows Na^+ to pass through).
- Under normal circumstances, AMPA receptor is unblocked and Na^+ is free to enter these channels.
 - The NMDA receptor is usually blocked by a Mg^{2+} ion; it is attracted to the negative inside, but does not fit through the channel.



- (b) If sufficient Na^+ enters the AMPA receptor to depolarize the cell, the Mg^{2+} leaves, unblocking the NMDA receptor.
- (c) Na^+ and Ca^{2+} enters the cell, which leads to an even further depolarization of the dendrite.
- (d) Ca^{2+} also triggers a series of biochemical events that lead to the expression of genes that increase the number of AMPA receptors in the synapse.
- (i) It activates a protein called **CAMKII**.

- (ii) CAMKII triggers the release of **CREB**.
- (iii) CREB enters the cell and alters gene expression (thus increasing AMPA receptor density).
- (iv) These effects are increased by **BDNF**.
 - BDNF guides the growth of new neurons (i.e. neurogenesis) and synapses. This increase leads to the strengthening of the synapse.
- (e) Only neurons with the greatest production of CAMKII, CREB, and BDNF will undergo LTP.
 - Only the *establishment* of LTP depends on NMDA receptors – these are not necessary to maintain *long-term changes*.
 - Once LTP has been established, the increase in the AMPA receptor density would be sufficient to maintain the strength of the synapse in the long run.



- LTP can also increase synaptic strength by increasing synaptic vesicles in the presynaptic cell.
 - In addition to increasing the number of receptors, retrograde neurotransmitters are also released (e.g. **Nitric oxide**), which travels back to the presynaptic cell and causes changes in the synaptic vesicles.
 - * More neurotransmitters are produced.
 - * More vesicles are stored in the presynaptic cell.
- Other presynaptic changes include:
 - Decreases in firing threshold (i.e. less depolarization is needed to cause the presynaptic cell to fire).
 - Axonal expansion.

3.5.5. Memory loss and memory disorders.

- (1) Hippocampal damage impairs **episodic memory** formation, while sparing other types of memory. In the case of H.M., he had:
 - **Anterograde amnesia:** inability to form memories for events that happened after brain damage.
 - **Retrograde amnesia:** loss of memory for events that occurred before the brain damage.
 - **Intact working memory:** if left undistracted, can remember names, numbers, etc.
 - **Intact procedural memory and better implicit than explicit memory** (because cerebellum and basal ganglia are undamaged).
- (2) Alzheimer's disease is a common type of dementia that leads to steadily worsening memory and cognition over a number of years.
 - It affects 5% of people between 65 and 74, and more than half of people over 85.
 - It is associated with an accumulation and clumping of the following brain proteins:

- Amyloid beta protein:
 - * Creates plaques from damaged axons and dendrites.
 - * Produces widespread atrophy of the cerebral cortex, hippocampus, and other areas.
- An abnormal form of the tau protein:
 - * Creates tangles.
 - * Part of the intracellular support system of neurons.

However, amyloid accumulation does not specifically predict the cognitive deficits caused by the disease.

3.6. Emotion.

3.6.1. Theories of emotion.

- (1) Emotions have three components: **cognition**, **action**, and **feelings**.
 - Although they are unobservable, feelings are what we associate more closely with emotions.
 - There is a distinction between **emotional experience** and **emotional expression**.

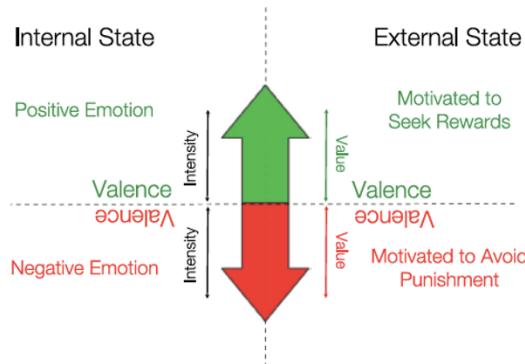
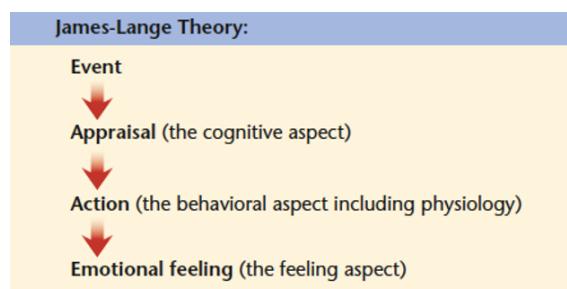


FIGURE 3.18. Emotion vs motivation.

- “Emotion” is a subjective internal state, and “motivated behaviours” are quantifiable readouts that serve as a proxy for the intangible “emotion”.
- (2) The **James-Lange Theory of Emotion** states that what we experience as an emotion is the label we give to our responses.



- For instance, the theory would support the claim that “I feel sad because I am crying” rather than “I cry because I am sad”.
- While the theory is difficult to completely discredit (e.g. forced to smile → perceive jokes as funnier), in most situations, arousal is neither necessary nor sufficient to produce emotions.

- (3) Psychologists currently have multiple theories of emotion, with their different merits and limitations.

- **Cannon-Bard Theory of Emotion:** states that emotional experience can occur independently of emotional expression.
 - In other words, sensory input received by the cerebral cortex does not play a role in emotion.
 - Instead, the thalamus produces emotion either by activating the amygdala, or causing physiological changes through descending signals.
 - Reaction to a stimulus and emotion occurs *at the same time*.

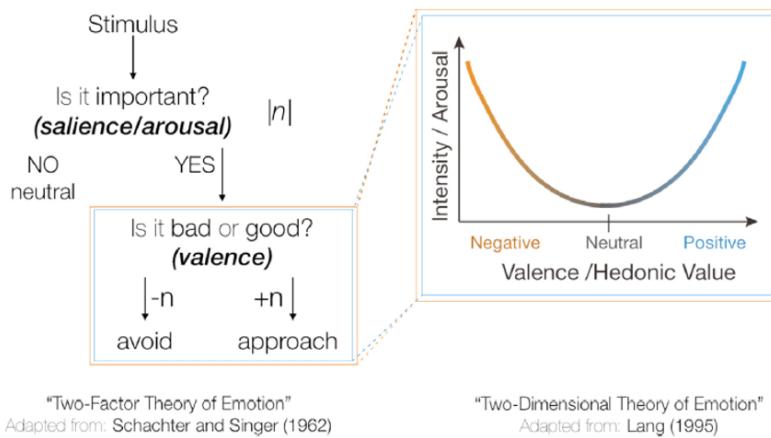


FIGURE 3.19. Two-Factor and Two-Dimensional Theories of Emotion.

- **Schachter-Singer Two-Factor Theory of Emotion:** states that the recognition of a salient/arousing stimulus is a distinct process that occurs before valence processing.
- **Two-Dimensional Theory of Emotion:** states that if something is not important to us (and we feel neutral about it), arousal would be low; if it has a strong positive/negative valence, the greater the arousal we would get.

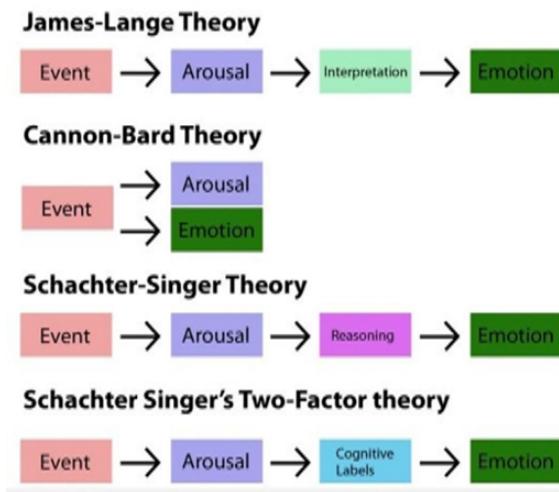


FIGURE 3.20. Theories of Emotion.

3.6.2. Emotions and the brain.

- (1) The **limbic system** is a network of forebrain areas surrounding the thalamus, that are involved in emotional processing.

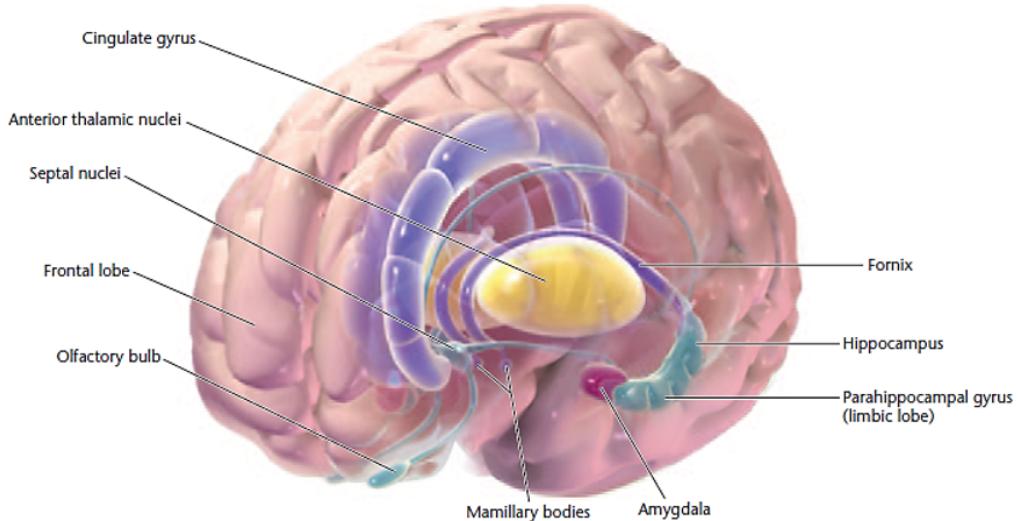


FIGURE 3.21. The limbic system.

It includes the amygdala, hippocampus, and cingulate cortex, among others.

- Although these structures are important for emotional processing, it is unlikely that one circuit generates the diversity of emotions that we have.
- (2) Across cultures, people agree on a set of 6 labels that map onto facial expressions:
 - (a) Happiness.
 - (b) Sadness.
 - (c) Anger.
 - (d) Fear.
 - (e) Disgust.
 - (f) Surprise.

However, facial expressions alone are not sufficient for raters to judge emotions in many situations.
 - (3) Attempting to localize individual emotions to specific brain areas has proven difficult, as most emotions activate a wide network of areas. However,
 - the **left prefrontal cortex** is important for happiness, and
 - disgust processing has been localized to the **insula**.
 - (4) The left hemisphere is associated with the **behavioural activation system (BAS)**, involved in “approach” emotions (e.g. happiness and anger).
 - It is marked by low to moderate autonomic arousal.
 - Individuals with stronger BAS are generally happier, more outgoing, and more fun-loving.
 - Damage to the left hemisphere leads to difficulty in processing positive emotions.

On the other hand, the right hemisphere is associated with the **behavioural inhibition system (BIS)**, involved in “avoid” emotions (e.g. fear and disgust).

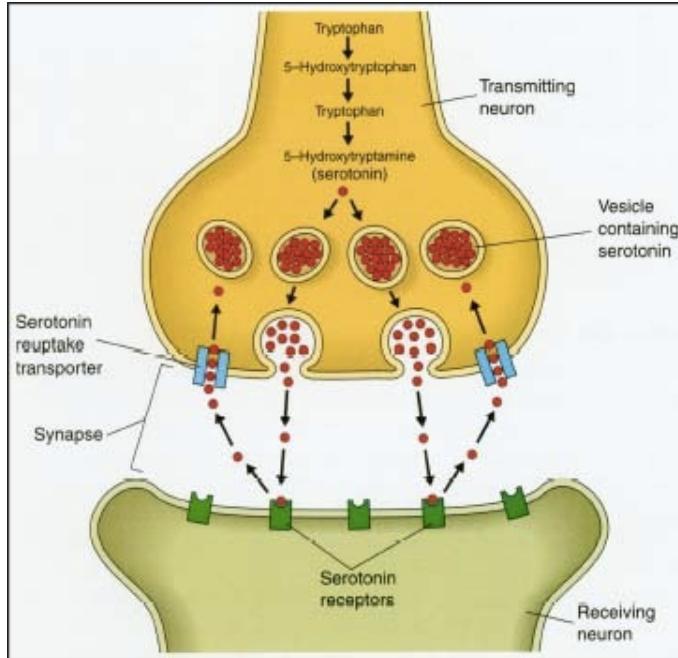
 - It is marked by high autonomic arousal.
 - Individuals with stronger BIS are generally socially withdrawn, less satisfied with life, and prone to unpleasant emotions.
 - Damage to the right hemisphere leads to difficulty processing negative emotions.

3.6.3. Emotions and moral decisions.

- (1) Emotions play a large role in how we make moral decisions.
 - Moral decisions can be **emotional** (deontological) or **rational** (utilitarian).
 - Separate brain networks are responsible for processing the emotional and rational aspects of moral decisions.
 - **Superior temporal sulcus:** representing the actions of others.
 - **Anterior prefrontal cortex:** moral emotions.
 - **Orbitofrontal cortex:** valuing the emotional consequences of decisions.
 - **Insula:** empathy for others' pain.
 - **Dorsolateral prefrontal cortex:** problem solving and executive function.
 - **Ventromedial prefrontal cortex:** integrates emotional and rational information to help us come up with our final decision.
- (2) Damage to the **prefrontal cortex** may impair emotions and lead to faulty decision making.

3.6.4. Attack behaviours.

- (1) Buildup of activity (due to an initial threat) in the **amygdala** predisposes an organism to aggressive behaviour.
 - Subsequent threats will be met with faster aggressive behaviours.
- (2) Aggressive behaviours are a function of an interaction between our genetic makeup (i.e. heredity, nature) and the environment in which we are raised (i.e. nurture).
 - For example, MAO_A is an enzyme that breaks down neurotransmitters dopamine, norepinephrine, and serotonin, thus lowering their available amounts.
 - Other genetic risk factors include:
 - Low IQ.
 - Poor emotional regulation.
 - Antisocial traits.
 - Other environmental risk factors include:
 - Lead exposure.
 - Witnessing violent abuse between parents.
 - Low parental involvement.
 - Overly harsh or lax discipline.
 - Playing violent video games does lead to a small but significant increase in aggressive behaviour, but it is not clear if this translates to committing real-world violent crimes.
- (3) The **Triple Imbalance Hypothesis** hypothesizes that the balance between **testosterone**, **cortisol**, and **serotonin** underlies aggressive behaviours.
 - Increases in testosterone is associated with high aggression.
 - Decreases in cortisol is associated with loss of inhibition and high aggression.
 - Decreases in serotonin (i.e. lower levels of serotonin turnover) is associated with high aggression.



- Neurons build serotonin from **tryptophan**, an amino acid which we cannot synthesize, and have to acquire through our diet.
- A byproduct of this chemical reaction is 5-hydroxyindoleacetic acid (5-HIAA). The concentration of 5-HIAA in the blood or CSF relates to how much serotonin is being used → **rate of turnover**.
- Serotonin is then stored in vesicles and ready to be released at the synapses.
- Vesicles release serotonin after an action potential reaches the axon terminal.
- Some of the serotonin released binds to the serotonin receptors in the postsynaptic cell.
- Leftover neurotransmitter is reabsorbed (recycled) by the presynaptic cell and it goes back into a synaptic vesicle.
- Some of these serotonin molecules may diffuse away, unable to be reabsorbed. This needs to be replenished by the cell by converting more tryptophan to serotonin.

However, these associations are relatively weak overall, and not useful for predicting individual behaviour (i.e. serotonin is not the “aggression neurotransmitter”). A new hypothesis is that:

- higher levels of serotonin *inhibit* a variety of impulses.
- lower levels of serotonin remove inhibitions.
- the resulting behaviour depends on what has been inhibited, which varies from person to person.

3.6.5. Fear.

- The **amygdala** plays a role in fear processing, through its deep interconnectivity with other limbic areas.

- We are born with the *startle reflex*, i.e. fear of loud noises.
 - The reflex is stronger if the startling sound is preceded by another stressful situation (e.g. pain).
 - Damage in the amygdala abolishes this effect: there is still a startle reflex, but it is not affected by recent experiences (i.e. precedence of another situation).

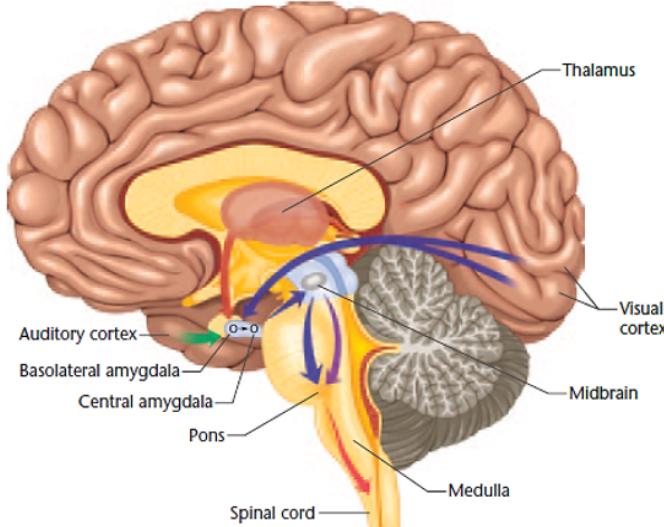
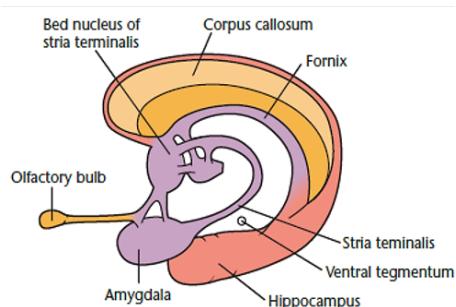


FIGURE 3.22. Connectivity of the amygdala.

- Inputs to the amygdala include:
 - Pain fibers.
 - Visual and auditory information.
- Output targets of the amygdala include:
 - Hypothalamus: control of autonomic fear responses, e.g. increase in heart rate.
 - Prefrontal cortex: approach and avoidance responses.
 - Midbrain, which in turn projects to the pons: control of the startle reflex.
- If a person has a fearful experience, he/she becomes fearful in a wide variety of circumstances.



- This is a result of the **bed nucleus of the stria terminalis**, which is connected to the amygdala and controls long-term generalized emotional arousal.
- (2) Damage to the amygdala leads to a decreased fear response in rats and primates.
- The parasite *Toxoplasma gondii* selectively destroys rats' amygdala, thus inhibiting rats' fear of cats.
 - Monkeys with damage to the amygdala develop the *Kluver-Bucy syndrome*, characterized by tame and placid behaviour. They also show less than normal fear responses, and have difficulty learning what to fear.

3.6.6. Anxiety.

- (1) **Anxiety** refers to a feeling of worry, nervousness, or unease about something with an uncertain outcome.
 - It is related to activity in the **hypothalamus** (i.e. decreases in GABA and increases in orexin).
 - Some disorders with anxiety as the major symptom include:
 - **Generalized anxiety disorder (GAD)**: persistent worry about many different things that is out of proportion to their importance.
 - **Post-traumatic stress disorder (PTSD)**: continuing distress after severe trauma, e.g. flashbacks, oversensitization to noises, sudden movements, etc.
 - **Panic disorder**: characterized by frequent periods of anxiety, and occasional attacks of rapid breathing, increased heart rate, sweating, and trembling (i.e. extreme arousal of the sympathetic nervous system).
- (2) Studies have indicated that anxiety is increased by the neurotransmitters **orexin** and **cholecystokinin (CCK)** in the amygdala and hypothalamus.
 - However, no drugs have been approved based on them.
 - Instead, most **anxiolytic** (i.e. anti-anxiety) drugs are **benzodiazepines** (e.g. Valium, Librium, Xanax).
 - They exert their effects by binding to GABA_A receptors → increases sensitivity to GABA → increases inhibition in the limbic system.

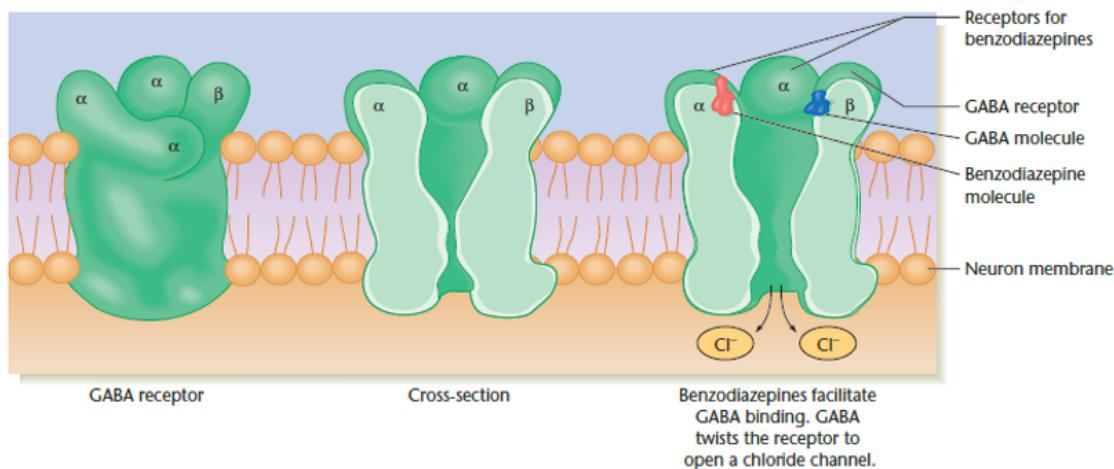
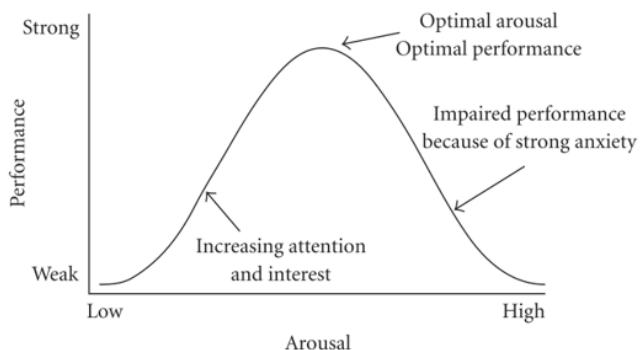


FIGURE 3.23. The GABA_A receptor.

- GABA_A is a receptor that binds to GABA to open a Cl⁻ channel.
 - Benzodiazepines bind to the receptor and increase its affinity to GABA → exert anti-anxiety effects in the limbic system.
 - However, GABA exerts effects throughout the brain, including the cortex and thalamus. This leads to side effects such as sleepiness, impaired memory, and addiction.
- (3) Anxiety may also be relieved through **cognitive behavioural therapy (CBT)**.
 - This is a common psychotherapeutic approach for treating anxiety disorders.
 - Our beliefs shape our thoughts which shape our feelings, so challenging these thoughts and beliefs can help to relieve anxiety.

3.6.7. Stress.

- (1) **Stress** is a non-specific physiological and psychological response to a threat or challenge.
- The **general adaptation syndrome (GAS)** describes the pattern of responses that the body goes through after being prompted by a stressor (e.g. illness, threat). The stages include:
 - Alarm: release of epinephrine and cortisol.
 - Resistance: continued cortisol release leads to adaptation to save energy.
 - Exhaustion: immune and nervous system can no longer sustain responses.
 - Cortisol increases metabolic activity, alertness, blood sugar levels, and suppresses the immune system.



- Brief or moderate stress can be beneficial (e.g. it improves attention and memory) and enhances immune system functioning.
- However, prolonged or excess stress impairs cognition and immune function, and can make the hippocampus more vulnerable to damage.

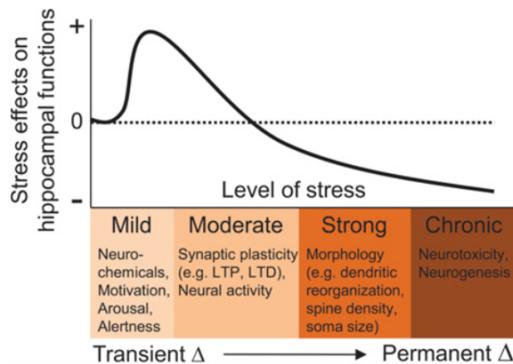


FIGURE 3.24. Effects of stress on the hippocampus.

- (2) In humans, this is related to activation of:
- the **sympathetic nervous system**,
 - the **hypothalamus-pituitary adrenal cortex (HPA) axis**,
 - The **hypothalamus** triggers a releasing factor from the pituitary gland.
 - The **pituitary** releases a compound, **ACTH**.
 - ACTH travels through the bloodstream down to the **adrenal cortex**, stimulating these glands to release **cortisol**.
 - The release of cortisol increases metabolic activity, alertness, elevate blood sugar levels, and suppresses the immune system.

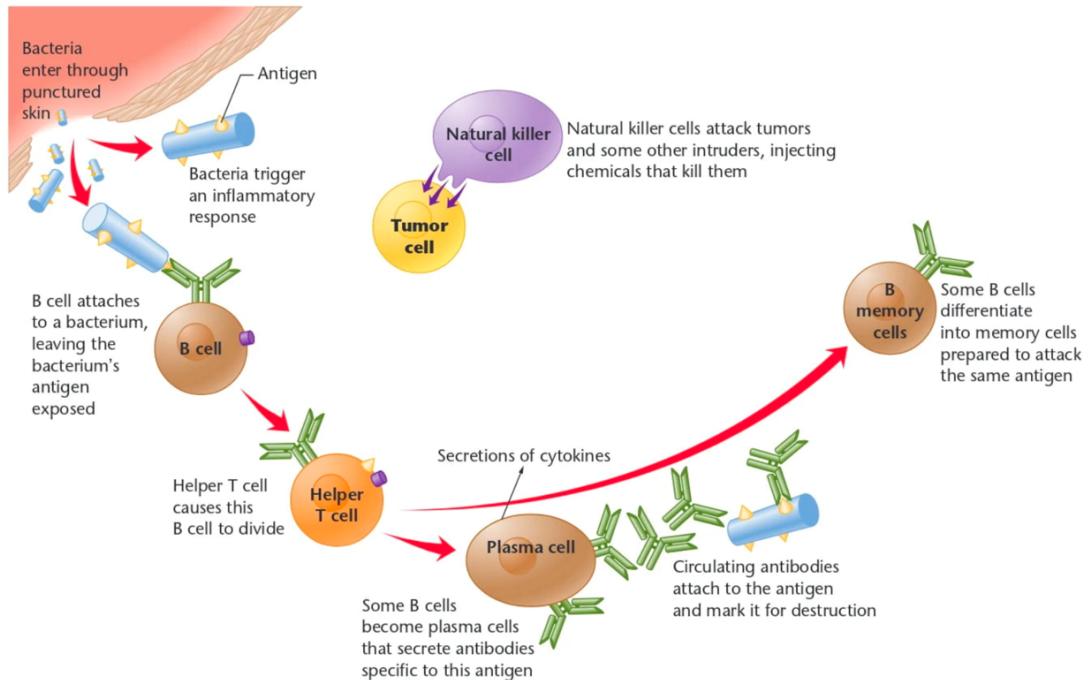


FIGURE 3.25. The immune system.

- the **immune system**.

- Leukocytes (i.e. white blood cells) produce small proteins called **cytokines**, which trigger the release of **prostaglandins**.
- Prostaglandins stimulate the hypothalamus to produce fever, sleepiness, fatigue, etc.

(3) **Resilience** refers to our ability to cope well with stress (e.g. recovering quickly from traumatic experiences). Some ways to reduce our stress levels include:

- Exercise.
- Deep breathing/meditation/mindfulness practice.
- Social support and physical contact.

3.7. Pleasure.

3.7.1. Reward value.

(1) One aspect of reward is its value.

- Reward value isn't absolute, but is based on our perception of the stimulus.
 - For example, the value of food decreases as we get fuller.
- Reward value is encoded in the orbitofrontal cortex (OFC), amongst other areas. Experiments which demonstrate this include:
 - There is decreased activity in the OFC in participants who have satiated from food, when the odour of the same food is presented. This decrease doesn't show if a different food was presented.
 - OFC activation is greater in the “expensive” condition (as compared to the “cheap” condition) when participants drink the wine.

(2) Reward has other features, including:

- Salience.
- Time delay.
- Risk and ambiguity.

3.7.2. Pleasure.

- (1) Pleasure has three components:
 - Liking.
 - Wanting.
 - Learning.
- (2) Liking is encoded by certain pleasure “hotspots” in the brain.
 - These can be found in some areas, e.g. the **ventral pallidum** and **nucleus accumbens**.
 - Activation of these regions result in greater “liking” responses in response to sweet foods, e.g. licking of lips, and opposite response to bitter foods, e.g. gaping mouths and shaking of head.
- (3) Liking isn’t the same as wanting.
 - Animals and humans who lack dopamine can still produce liking reactions.
 - Dopamine stimulation doesn’t produce greater pleasure.
 - Animals will eat more and “want” the reward more instead.
 - Humans report feeling a desire to stimulate the dopamine system again, but do not report feeling pleasure in response to the stimulation.

3.7.3. Learning, dopamine, and reward prediction error (RPE).

- (1) Learning occurs at a cellular level.
 - A conditioned stimulus will block other stimuli from being conditioned.
- (2) Dopamine neurons are found in the midbrain (i.e. the substantia nigra and the VTA).
 - They project to the striatum, amygdala, and cerebral cortex (e.g. mesolimbic pathway: VTA → ventral striatum).
 - Dopamine is associated with movement and reward.
 - Damage to dopaminergic neurons in the substantia nigra results in Parkinson’s disease.
- (3) Dopamine neurons act through RPE.
 - Almost all abused drugs act upon the dopamine system.
 - Some drugs activate dopamine neurons, e.g. nicotine, morphine.
 - Some drugs block the reuptake of dopamine, e.g. cocaine, methamphetamine (meth).
 - Dopamine neurons can respond to “errors” in predicted reward values.

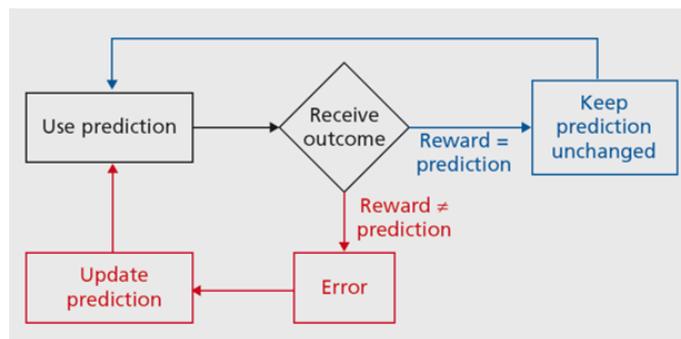


FIGURE 3.26. Scheme of learning by prediction error.

- They alert the brain to the presence of stimuli.
- Then, they begin encoding for the rewarding-ness of the stimuli (i.e. develop “expectations” of a reward).

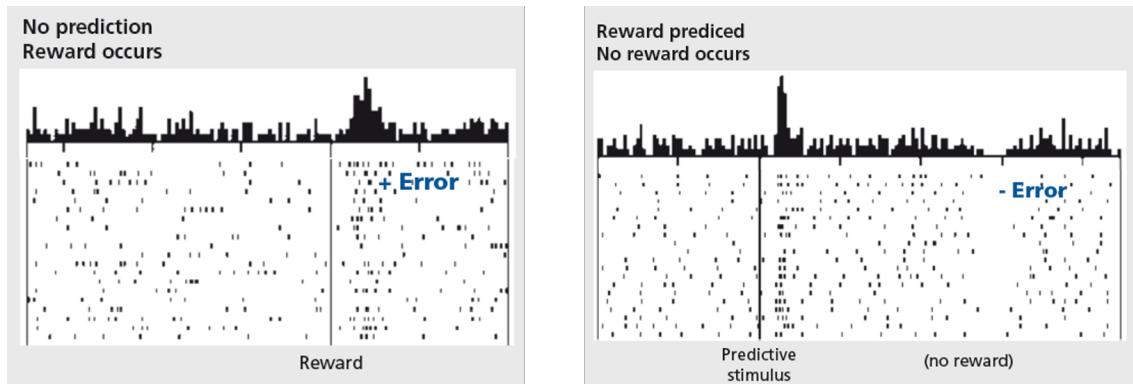


FIGURE 3.27. Dopaminergic neuron activity in response to RPE.

- Feelings of pleasure can adapt to new baselines.
 - Dopamine neurons update their firing rate after several exposures.
 - A repeat of the initial dopamine “rush” requires greater stimulation than before.

3.8. Psychological Disorders.

3.8.1. What is a mental disorder?

- (1) Mental disorders are currently classified by checklists of symptoms.
 - This is problematic because of **diagnostic heterogeneity**.
 - For the majority of conditions, two people can receive the same diagnosis without any common symptoms.
 - In DSM-5, there are over 270 million combinations of symptoms that would meet the criteria for both PTSD and MDD. When 5 other common diagnoses are added, this rises to one quintillion combinations.
 - There are over 24,000 possible symptom combinations for panic disorder in DSM-5, but only 1 combination for social phobia.
 - There is a large overlap in genes that increases risk across multiple disorders, as well as other physiological biomarkers.
 - Our understanding of the underlying causes of mental illnesses is still relatively poor.
- (2) The current dogma is that mental disorders are *categorical* (i.e. discontinuous from health and from each other).
 - There is an alternative view that mental disorders are an arbitrary division along a continuum (from health and from each other).
 - For example, everyone has some degree of depression (and low levels are considered “healthy”).

3.8.2. Substance abuse.

- (1) Drugs bind to receptors and up- or down-regulate synaptic activity in a variety of ways.
 - **Agonists** are drugs that occupy receptors and activate them.
 - **Antagonists** are drugs that occupy receptors but do not activate them; they block receptor activation.
 - **Drug affinity** refers to the tendency of a drug to bind to a receptor.
 - **Drug efficacy** refers to the tendency of a drug to activate a receptor.
 - Different people have different types of receptors, so they may respond differently to drugs (i.e. variability).

- Some examples of how drugs may influence the synaptic activity of dopamine are shown in the diagram below:

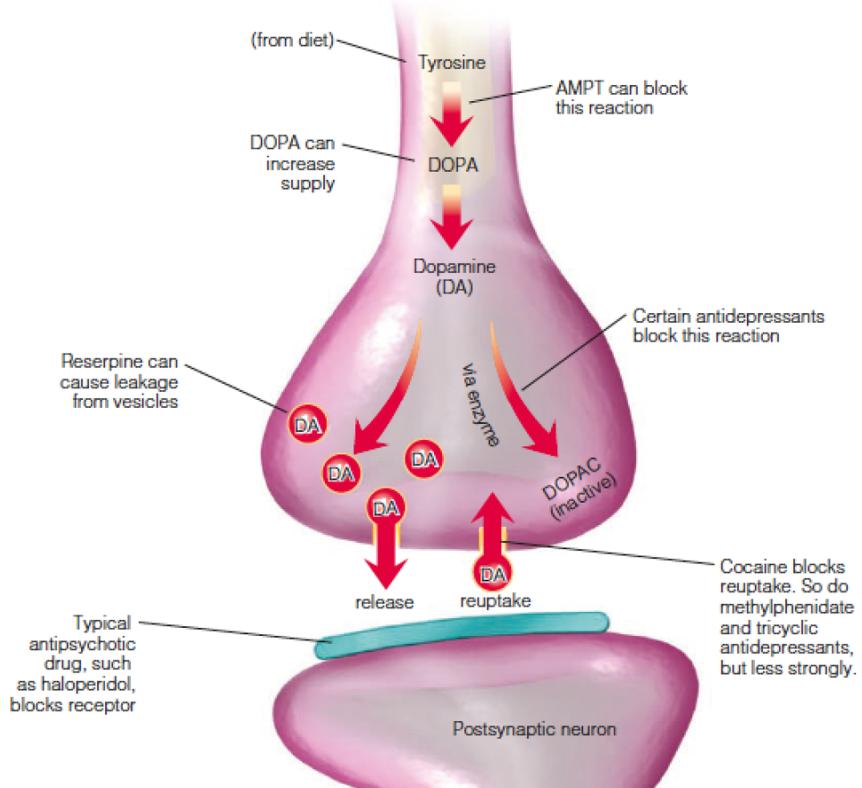


FIGURE 3.28. Dopamine activity in response to different drugs.

Drugs may affect:

- the production of dopamine.
- the release of dopamine.
- dopaminergic receptors.
- how long dopamine is present in the synaptic cleft.

(2) Genetic and environmental factors can predispose individuals to developing substance abuse disorders.

- **Addiction** is the compulsive engagement in *rewarding* stimuli, despite adverse consequences.
 - Even though there are differences between addictive substances and activities, they are similar in that both affect either dopamine or norepinephrine.
- Genetically, many addiction-related genes have been identified (e.g. genes that influence the effect of alcohol), but each gene has a very small effect on the risk of substance abuse.
- Environmentally, the prenatal, childhood, and adult environments are critical on the risk of substance abuse (e.g. use of heroin in the Vietnam war).

- (3) Substance abuse leads to alterations in the dopamine system, which causes **tolerance** and **withdrawal**.
- Nearly all drugs of abuse increase the activity of the dopamine and norepinephrine synapses.

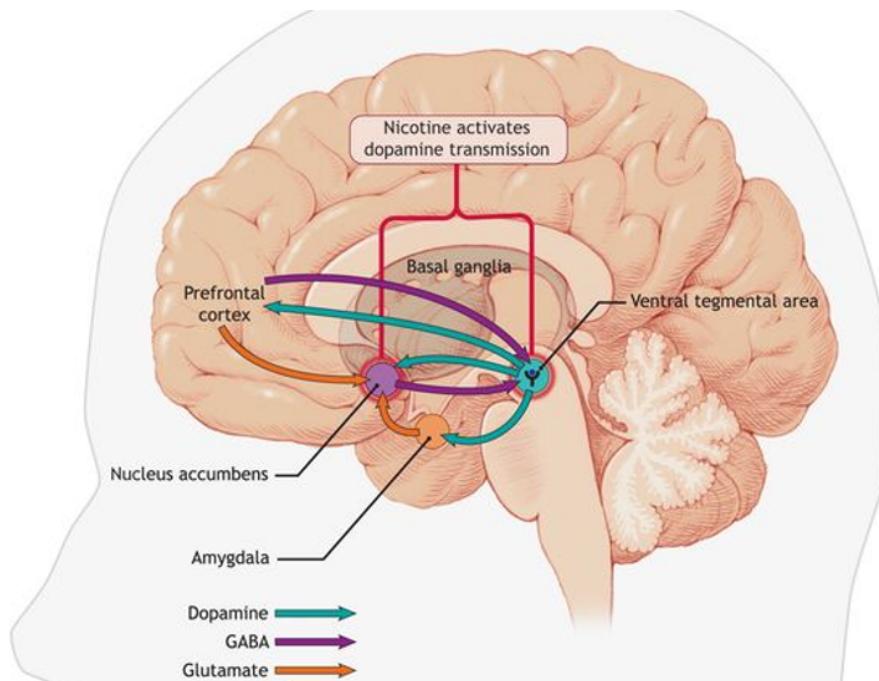


FIGURE 3.29. Effects of nicotine on the brain.

- These neurotransmitters are released in the **nucleus accumbens**.
 - The nucleus accumbens activates in response to drug consumption. It also responds to sexual excitement, music, taste of sugar, and other pleasurable experiences.
 - Repeated exposure to addictive substances may:
 - Increase the number of receptors on GABA-ergic neurons in the nucleus accumbens.
 - Increase receptor sensitivity.
 - Increase the metabolism of substances in the bloodstream (e.g. alcohol).
- These changes lead to **drug tolerance**: the effects of the drug decreases, thus requiring a higher dose to achieve the same effect.
- This may result in the **reward deficiency syndrome**, where patients experience reduced subjective pleasure, and so they seek out stronger rewards. For example:
 - Cocaine abusers have reduced dopamine release in the nucleus accumbens, and a reduced “high” compared to controls.
 - They also had increased response in the thalamus, which was associated with cocaine **craving** (i.e. uncontrollable desire for the substance).
 - These changes also lead to **withdrawal symptoms** (i.e. symptoms that occur after drug cessation), which include:
 - Shaking.
 - Vomiting.
 - Fatigue.
 - Hallucinations.
 - Convulsions.
 - Addicts develop **conditioned tolerance** to the place where they usually take drugs.
 - Taking the usual dose of drugs in an unusual setting can cause the effects of an overdose.

3.8.3. Depressive disorders.

- (1) Depressive disorders cause decreased mood, energy, and motivation, changes in sleep and appetite, and cognitive impairment.
 - They are more common in women during the reproductive years.
 - Genetic and environmental factors both cause them to develop.
 - Many genes have been linked to depression (but each has a very small effect).
 - People with early-onset depression (i.e. before the age of 30) are more likely to have relatives with depression.
 - Late-onset (after the age of 45) are linked to relatives with circulatory problems.
 - Stressful events can also help precipitate depression in vulnerable individuals.
 - Young adults with the short form of the *serotonin transporter gene* who experienced stressful experiences have a major increase in the probability of developing depression.
- (2) Depression is associated with a hyperactive right hemisphere and a hypoactive left hemisphere.
 - Depressed patients may have insufficient release of dopamine.
 - The activation of the nucleus accumbens is lower in depressed patients who were asked to sustain positive emotions.
 - Drugs like *bupropion*, which inhibits dopamine reuptake, can be effective in treating depression.
- (3) Depression is also strongly associated with sleep.
 - Insomnia is a common symptom of depression.
 - Sleep difficulties often precede and predict the onset of depression.
 - Sleep deprivation (temporarily) relieves symptoms of depression.
 - This is thought to be due to a build-up of adenosine.
- (4) Seasonal affective disorder (SAD) is depression that occurs during certain seasons (usually winter).
 - Patients usually have phase-delayed rhythms.
 - **Light therapy/Light-box treatment** is often used to help regulate circadian rhythms.
- (5) Established treatments for depression include antidepressant medication and psychotherapy.
 - Most common antidepressants alter **serotonin**, **norepinephrine**, and/or **dopamine** neurotransmission (mainly by inhibiting their reuptake).
 - Less reuptake of these neurotransmitters would like to a prolonged presence of these neurotransmitters in the synaptic cleft.
 - However, it is very likely that this is **not** the reason why antidepressants work.
 - Other treatments include:
 - **Cognitive-behavioural therapy (CBT)** has proved to have strong antidepressant benefits (on par with drugs).
 - **Exercise** also has modest antidepressant benefits.
 - **Electroconvulsive therapy** is often used as a last recourse, and its mechanism is unknown.
 - Newer treatments, e.g. transcranial magnetic stimulation (on the left dorsolateral prefrontal cortex) and deep brain stimulation, are promising alternatives.
- (6) **Bipolar disorder** is characterized by episodes of mania and depression.
 - Bipolar I: full blown manic disorder.
 - Bipolar II: hypomania.
 - It can be treated by mood stabilizers such as **lithium**.
 - Affected individuals have deteriorating ability to function in everyday life for at least 6 months, paired with at least two of the following symptoms (including at least one of the first three):
 - Hallucinations.
 - Delusions.
 - Disorganized speech.
 - Grossly disorganized behaviour.
 - Weak or absent signs of emotion, speech, and socialization.

3.8.4. *Schizophrenia.*

- (1) **Schizophrenia** is a psychotic disorder that features **positive** (i.e. behaviours that are present but should be absent) and **negative** (i.e. absent behaviours that should be present) symptoms.
 - Positive symptoms include delusions and hallucinations.
 - Negative symptoms include disorganized thought, due to a dysfunction of working memory, which in turn is due to abnormal connections between the cortex, thalamus, and cerebellum.
- (2) It is caused by a complex combination of genetic and environmental factors.
 - The more closely an individual is biologically related to someone with schizophrenia, the greater their probability of having schizophrenia.
 - A large number (>100) of genes are associated with schizophrenia risk. They code for proteins which affect dopamine and glutamate synapses, as well as calcium channel functioning.
 - An important factor in the development of schizophrenia is a disturbance in the development (in-utero and in early childhood).
 - Intermediate risk factors include living in a crowded city, and owning cats during childhood.
 - Lower risk factors include poor nutrition, infections, and stress during pregnancy, as well as head injury during early childhood.
 - Most results are not consistent across patients, but in general, brains of people with schizophrenia have:
 - Smaller left prefrontal and temporal cortices.
 - Smaller cell bodies in the hippocampus and dorsolateral prefrontal cortex.
 - A more dominant right hemisphere.
 - A difficulty in perceiving and identifying smells is also a diagnostic indicator of schizophrenia.
- (3) **Dopamine** and **glutamate** are the two neurotransmitters primarily implicated in the disorder.
 - The dopamine hypothesis:
 - Drugs that block dopamine synapses work as antipsychotic drugs.
 - There is increased dopamine release during the first psychotic episodes.
 - Substance-induced psychotic disorder, with similar symptoms as schizophrenia, is induced by drugs such as cocaine, which increase dopamine in synapses.
 - The glutamate hypothesis:
 - Drugs that block dopamine synapses also affect glutamate activity indirectly.
 - Schizophrenia is associated with less release of glutamate, and a lower count of NMDA receptors.
 - PCP (“angel dust”) is a drug that inhibits NMDA receptors, and it induces many of the positive and negative symptoms of schizophrenia.

3.8.5. Antisocial personality disorder.

- (1) **Antisocial personality disorder** is characterized by repeated disregard for the rights and feelings of others, and may lead to **psychopathic behaviour** (i.e. persistent violent social behaviour).
- It develops because of deficits in empathy and emotional responses to wrongdoing, rather than due to deficits in knowledge of what is moral.
 - There are differences in the brain between individuals with APD and normal individuals.

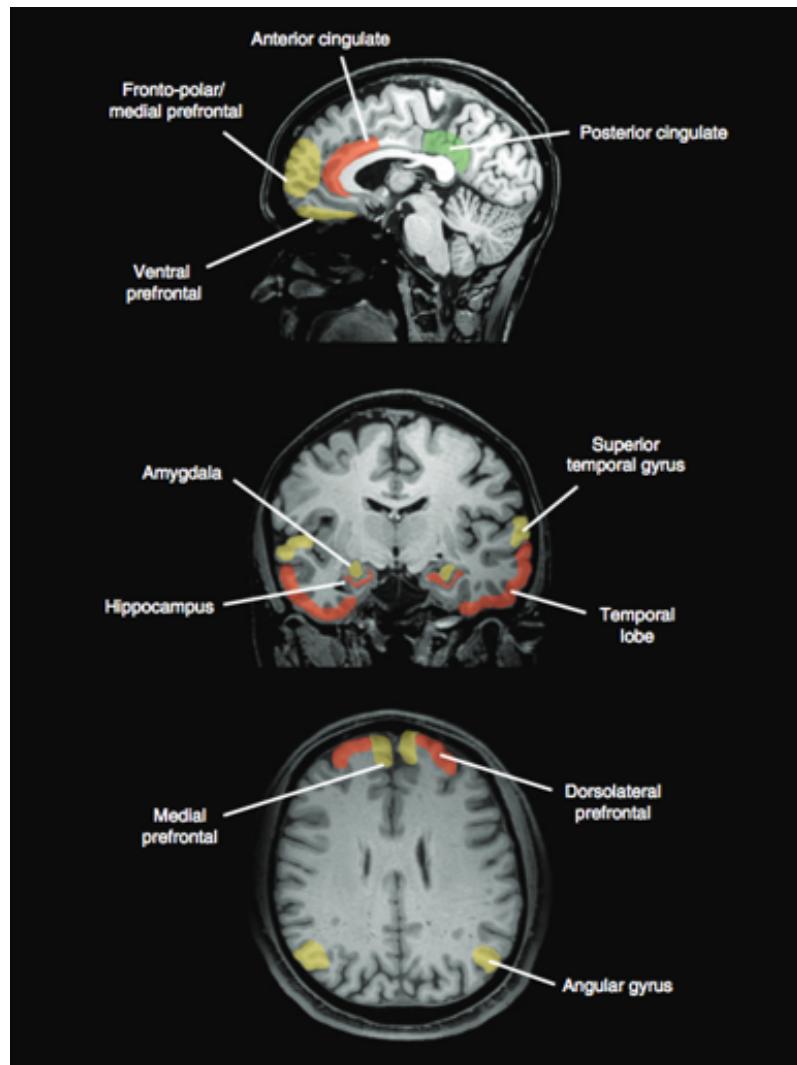


FIGURE 3.30. Brain regions affected by APD.

- The red regions are impaired in antisocial individuals.
 - The green regions are impaired in individuals with impaired moral decision-making.
 - The yellow regions are impaired in both groups of individuals.
- These areas generally have less gray matter and poorer functioning.