Emotions

- Common emotions– happiness, anger, surprise, fear, sadness
- Very subjective– same stimulus does not give same response in all people in all situations
- Emotions are strongly tied to the visceral motor system (emotional feeling)
- Also tied to somatic muscle responses– especially facial muscles (emotional expression)
- Limbic system– brain areas especially important for emotions (emotional thinking)
- Affective (mood) disorders– e.g. depression

Speaker notes

emotion
: a natural instinctive state of mind deriving from one's circumstances, mood, or relationships
: instinct

viscera
: of or relating to viscera
: relating to deep inward feelings rather than to the intellect

intellect
: the faculty of reasoning and understanding objectively

objective
: not influenced by personal feelings or opinions in considering and representing facts

subjective
: based on or influenced by personal feelings, tastes, or opinions

Lincoln's melancholy

Abraham Lincoln:

> *I am now the most miserable man living. If what I feel were equally distributed to the whole human family, there would not be one cheerful face on earth. Whether I shall ever be better, I cannot tell; I awfully forebode I shall not. To remain as I am is impossible. I must die or be better, it appears to me.*

Speaker notes

Abraham Lincoln:

> *I am now the most miserable man living. If what I feel were equally distributed to the whole human family, there would not be one cheerful face on earth. Whether I shall ever be better, I cannot tell; I awfully forebode I shall not. To remain as I am is impossible. I must die or be better, it appears to me.*

Lincoln was unconscious following a horse kicking him in the head for 24hrs at 9 yrs old.

He was clubbed on the head during a robbery attempt in 1828.

mild traumatic brain injuries and mental health.

https://en.wikipedia.org/wiki/Medical_and_mental_health_of_Abraham

https://www.theatlantic.com/magazine/archive/2005/10/lincolns-great-depression/304247/

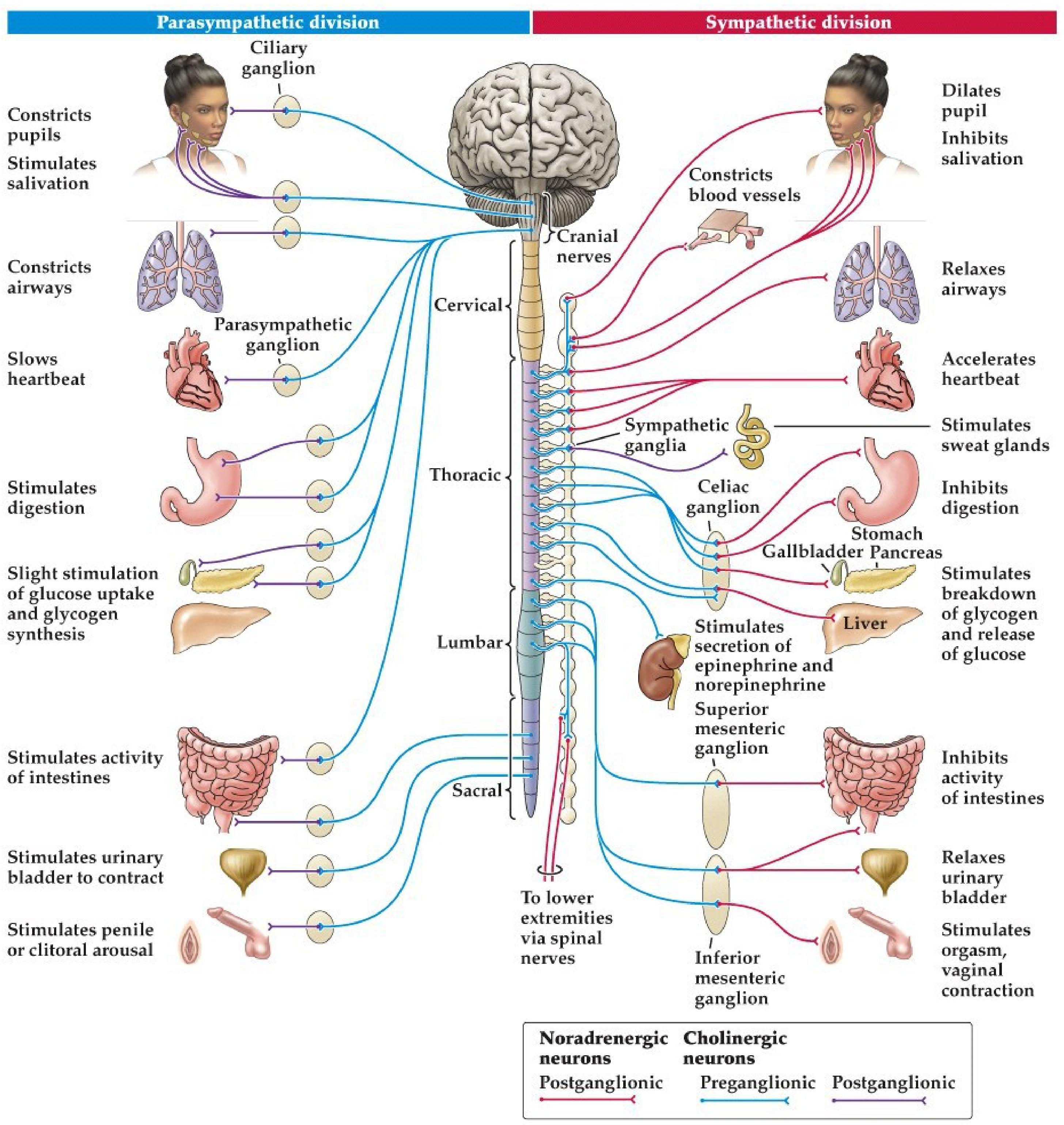
Visceral (autonomic) motor system

- Two main subdivisions– sympathetic and parasympathetic subsystems
- Sympathetic mobilizes the body’s resources for dealing with challenges. Fight or flight response
- Parasympathetic deals with energy storage. Calms the body
- Major locus of control is the hypothalamus and brainstem areas

Speaker notes

No notes on this slide.

Autonomic motor system



Neuroscience 5e Fig. 21.1

Speaker notes

Sympathetic Fight or flight, preganglionc: in the intermediolateral column. Postganglionic: Sympathetic chain

blood vessels in skin and gut contract, rerouting blood to muscles

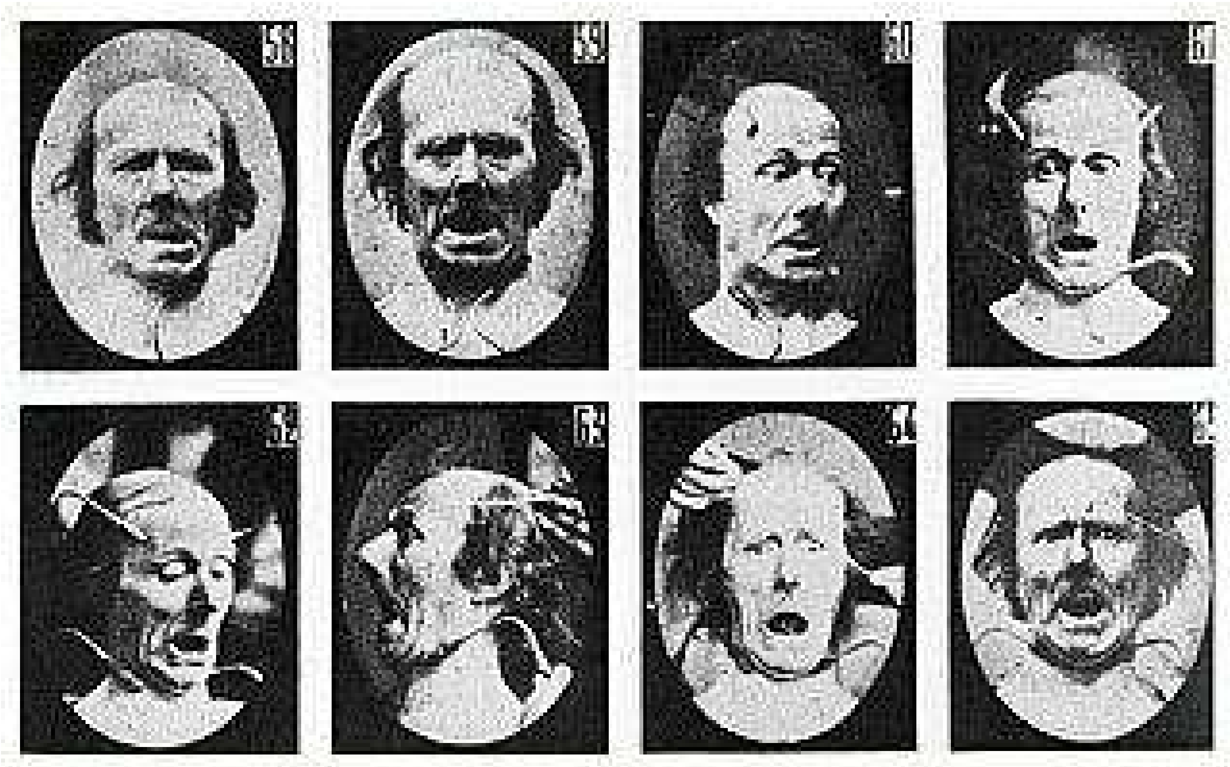
hairs stand on end, piloerection making us look more fearsome, bronchi dilate for incr oxygenation, heart rate accelerates. Sympathetic activity also stimulates adrenal medulla to relesase adrenaline and noradrenaline into the bloodstream to mobilize glucagon release from pancreas.

Parasympathetic:
Preganglionic is in the brainstem or sacral spinal cord, Peripheral ganglia in close to the organ they control (think ciliary ganglion or cardiac plexus)

sympathetic:
preganglionic is in spinal cord, peripheral ganglia is in the specialized sympathetic chain ganglia

Facial expression of emotion

- Duchenne de Boulogne
- Facial muscle stimulation can create a variety of expressions recognizable as emotion



Duchenne de Boulogne *Mecanisme de la Physionomie Humaine* 1862

Speaker notes

Emotions can trigger facial muscles that can't be done on purpose.

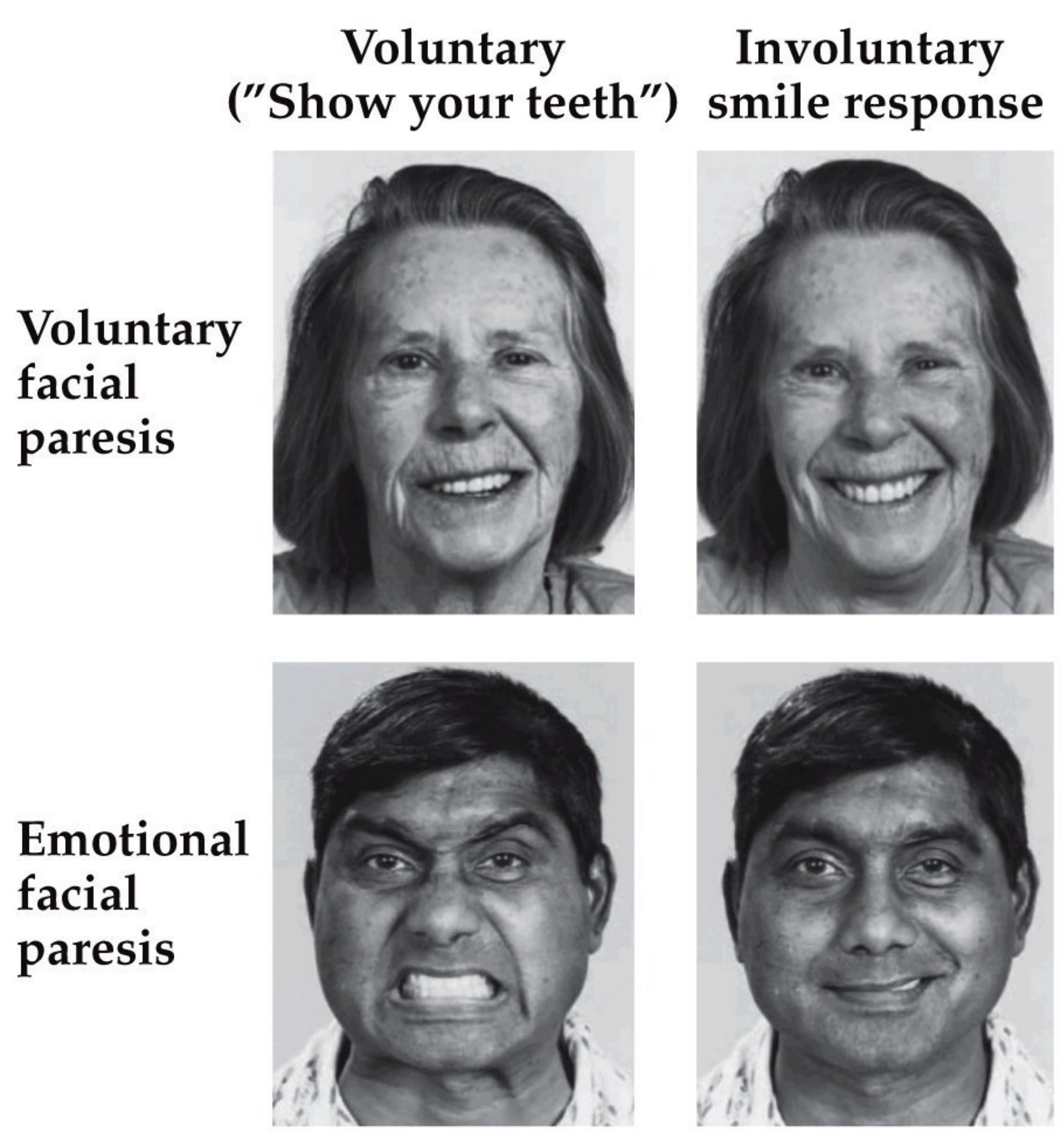
Expression of emotion

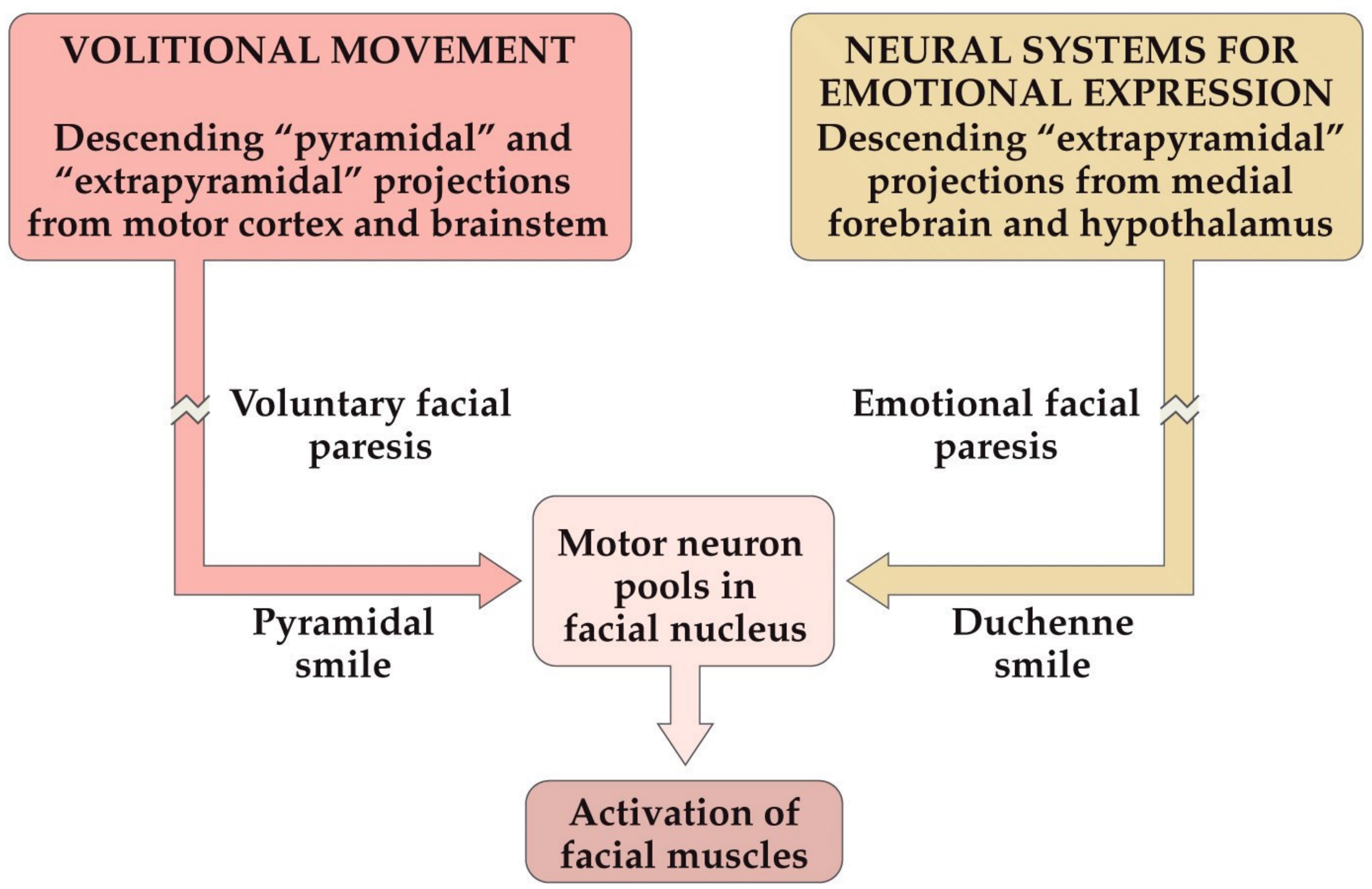
Speaker notes

animals express emotion as well—

Facial expression of emotion

Two pathways to get to facial muscles that display emotion– voluntary and emotional pathways are separable.





Neuroscience 5e Box 29A, Ross and Mathiesen *N Engl J Med* 1998Neuroscience 5e Box 29A

Speaker notes

extrapyramidal system: is a neural network that is part of the motor system causing involuntary movements

pyramidal pathways (corticospinal and some corticobulbar tracts) may directly innervate motor neurons of the spinal cord or brainstem

extrapyramidal system centers on the modulation and regulation (indirect control)

Extrapyramidal tracts are chiefly found in the reticular formation of the pons and medulla, and target neurons in the spinal cord involved in reflexes, locomotion, complex movements, and postural control

paresis: muscle weakness

Hypothalamus as a coordinator of emotional behavior

- Hypothalamus as a critical center for coordination of both the autonomic and somatic components of emotional behavior
- Lesion huge areas of the forebrain in cats and angry behavior occurs spontaneously, including the autonomic correlates of anger. Increased blood pressure and heart rate, dilation of pupil, hair raising. Also contained somatic motor components such as arching the back and tail. Called sham rage
- Sham rage found to require the hypothalamus
- Stimulation of discreet parts of hypothalamus could elicit different behaviors associated with anger

Speaker notes

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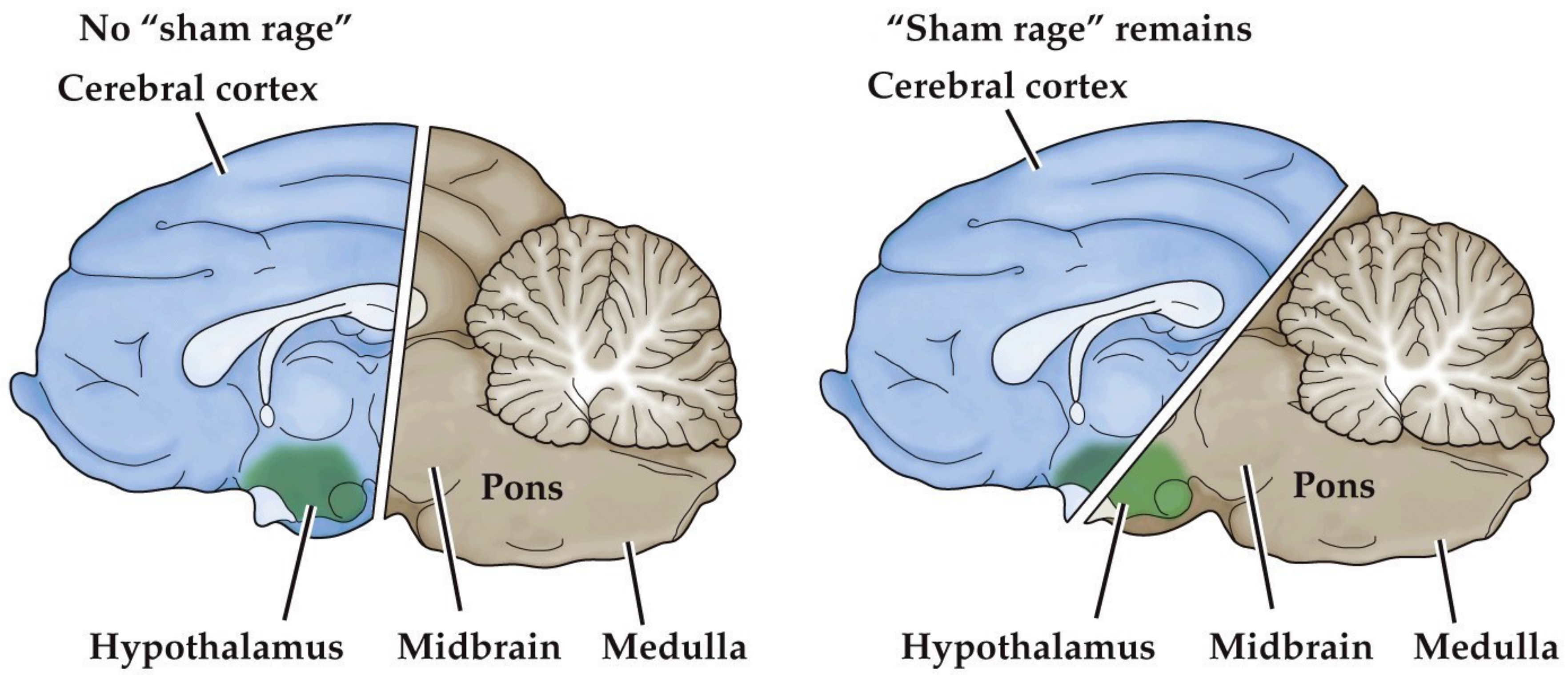
Hypothalamus as a coordinator of emotional behavior

- Phillip Bard / Walter Hess, early 1900s. Conducted seminal studies that determined the hypothalamus is a critical center for coordination of both the autonomic and somatic components of emotional behavior



Neuroscience 5e Fig. 29.1, LeDoux *Handbook of Physiology* 1987

Speaker notes

started by removing cerebral hemispheres of cats, when anesthesia wears off they acted as if enraged. Involved all the autonomic components of the sympathetic nervous system. Called sham rage because no obvious target.

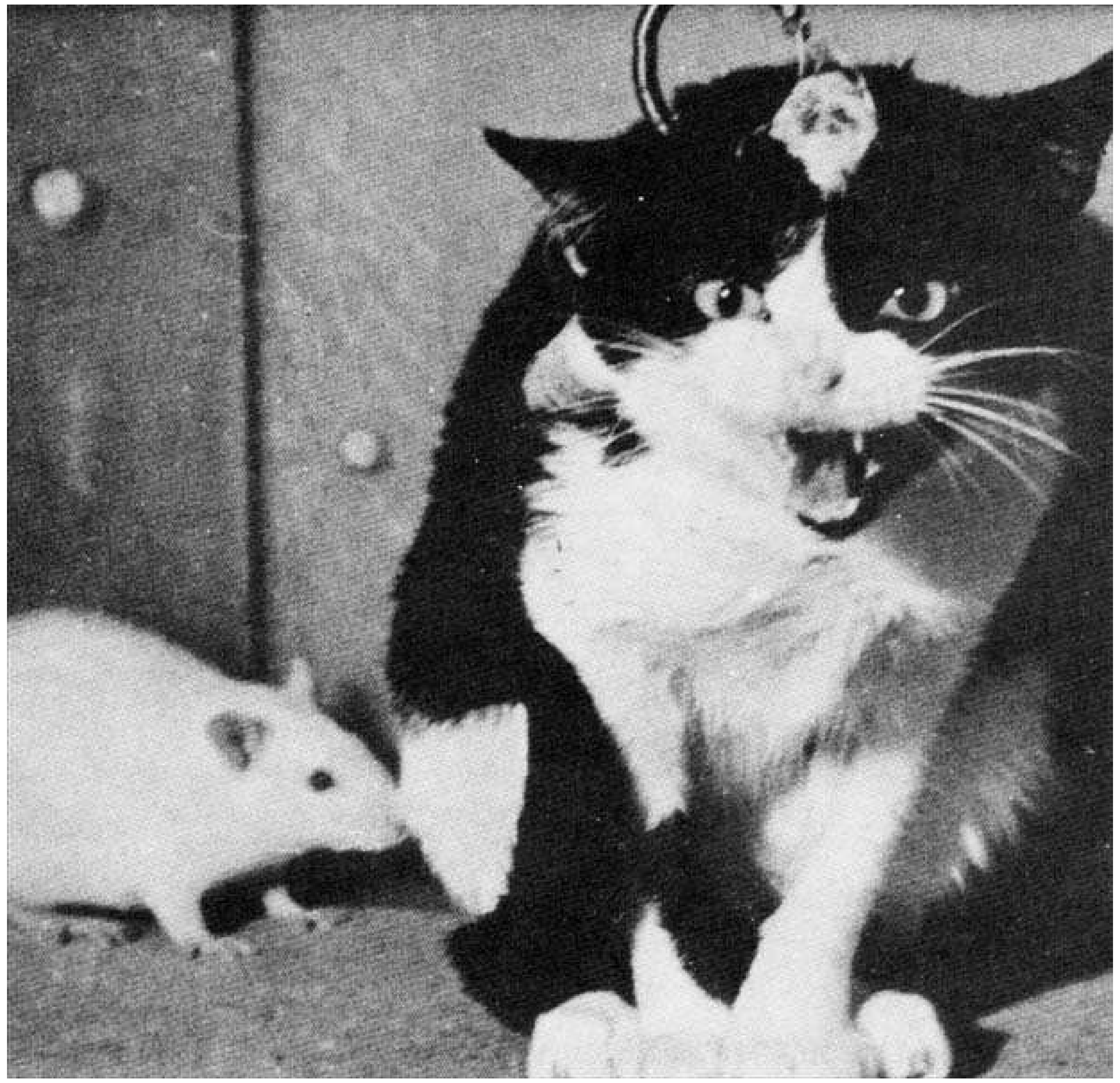
Sham rage: Angry behavior occurred spontaneously included autonomic correlates of anger. Increased blood pressure and heart rate, dilation of pupil, hair raising. Also contained somatic motor components such as arching the back and tail.

Connection from ventral hypothalamus to midbrain needs to be present to elicit sham rage.

Bard suggested that emotional behaviors are often directed towards self-preservation (point also made by Charles Darwin).

Affective attack expression

Sham rage after stimulation of cat medial hypothalamus



Speaker notes

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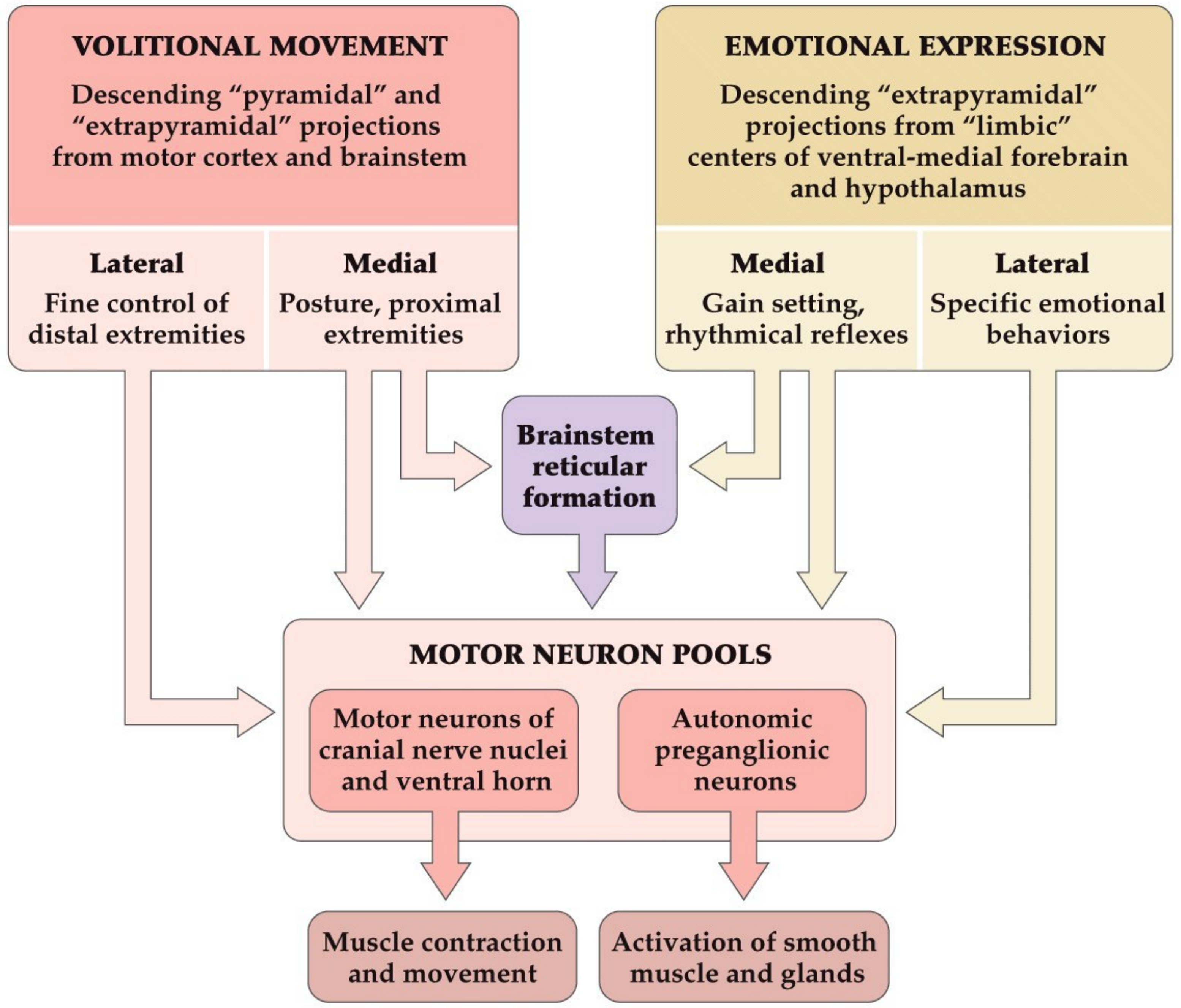
General connectivity of emotions

- Both a volitional (with deliberate action) and a non-volitional component. Are in separate pathways. Both pathways ultimately lead to motor neuron pools that activate muscle contraction or smooth muscle/gland secretions
- Lateral projections control specific movements or emotional behaviors, medial projections provide support for these behaviors

Speaker notes

No notes on this slide.

Descending systems that control somatic and visceral motor pathways in the expression of emotion



Neuroscience 5e Fig. 29.2

Speaker notes

- major targets of the hypothalamus is the reticular formation (tangled nerve web of over 100 cell groups including those that regulate sleep/wakefulness, cardiovascular function, respiration, urination, vomiting, swallowing). Reticular output is to somatic and visceral motor effector systems.

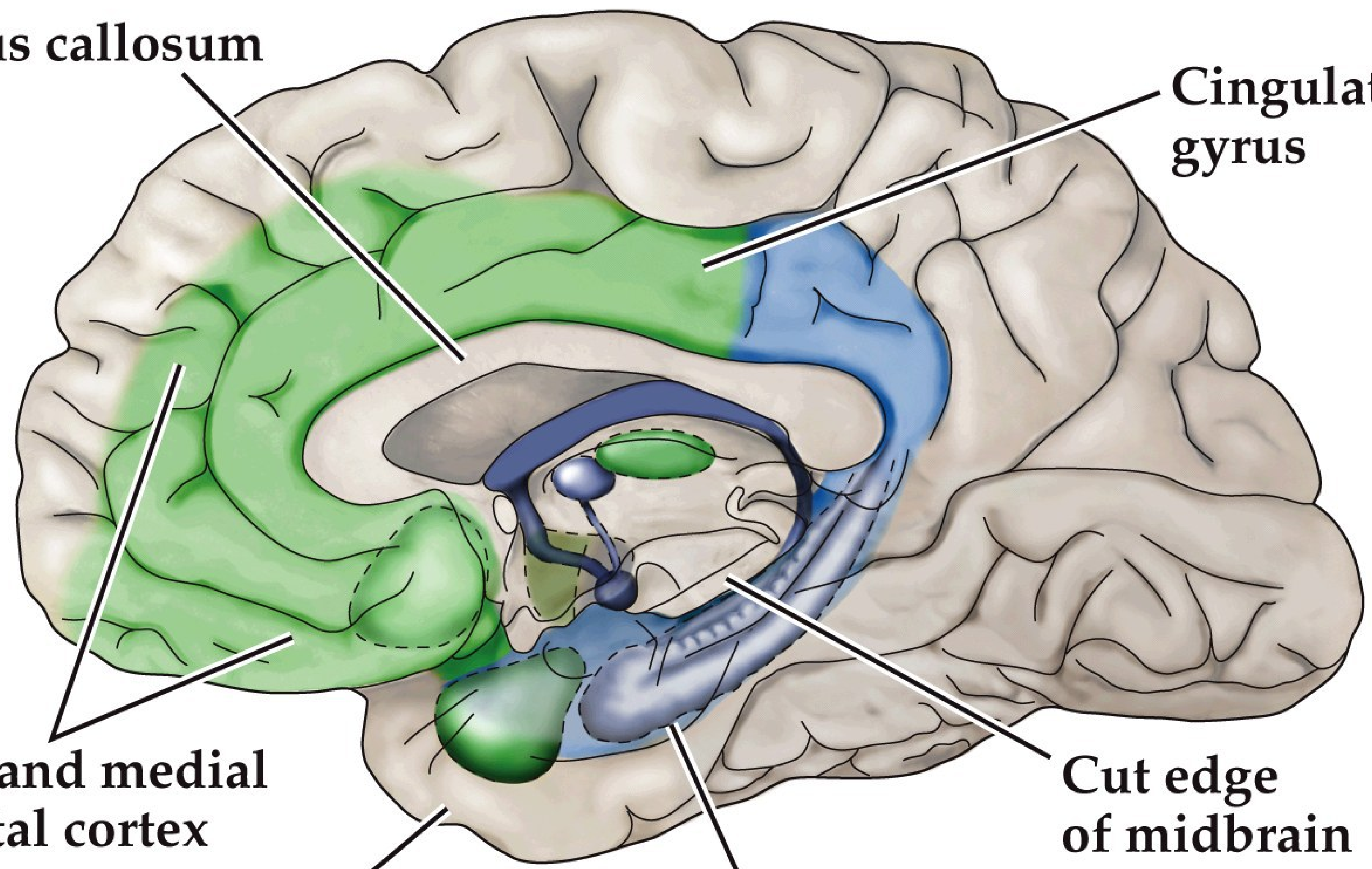
How does your brain regulate emotions?

- Anatomists had shown that there was a subregion of the brain that formed a rim around the corpus callosum and the medial aspects of the cerebral hemispheres
- Contains the hippocampus and cingulate gyrus
- These areas found to form a circuit with other areas, including hypothalamus, amygdala, and parts of the thalamus. Together these areas make up the **limbic system**

Speaker notes

excellent article about emotional control

Limbic system



Neuroscience 5e Fig. 29.4

≡

Speaker notes

The limbic system.

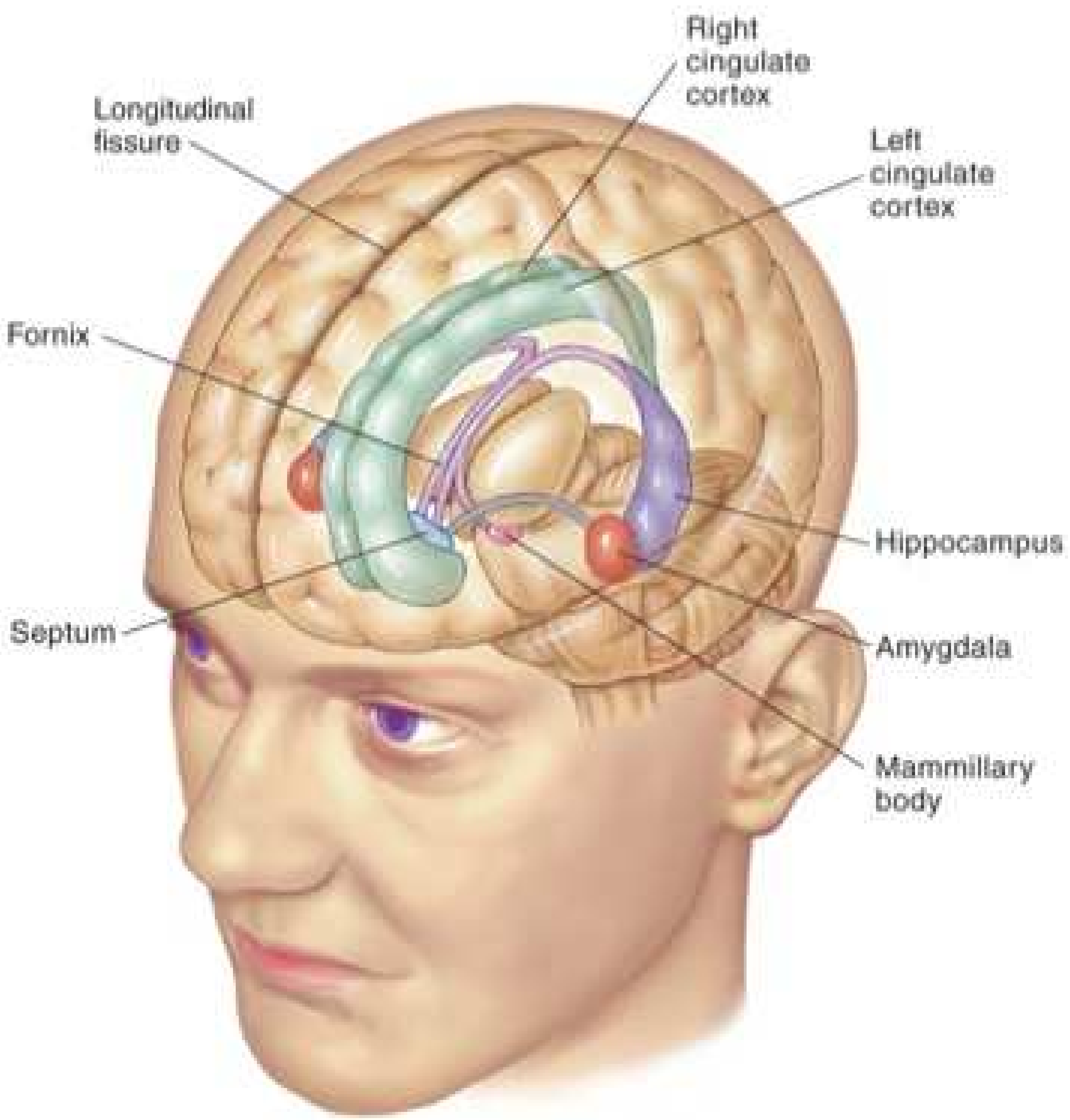
Green is modern view of limbic system critical for processing emotion. Blue includes other areas of the traditional limbic system such as the hippocampus and mammillary bodies that are not considered critical to circuits for emotional processing.

orbitofrontal and medial prefrontal cortex together with the amygdala are especially important components of the limbic systm.

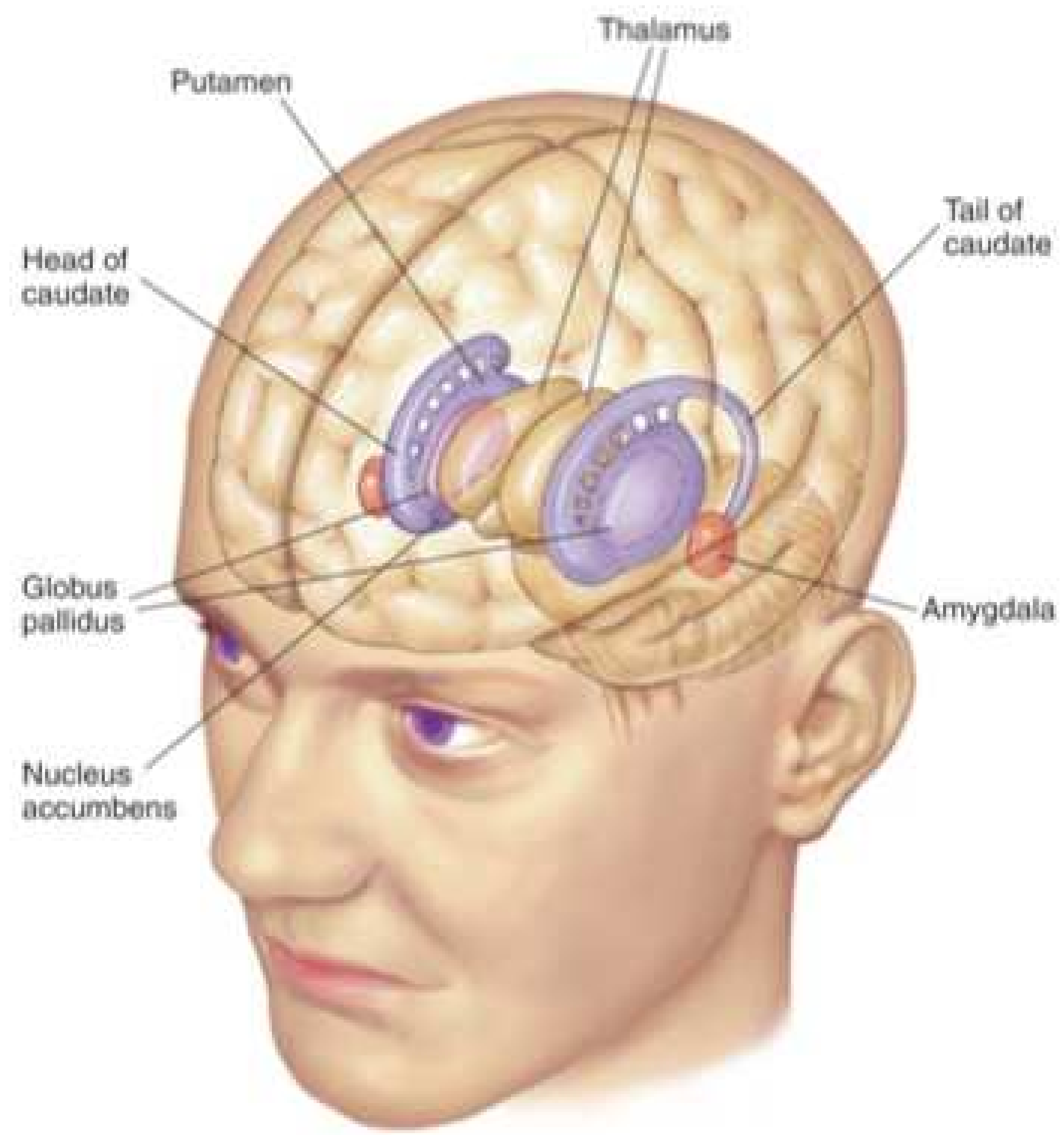
- mammilary bodies are part of the posterior hypothalamus and is important for interconnecting the cingulate cortex with the hypothalamus through the anterior nucleus of the thalamus
- hippocampus projects back to the hypothalamus via the fornix

Limbic system

Limbic system



Basal ganglia



Speaker notes

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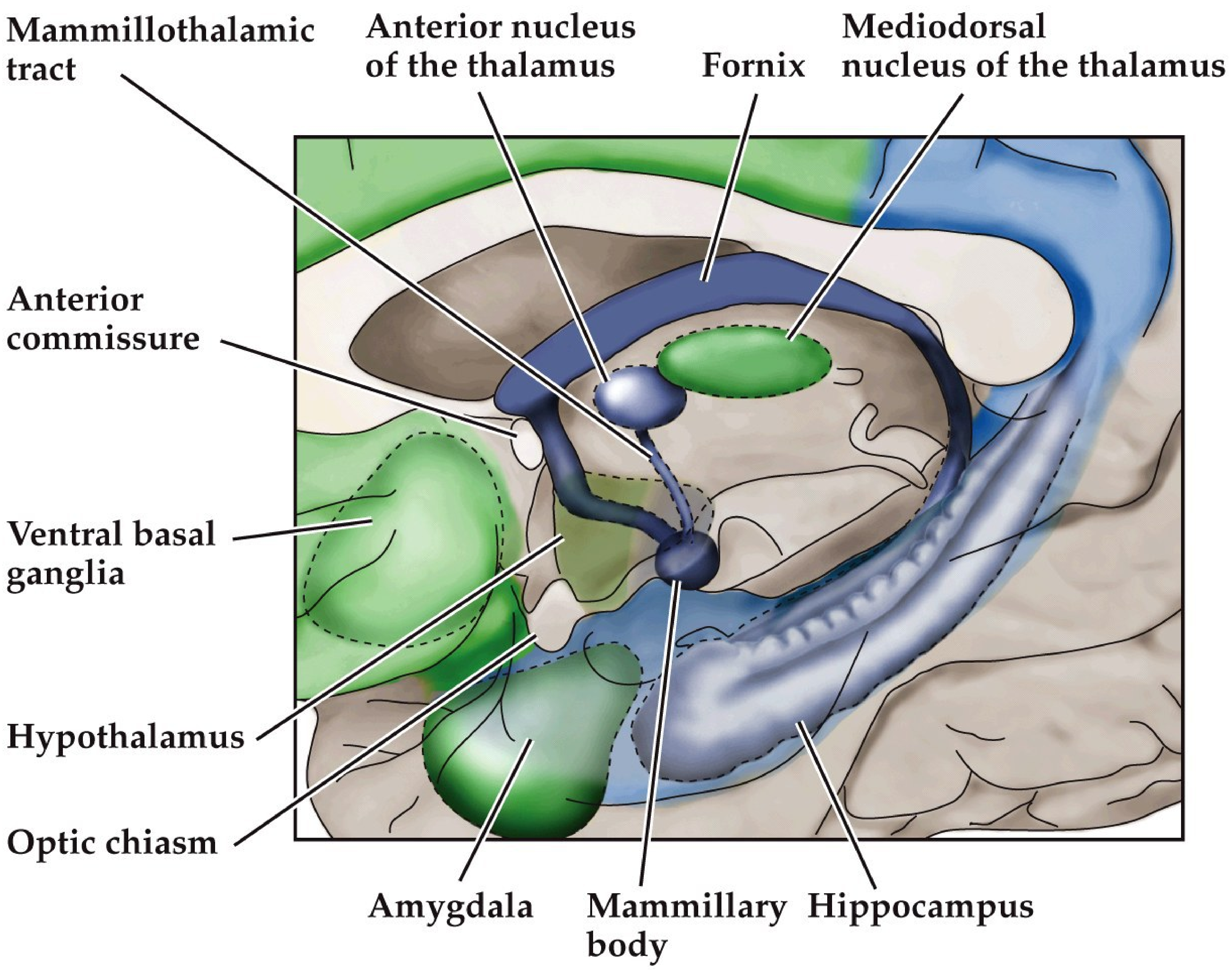
Limbic system



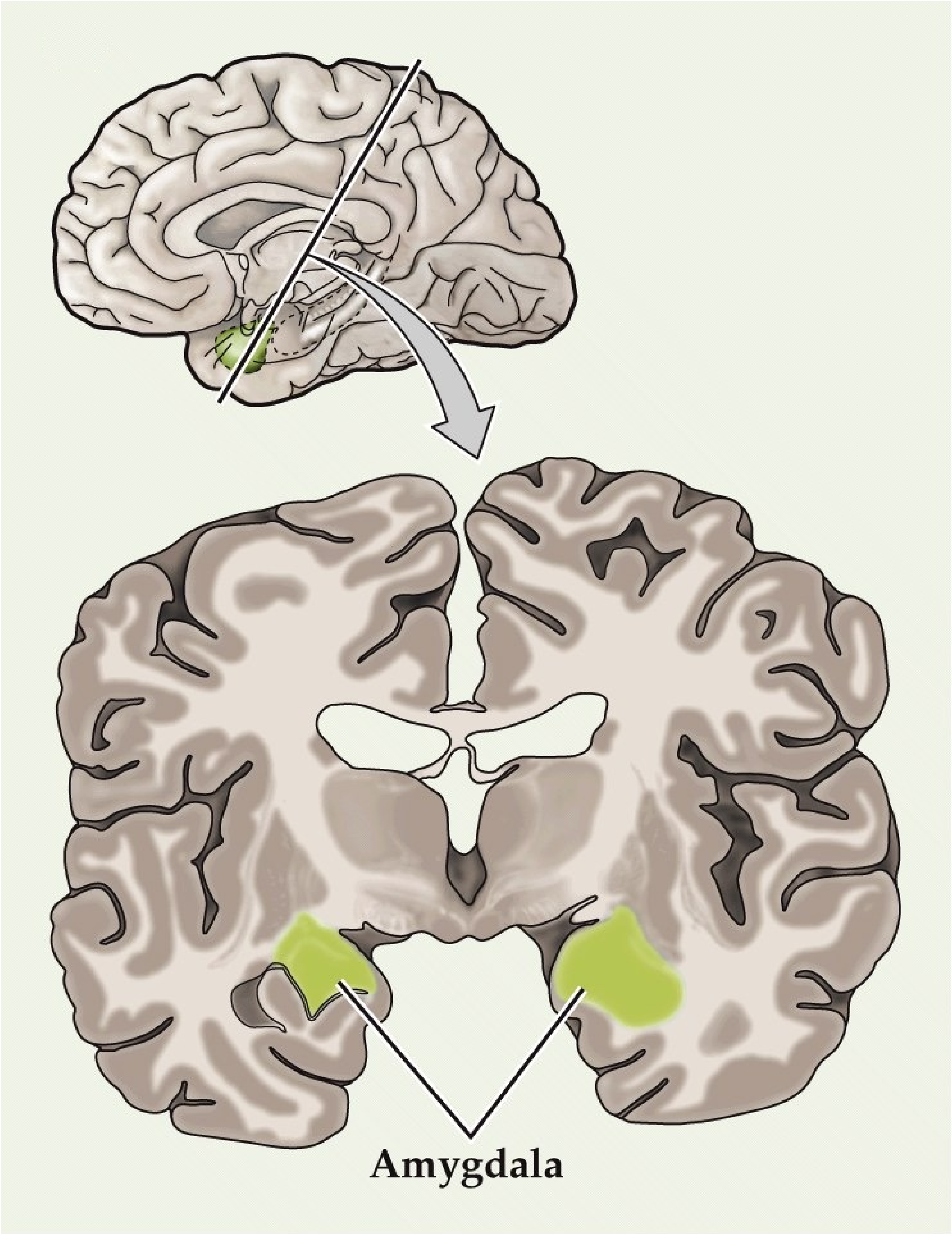
Neuroscience 5e Fig. 29.4

Speaker notes

amgydala—> ventral basal ganglia —> mediodorsal nucleus of thalamus —> orbital and medial prefrontal cortex —> amygdala

amgydala, Latin for ‘almond’

Amygdala



Neuroscience 5e Box 29B

Speaker notes

- amgydala is in the anteior-medial part of the temporal lobe. Rostral to hippocampus
- three major functional and anatomical subdivisions
- medial group
  - connections with olfactory bulb and olfactory cortex
- basal-lateral group
  - large in humans
  - major connections to orbital and medial prefrontal cortex of frontal lobe and association cortex of anterior temporal lobe
- central and anterior group
  - connections to hypothalamus and brainstem (visceral sensory structures like nucleus of solitary tract and parabrachial nucleus)
- hypothalamus receives unprocessed sensory inputs, amygdala receives processed sensory inputs (cortex and thalamus)
- highly complex stimuli often needed to evoke response in amygdala (e.g. facelike neurons)

Crude lesion studies

- John Downer (London in 1950’s) removed the temporal lobes of monkeys and witnessed weird emotional behaviors
- Unable to recognize objects, although not blind (why?)
- Bizarre oral behaviors
- Hyperactivity and hypersexuality, making physical contact with virtually anything
- No longer showed fear. Neither to humans or to snakes
- Eventually the fear behaviors was narrowed down to a region called the amygdala through selective lesion studies

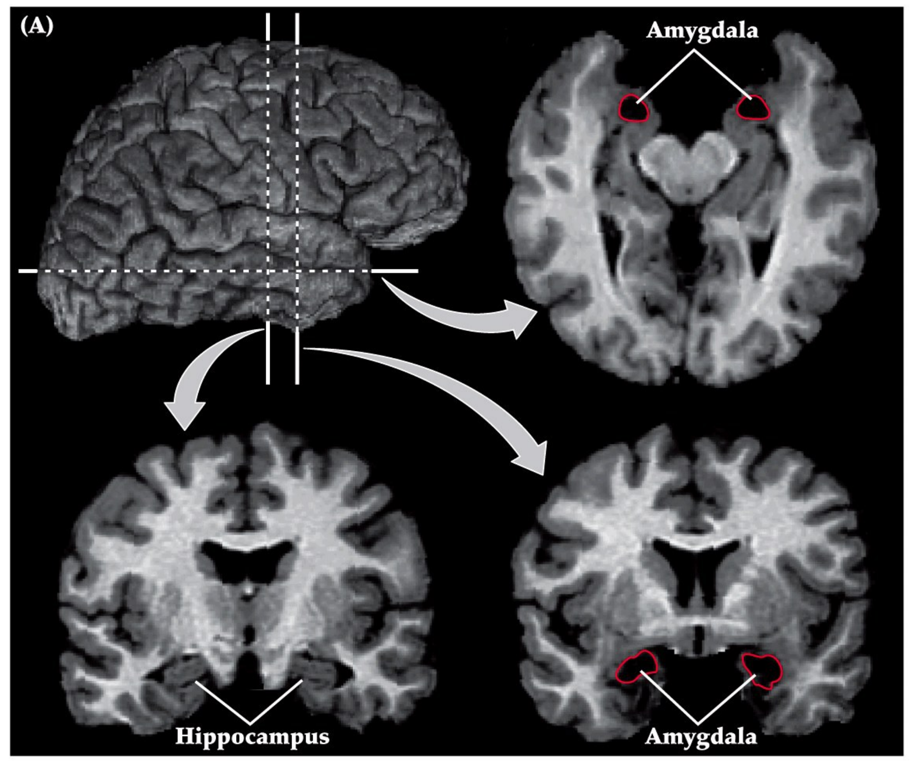
Speaker notes

- Kluver-Bucy syndrome– a disease due to damage of temporal lobe and limbic system https://www.youtube.com/watch?v=7RDFRASiq4M

Patients with amygdala damage exhibit diminished emotional fear recognition and expression

Patient S.M. can't recognize the emotion of fear in photographs. She also exhibits little fear herself (e.g. to dangerous animals, scary houses, films, etc)

Amygdala damage in patient S.M



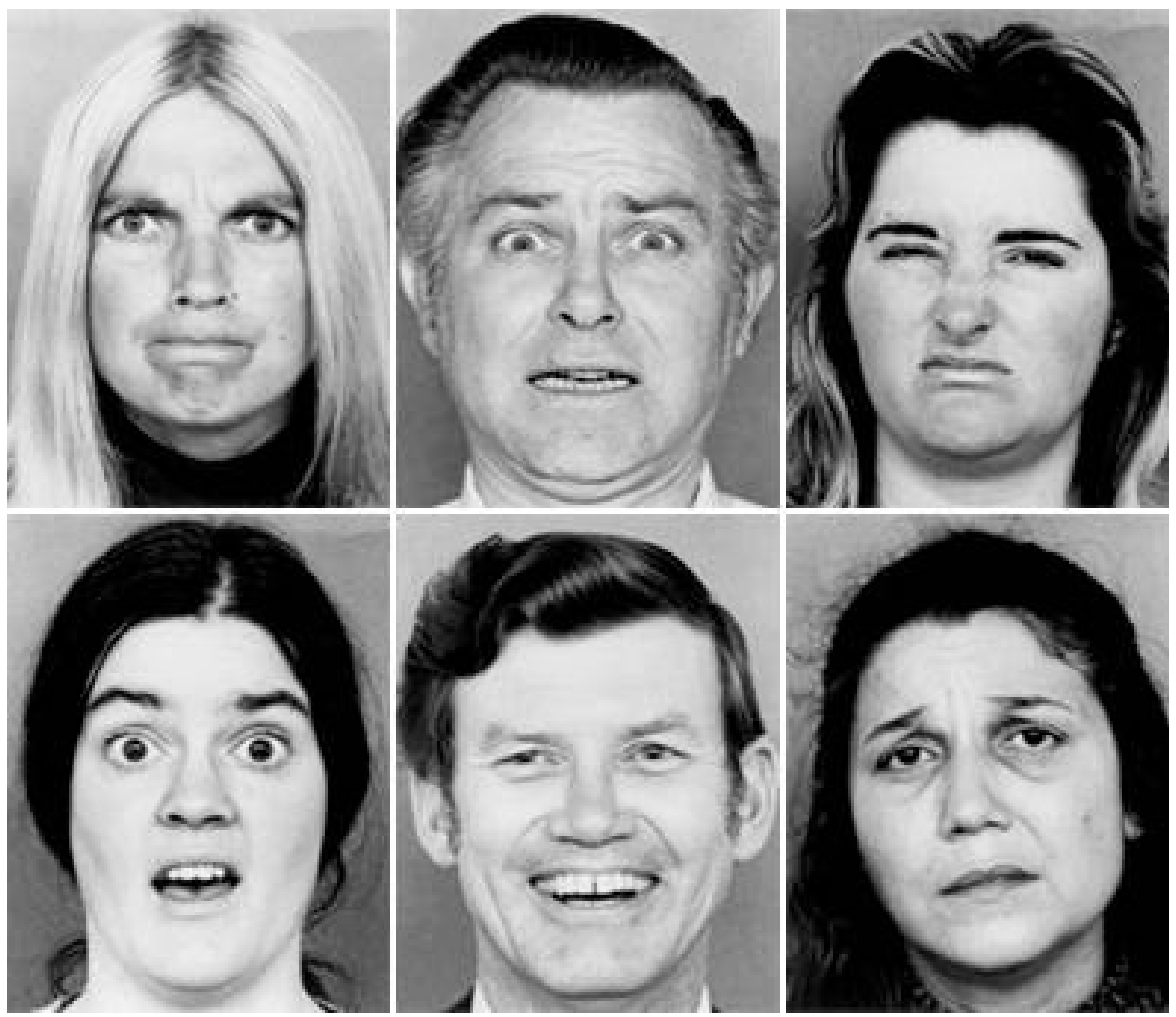
Neuroscience 5e Box 29d

Speaker notes

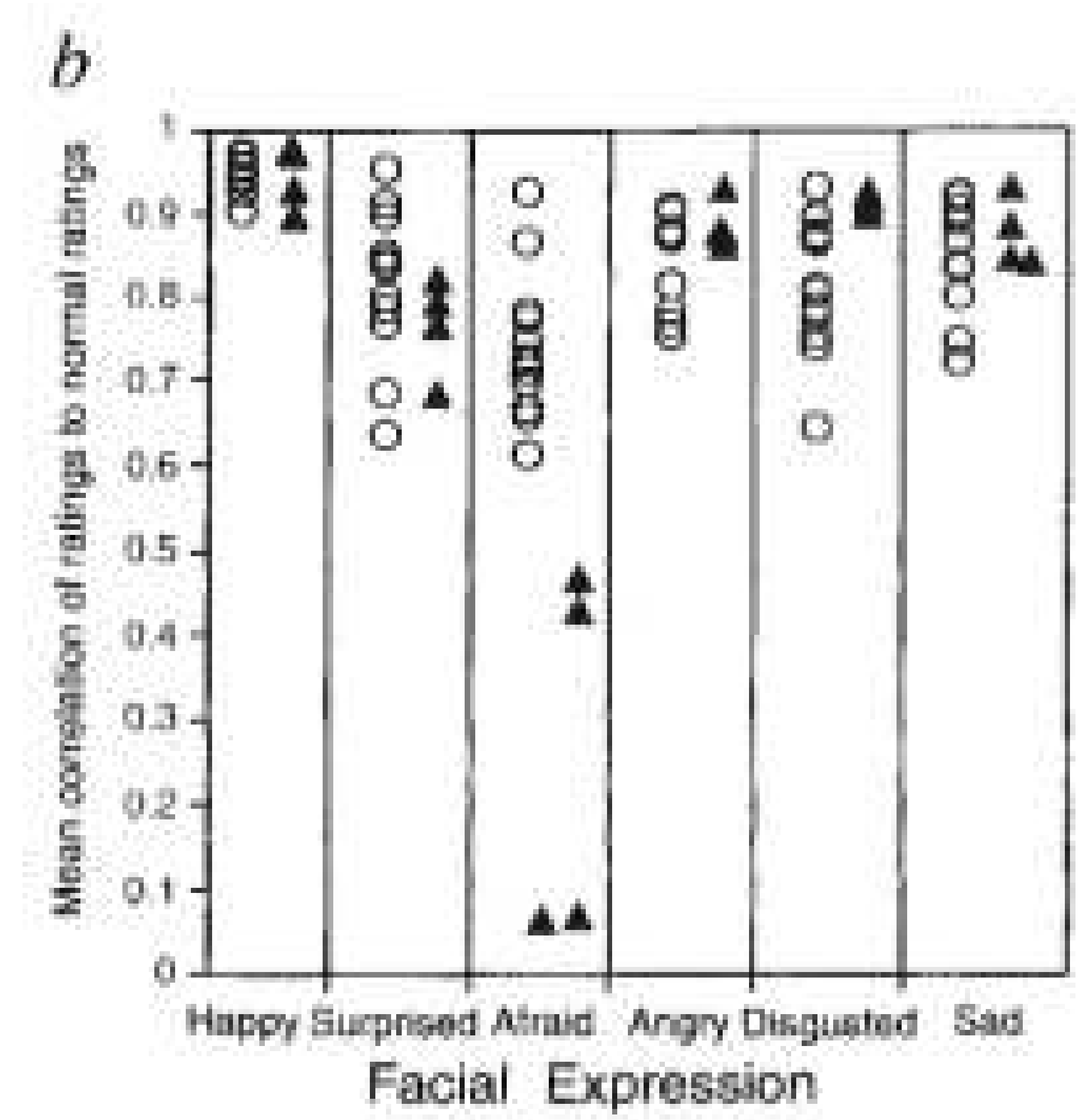
patient SM has rare autosomal recessive condition called Urbach-Wiethe disease. Disorder of bilateral calcification an atrophy of anterior-medial temporal lobes. Both amygdalas are extensively damaged. Little to no injury of the hippocampus.

She has no motor or sensory or intelligence or memory or language impairment. However she can't recognize the emotion of fear in photographs. Furthermore, she exhibits little fear herself (to dangerous animals, scary houses, films, etc).

Patients with amygdala damage exhibit diminished emotional fear recognition and expression



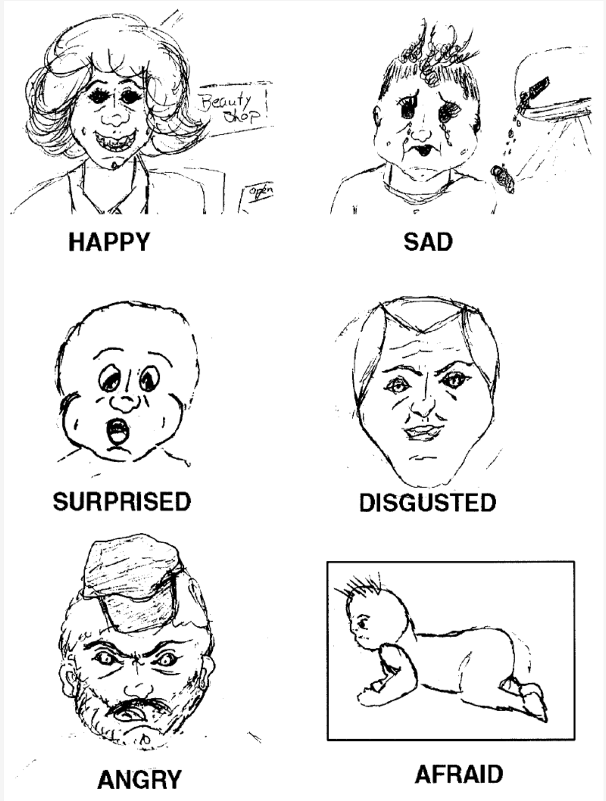
circles: control patients, triangles: amygdala lesion patients



Adolphs et al., *J. Neurosci* 1995

Speaker notes

Adolphs et al., 1995. Subject with bilateral amygdala lesions was asked to draw facial expressions of emotions.



Fear conditioning

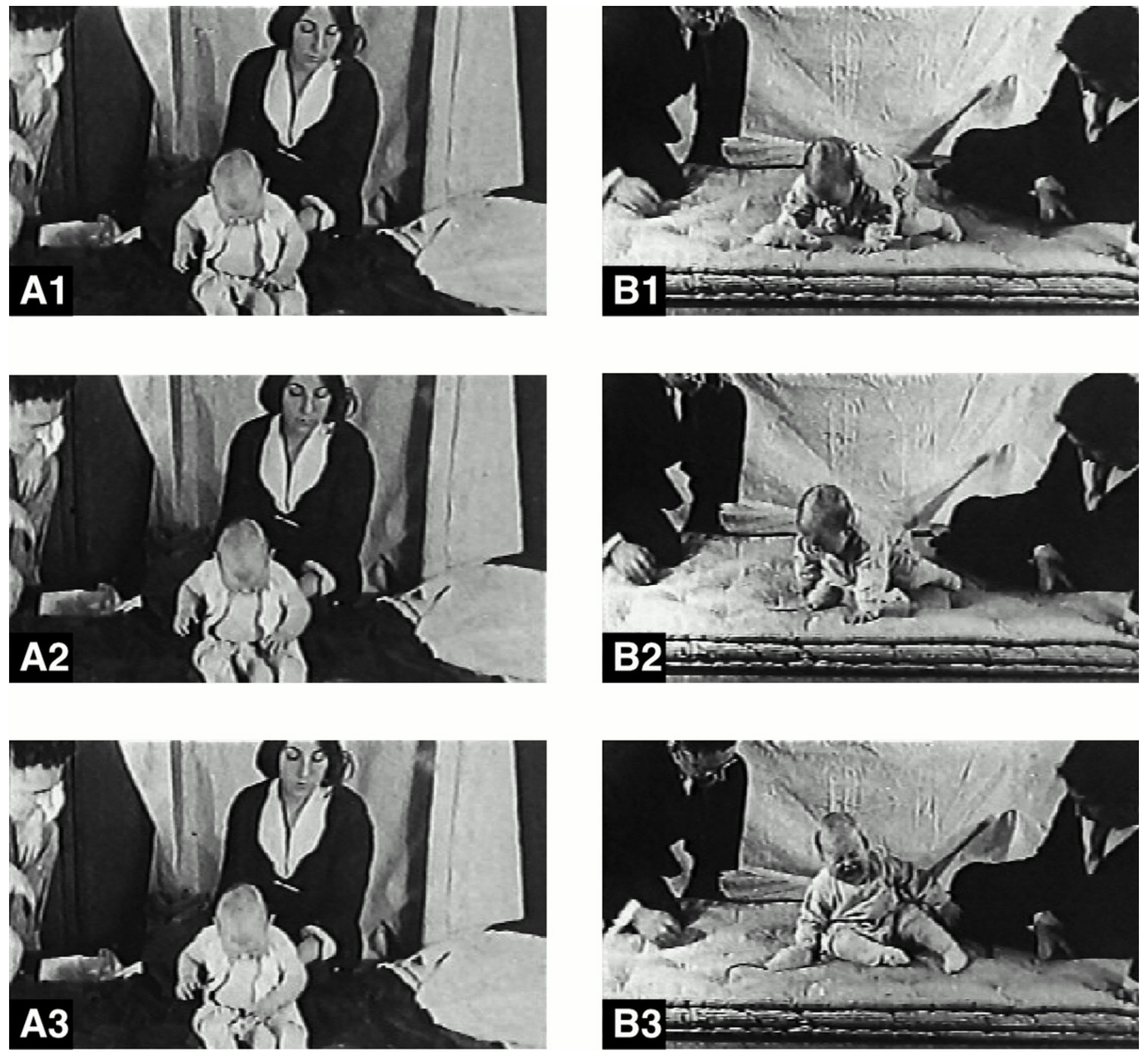
- Pair a normally neutral stimulus with an inherently aversive one. Over time the animal will show behaviors to the neutral stimulus similar to that when given the aversive one. The animal learns to attach new meaning to a stimulus through classical conditioning
- Can use this assay to determine what areas of the brain are required for the learned behavior

Speaker notes

No notes on this slide.

Classic experiments demonstrating fear conditioning in an infant

A white rat presented to an infant does not innately elicit fear, but pairing the rat with an aversive noise, produces crying and attempts to crawl away, even when the rat was presented without the noise.



'Little Albert' experiment, Watson and Rayner *J Exp Psychol* 1920

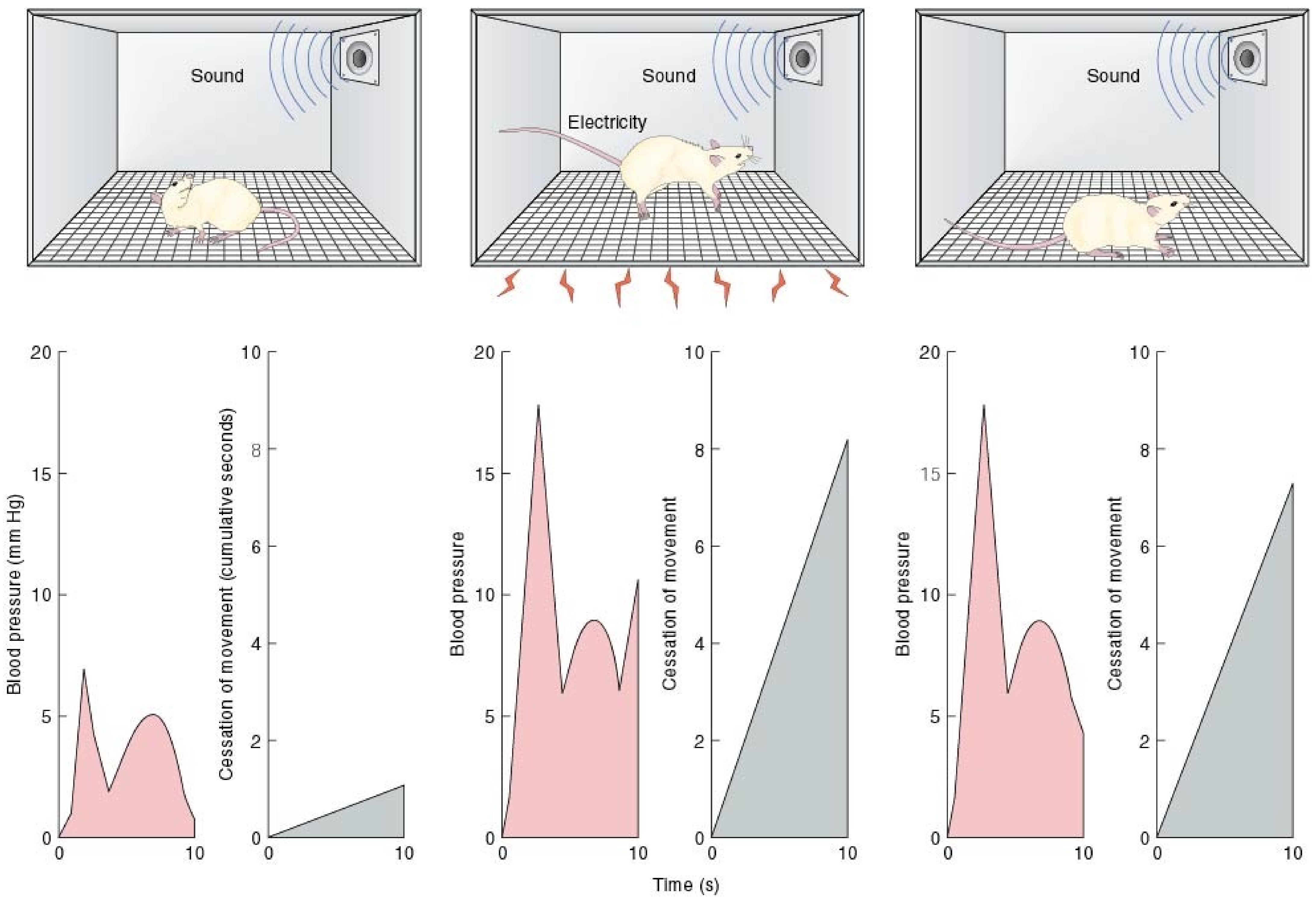
Speaker notes

Classic experiments from Watson and Rayner demonstrating fear conditioning in an infant

As early as the 1920s, fear conditioning was demonstrated in infants. A white rat presented to an infant does not innately elicit fear, but pairing the rat with an aversive noise, produces crying and attempts to crawl away, even when the rat was presented without the noise.

Fear conditioning in rats

Conditioned fear response in rats after associating foot shocks with sound



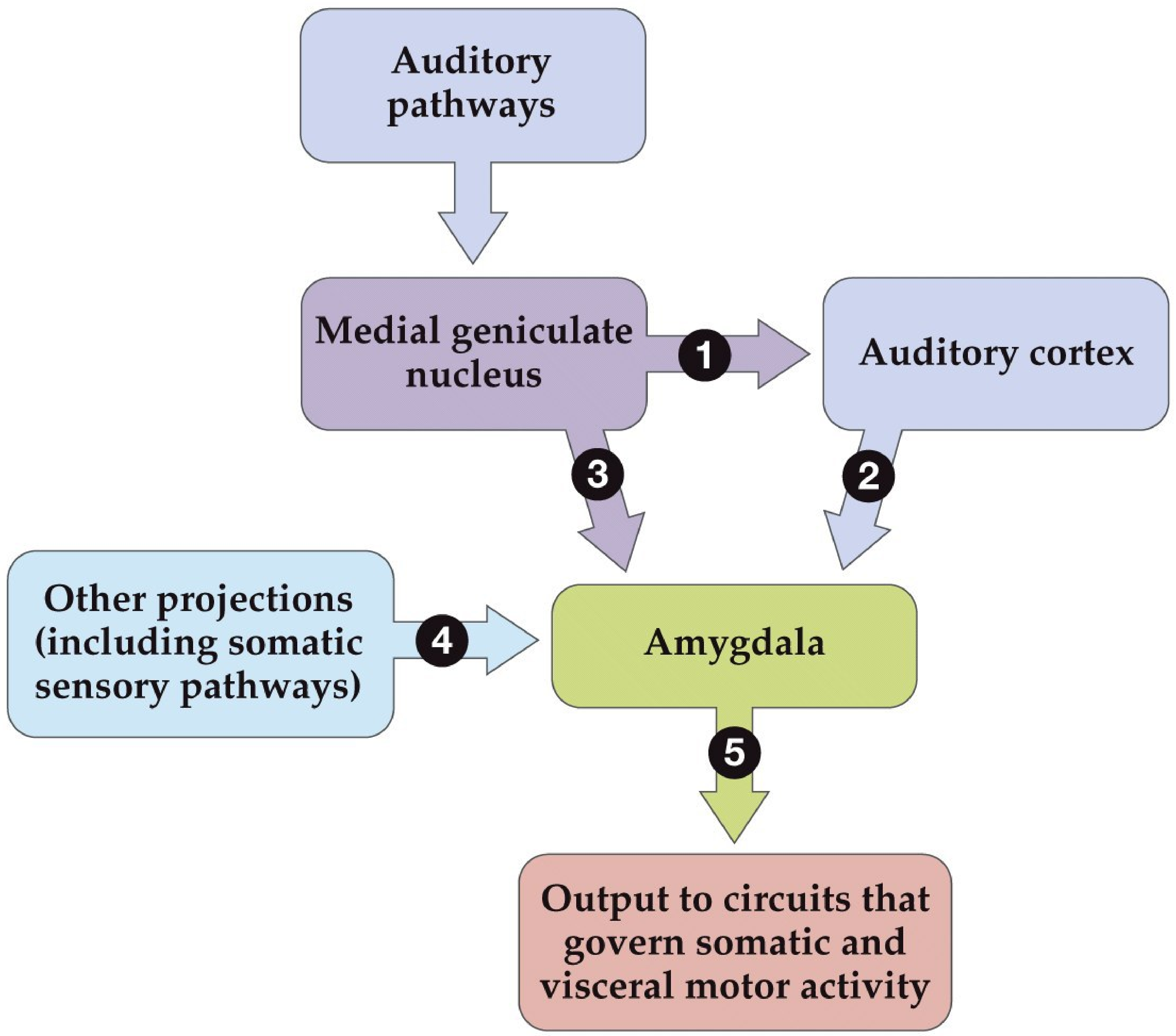
Principals of Neural Science, Kandel, Schwarz, Jessel Fig. 50.07

Speaker notes

notice incr blood pressure, visceral response after the association is made and how it is maintained

Pathways involved in fear conditioning

Amygdala can associate diverse sensory inputs



Neuroscience 5e Fig. 29.5

Speaker notes

CE – central nucleus, LA lateral Nucleus

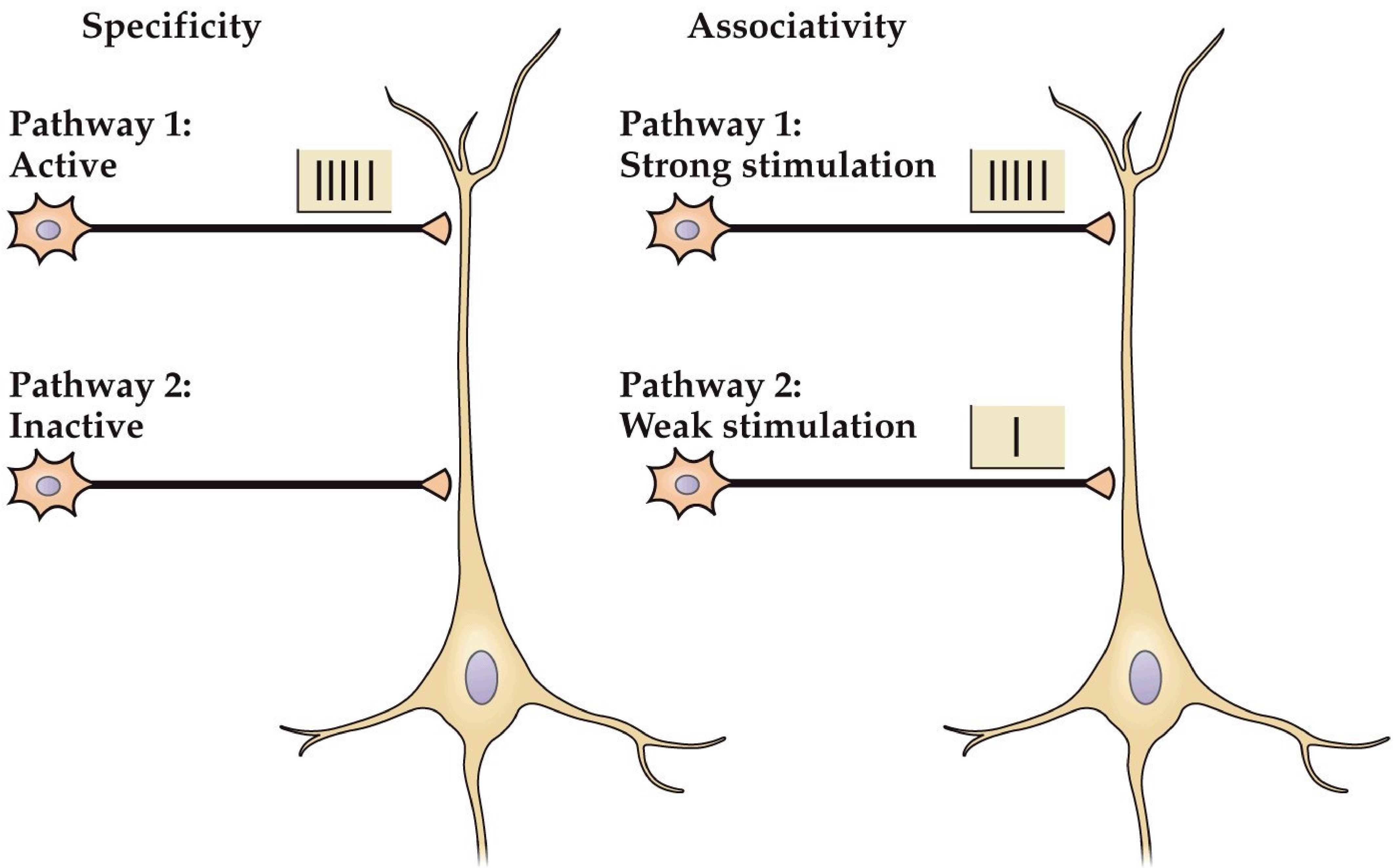
CG– central gray or PAG (periaqueductal gray). Primary control center for descending pain modulation. Enkephalin releasing neurons that project to raphe nuclei (and 5-HT in turn excites inhibitory interneurons in the spinal cord dorsal horn). Role in analgesia and defensive behavior. Responsible for the ‘freezing’ behavior of conditioned fear, the arresting of somatomotor activity.

LH– lateral hypothalamus. Contains orexinergic neurons. Projects widely throughout nervous system. Promotes feeding behavior, arousal, reduces pain perception, regulates body temperature, digestive functions and blood pressure. Glutamate, endocannabinoids (anandamide), and orexin neuropeptides are main neurotransmitters in orexin neurons. Robust projections to posterior hypothalamus, tuberomammillary nucleus (histamine projection nucleus in posterior hypothalamus. Sole source of histamine pathways in human), arcuate nucleus (neuroendocrine neurons in mediobasal hypothalamus, prolactin, GHRH, ghrelin, neuropeptide-Y), paraventricular hypothalamic nucleus.

PVN– paraventricular nucleus of hypothalamus. Contains groups of neurons activated by stressful or other physiological changes. Release oxytocin or vasopressin into circulation through terminals in the pituitary.

Important properties of long-term potentiation

- Spatial localization (synaptic input specificity)
- Associativity (between synapses within the post-synaptic neuron)



Neuroscience 5e Fig. 8.9

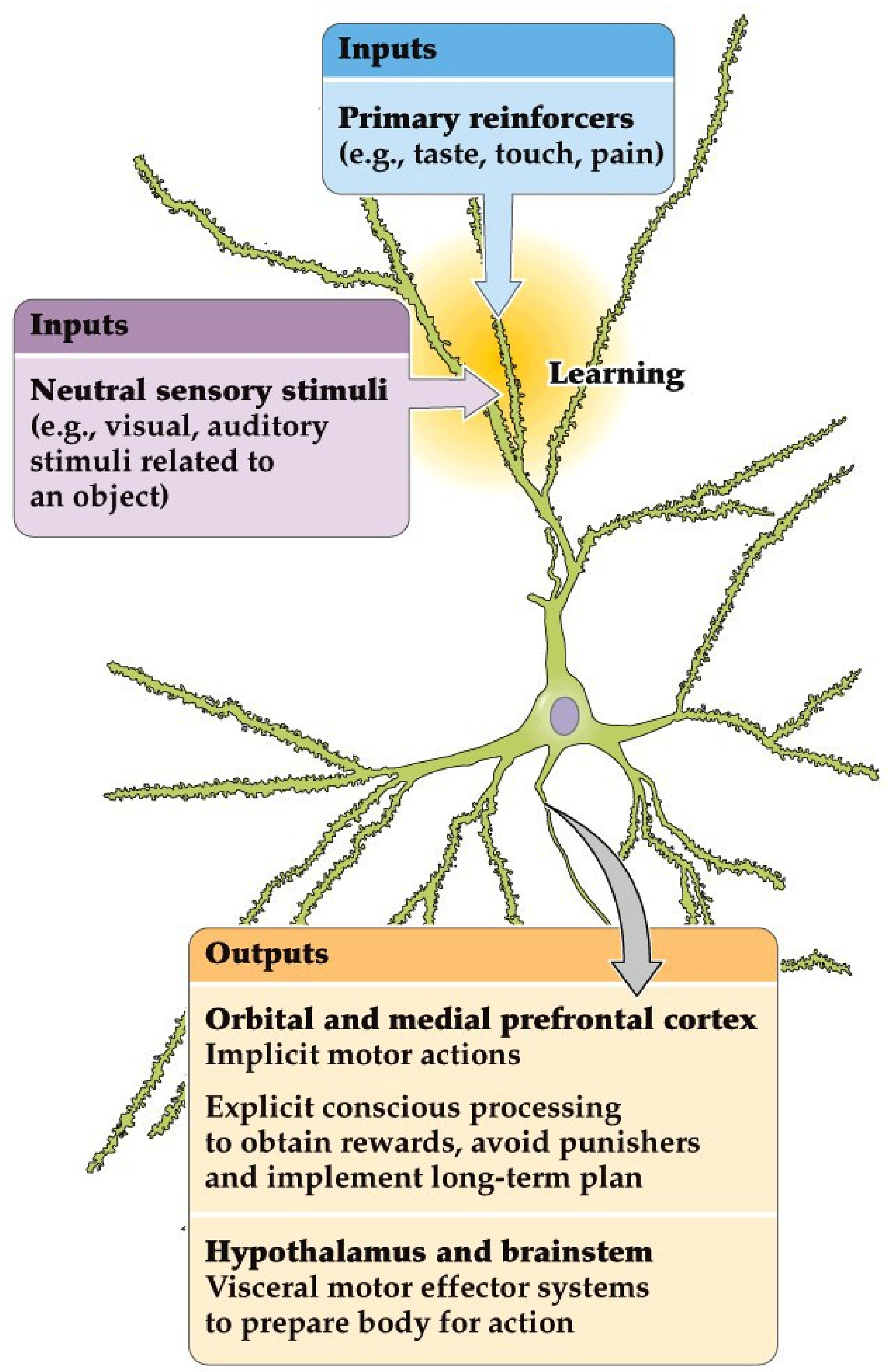
Speaker notes

- Properties consistent with role as specific coincidence detector
- Not generalized across whole neuronal ensembles, but localized
- Associativity utilized for associative learning or classical/Pavlovian conditioning (great early 20c russian physiologist, Pavlov's dogs (dinner bell association with food presentation and salivation))

at Schaffer collateral axon synapse betwen CA3 and CA1

- NMDA receptor opening leads to strengthening of synapses
- weak stimulation at pathway 2 can lead to synapse strengthening/potentiation through associative mechanisms--EPSP summation

Model for associative learning in the amygdala



Neuroscience 5e Fig. 29.6, E.T. Rolls *The Brain and Emotion* 1999

Speaker notes

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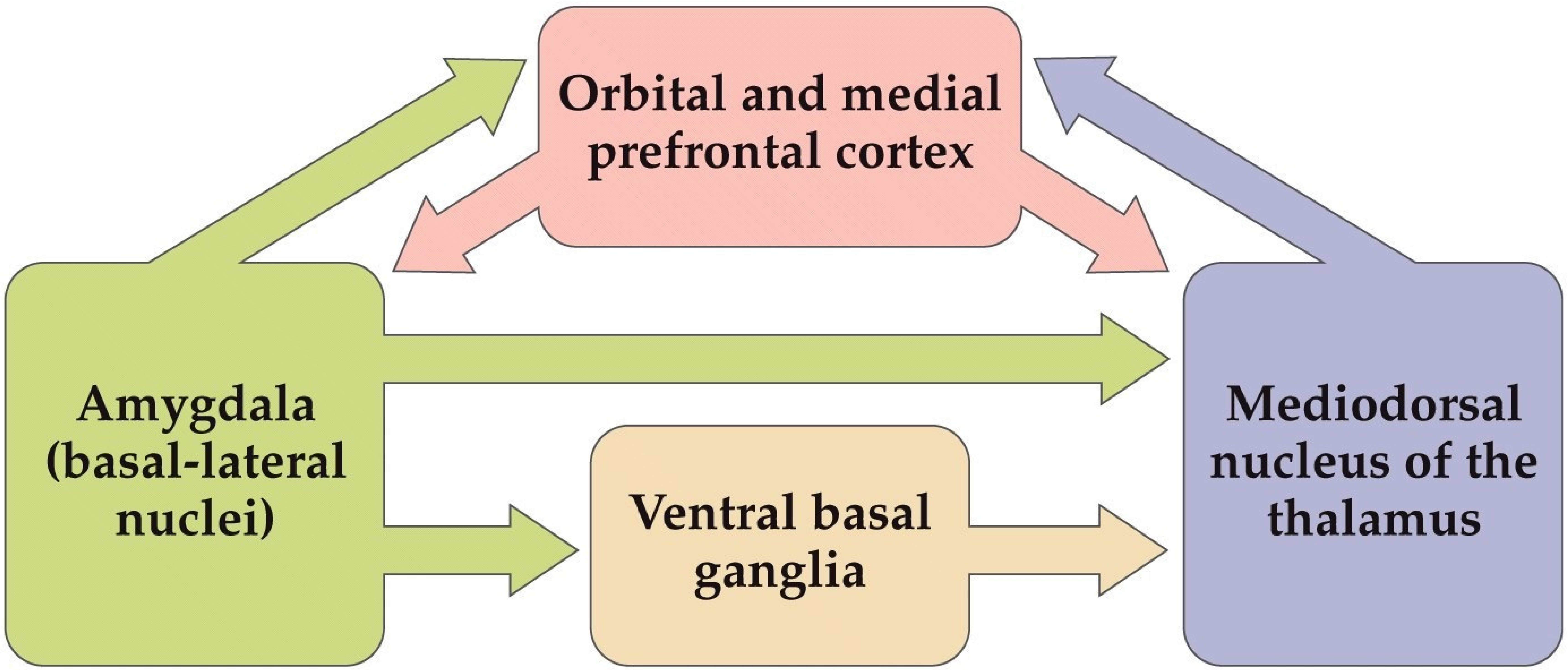
The amygdala as a key node in the brain network for emotional processing



Neuroscience 5e Box 29B

Speaker notes

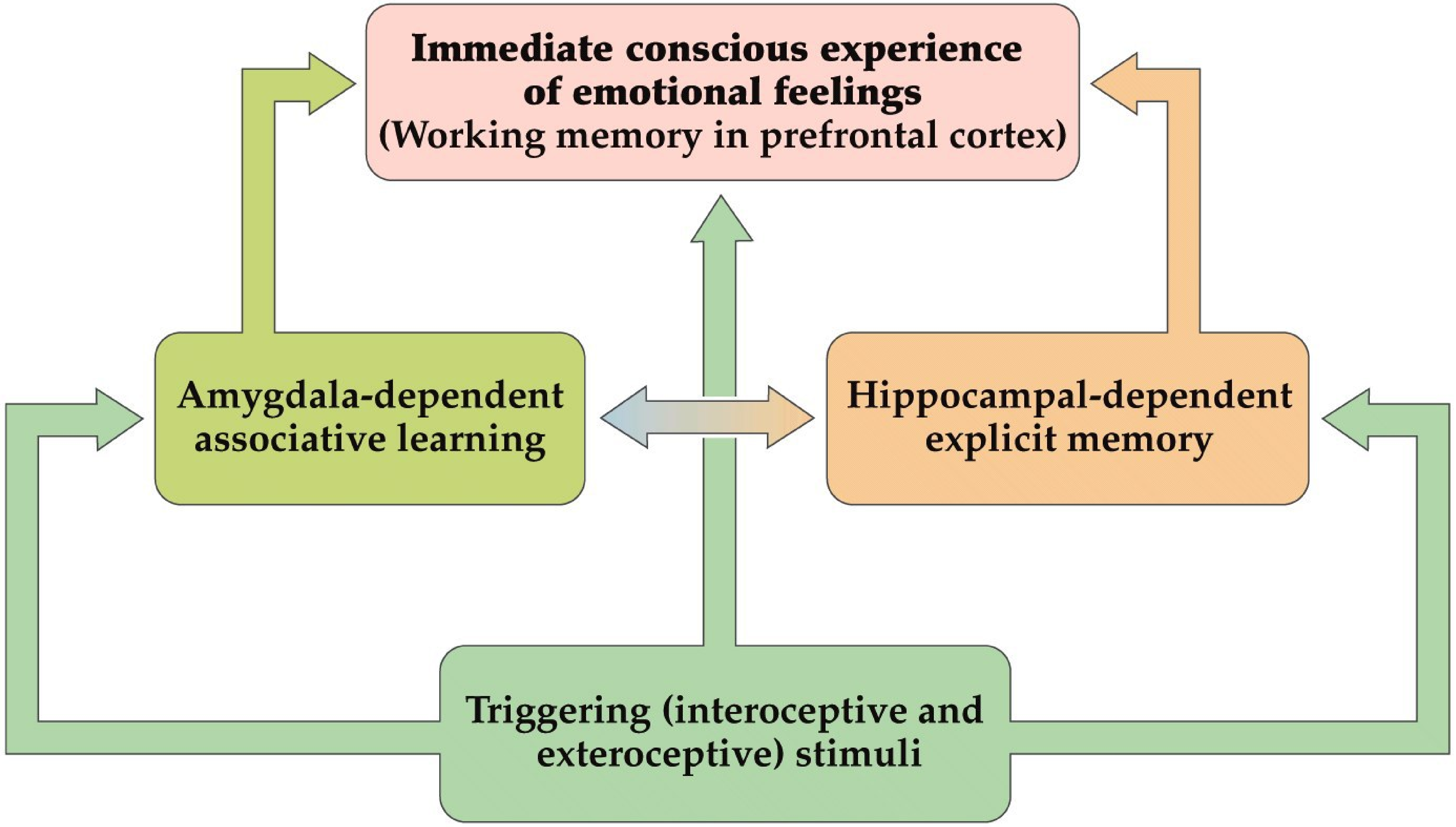
orbito and medial prefrontal cortex
: prefrontal cortical regions in the frontal lobe associate information from every sensory modality

- amygdala projects to mediodorsal nucleus of thalamus-- this in turn projects to the prefrontal association areas
- innervates nueons in ventral basal ganglia that receive major corticostriatal projections

Amygdala and connections to prefrontal cortex and basal ganglia regulates selction and initiation of behaviors need to obtain rewards (and avoid punishments)

Feelings may be a kind of emotional working memory. Containing both immediate conscious experience of implicit emotions and explicit processing of semantic thought, orbito and medial sectors likely areas for these assocaition be maintained in conscious awareness

Model for the awareness of emotional feelings



Neuroscience 5e Fig. 29.7, LeDoux 2000

Speaker notes

No notes on this slide.

Emotions are lateralized

- Right hemisphere is especially important for the expression and comprehension of the affective aspects of speech (emotional sides of language)
- People with lesions on the right side equivalent of Broca's area speak in monotones. Unable to change tone to relay things like anger
- Mood. Left side more associated with positive emotions and the right side more associated with negative emotions
- Depression often associated with left side damage, right side damage leads to undue optimism

Speaker notes

smile asymmetries in facial expressions, most individuals more quickly and fully express emotions with left facial musculature than the right

Mood disorders– depression

- Can be unipolar or bipolar
- Unipolar depression affects 5% of world's population. 8 million Americans at any given time
- Average age of onset 28 years. More common in women than men
- Bipolar disorders– have a manic phase. 1% of people have it at some point during lifetime. Affects men and women equally
- Account for a large fraction of suicides

Speaker notes

No notes on this slide.

Treatments for depression

- Monoamine oxidase inhibitors that increase monoamine concentration at synaptic terminals– e.g. Iproniazid
- Monoamine transporter inhibitors– e.g. Imiprmine and fluoxetine (Prozac). Fluoxetine selectively inhibits serotonin reuptake as a selective serotonin reuptake inhibitor

Speaker notes

No notes on this slide.

Anxiety disorders

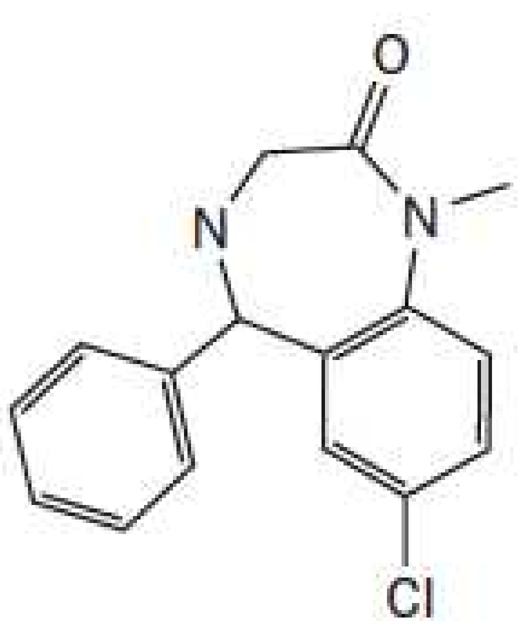
- Most common types of psychiatric disorders, include anxiety, phobias, panic disorders, obsessive-compulsive disorder
- Often associated with fatigue, muscle tension, and sleep disturbance. 5% of people *report* some type of general anxiety disorder
- Barbiturates– reduce anxiety but also are potent sedatives. Overdose is lethal
- Benzodiazepines– reduce anxiety without as much sedation. Harder to overdose on benzodiazepines
- Both drugs bind to the ionotropic GABA receptors and enhance GABA transmission

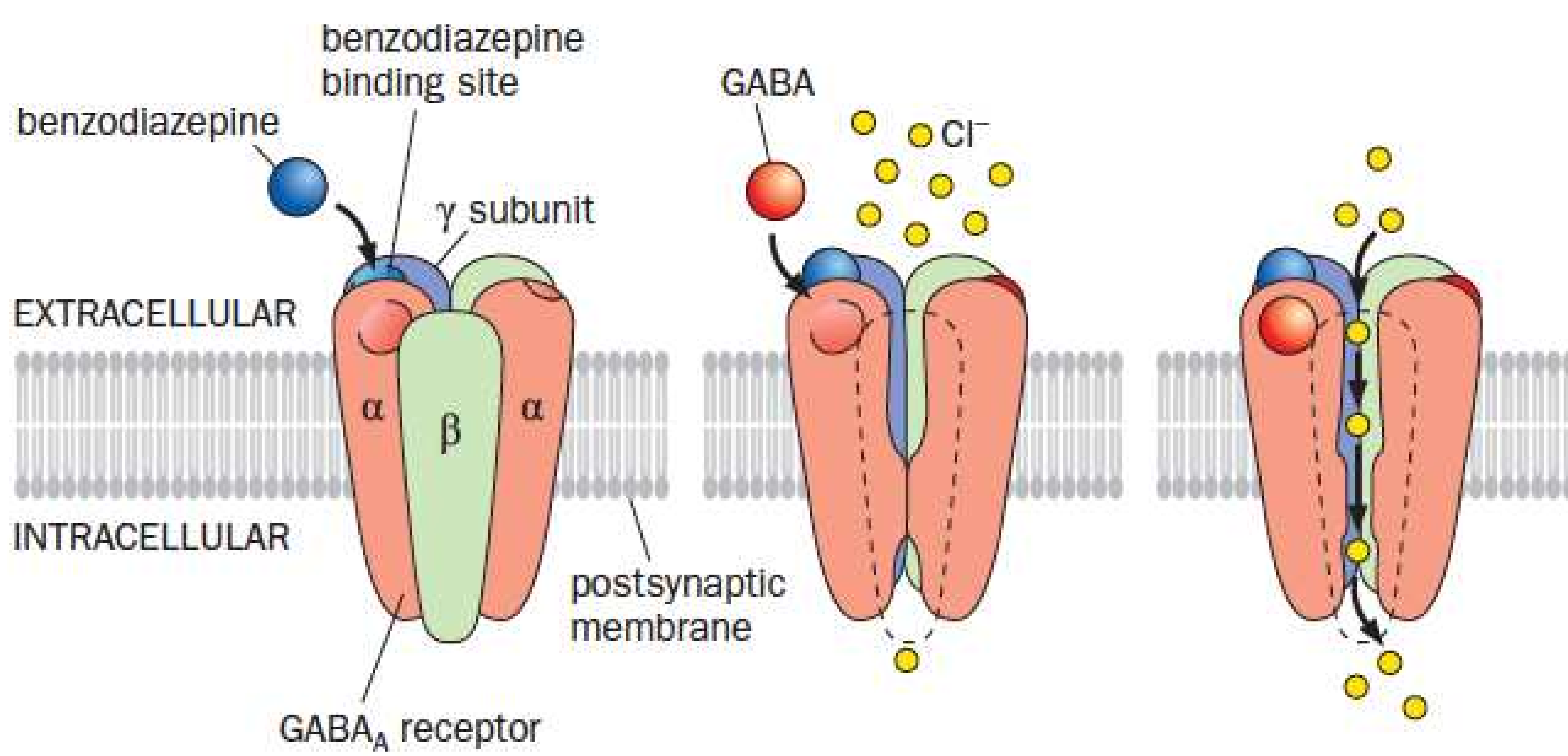
Speaker notes

No notes on this slide.

Benzodiazepine mechanism of action

- Benzodiazepines increase the affinity of the receptor for GABA
- Barbituates can activate the GABA receptor independent of GABA





Speaker notes

Act at the level at the interface of the alpha and gamma subunits. Different neurons express different gamma subunits. Six different genes for the alpha subunit. Benzodiazepines only can interact with the a1,a2, and a5 subunits, have a conserved histidine.

TODO: src

Drug abuse and addiction

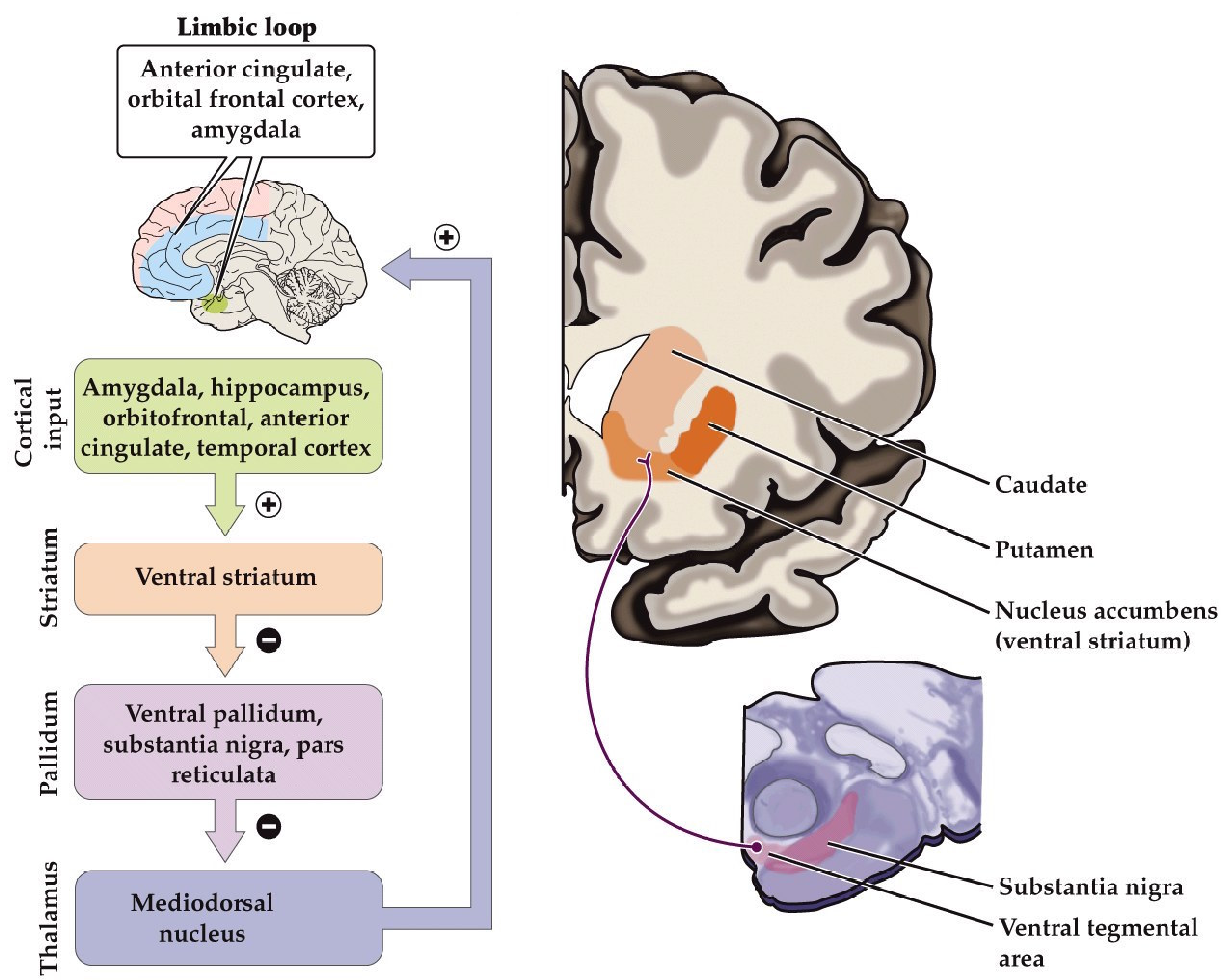
- Emotional processing in the limbic system signals the presence or prospect for reward and punishment, and activates programs to procure rewards and avoid punishment
- Most known drugs of abuse (heroin, cocaine, ethanol, opiates, marijuana, nicotine, amphetamines) act on the limbic circuits
- Most act by altering dopamine circuits that go through the ventral basal ganglia

Speaker notes

all act by changing the neuromodulatory influence of dopamine for processing reinforement signals in nucleus accumbens, leading to the strenghthening of circuits underlying addictive behavior in limbic systems

Functional and anatomical organization of the limbic loop through the basal ganglia

- Nucleus accumbens– contains MSNs
- Ventral tegmental area (VTA)– provides dopaminergic input to the to nucleus accumbens



Neuroscience 5e Fig. 29.10

Speaker notes

Recall the non-motor loops we discussed in our study of the basal ganglia.

Much like the direct pathway. Inputs from different parts of cortex, including amygdala.

to MSNs in ventral striatum the nucleus accumbens. These gabaergic projections then inhibit inhibitory projections in the in the ventral globus pallidus called the ventral pallidum. So there is a disinhibitory effect, much as we discussed before for other basal ganglia loops.

nucleus accumbens and VTA are the main sites wher drugs of abuse interact with signals for emotional reward

serotonin pathways

- mood
- memory processing
- sleep
- cognition

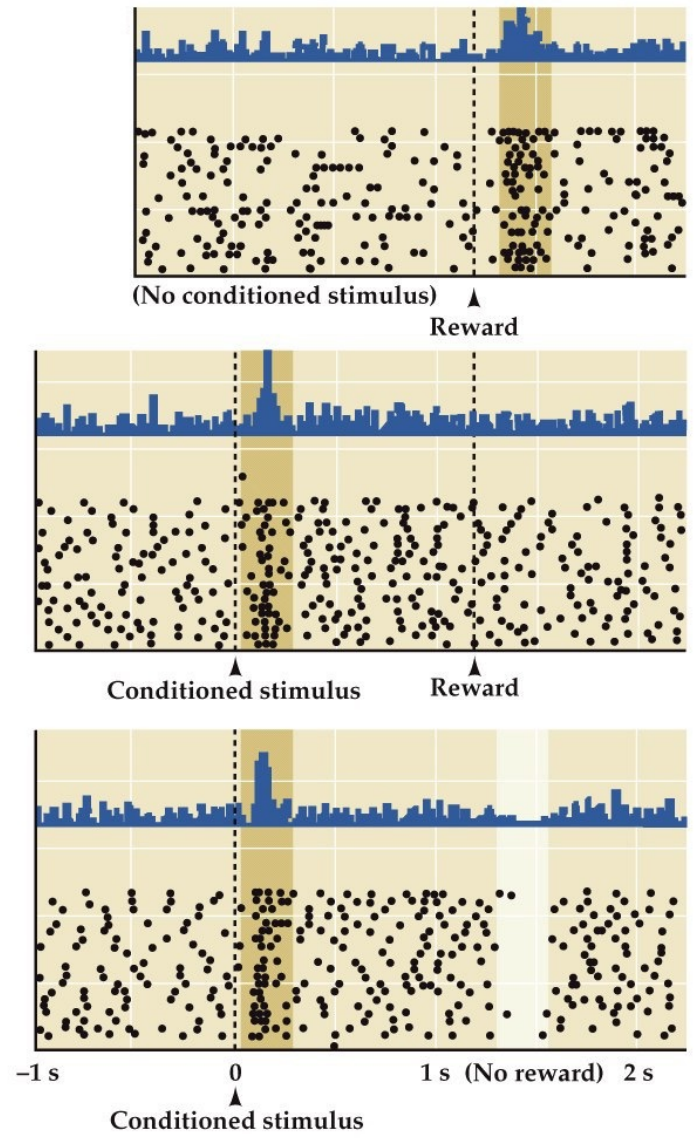
dopamine pathways

- reward (motivation)
- pleasure, euphoria
- motor function (fine tuning)
- compulsion
- perserverance
- decision making

Changes in the activity of dopamine neurons in the VTA during stimulus–reward learning

Recordings from VTA dopamine neurons in awake monkey. VTA signals the presence of an **expected** reward.

Raster plots of experiment trial showing spike times and peristimulus time histograms. top: Surprise juice reward response middle: Learned conditioned stimulus (e.g. visual cue) and presence of expected reward bottom: Learned conditioned stimulus and absence of expected reward



Neuroscience 5e Fig. 29.12, Schultz 1997

Speaker notes

The VTA signals the occurrence of a reward relative to its prediction

- Schultz Neuron 1997

Stimulation of reward pathway is incredibly powerful

- Self stimulation experiments have demonstrated that rats will bar press for stimulation of the VTA or NAc
- Olds and Milner, 1954, J Comp Physiol Psychol, 47
- This behavior can be blocked by cutting the pathway from the VTA or by administering dopamine antagonists

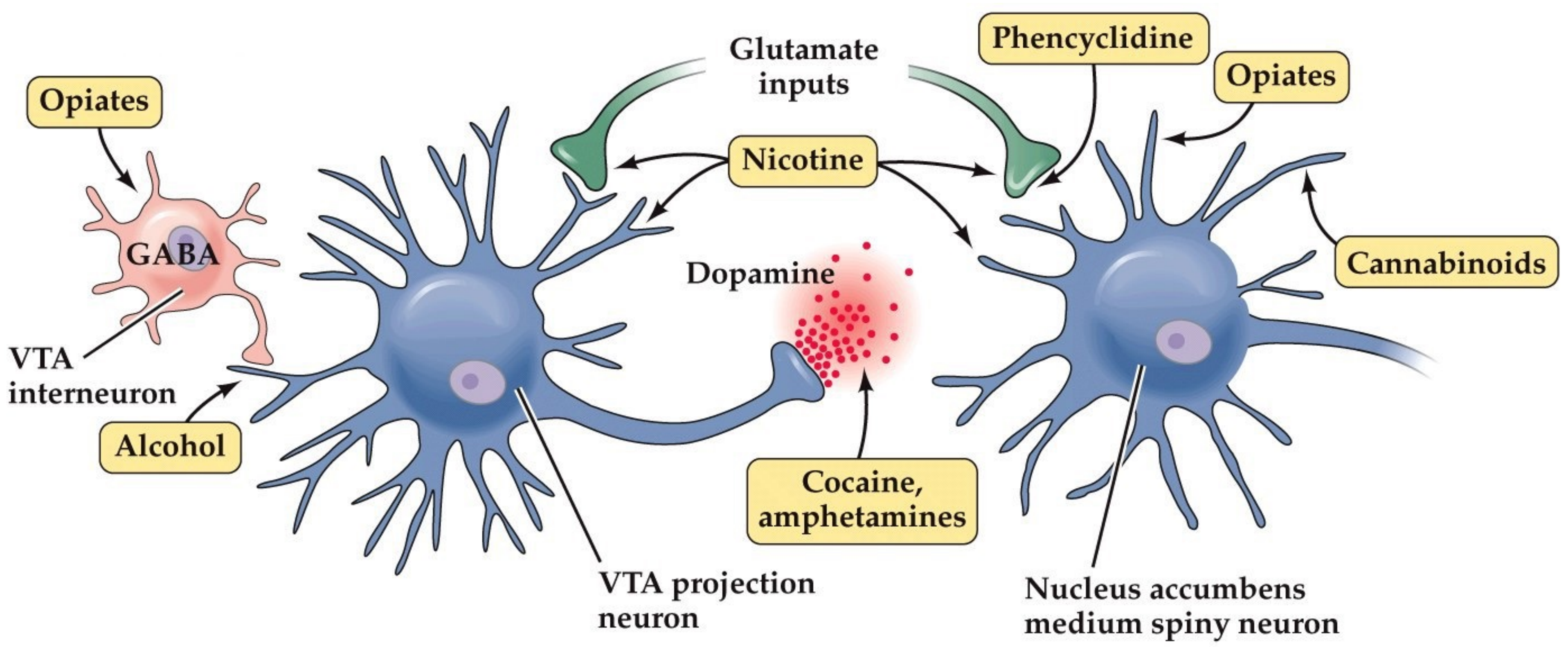
Rat self reward stimulation

Speaker notes

No notes on this slide.

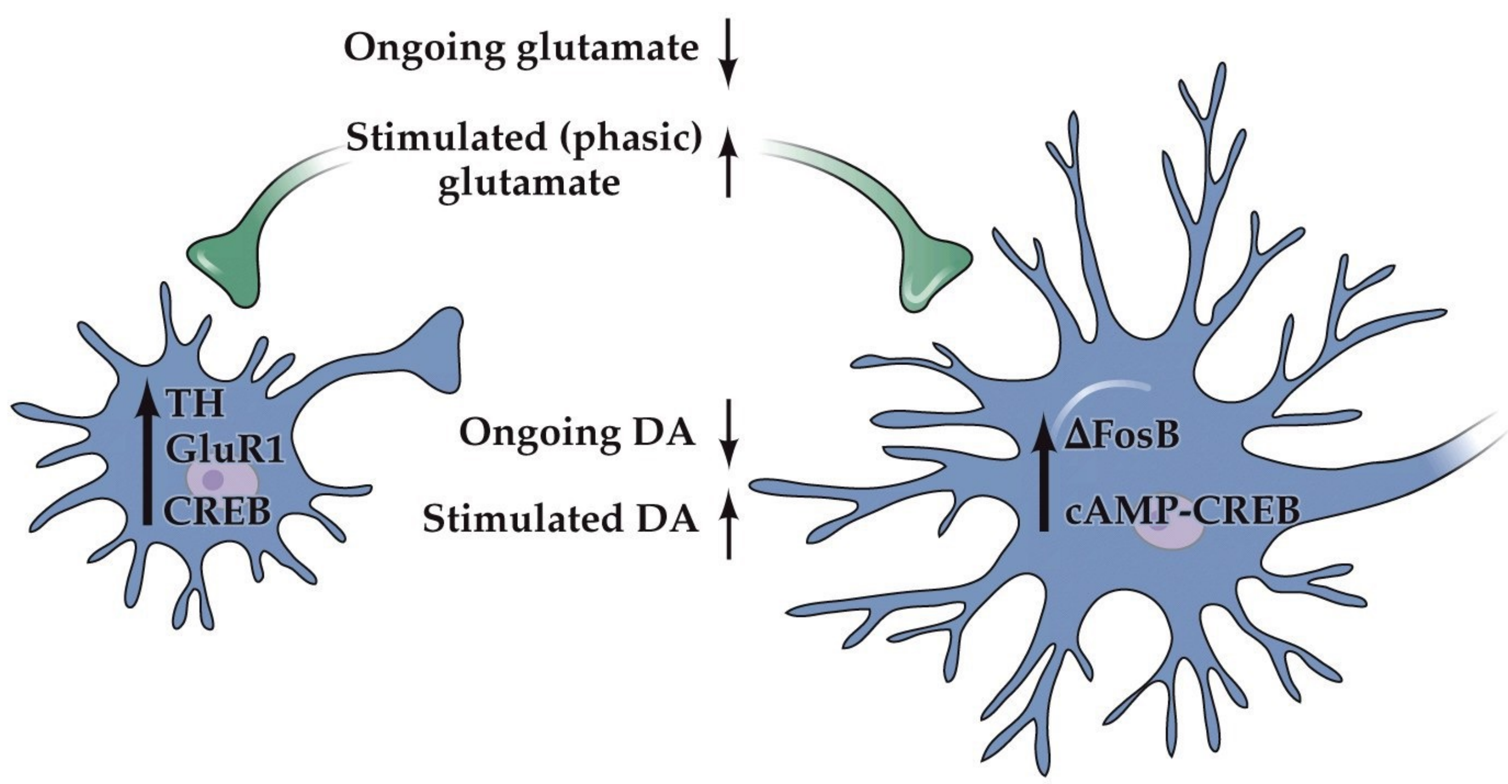
Drugs of abuse affect dopamine projections from the VTA to the nucleus accumbens

Synaptic locations of action for psychoactive drugs of abuse



Neuroscience 5e Fig. 29.11

Functional changes at VTA projections in addicted individuals



Neuroscience 5e Fig. 29.11

Speaker notes

Exposure to drugs of abuse causes long-lasting enhancement of excitatory input to VTA dopamine neurons, increasing AMPA/NMDA receptor ratio at these synapses.

Circuits involved in drugs of abuse

- Nicotine enhances input onto VTA by presynaptic excitation
- Opioids, benzodiazepines, and cannabinoids act by hyperpolarizing GABAergic neurons
- Ethanol boosts dopamine concentrations– mechanism unknown
- Cocaine blocks dopamine reuptake via the plasma membrane dopamine transporter (DAT)
- Ecstasy causes dopamine release in vesicle independent manner, inhibits
- Dopamine degradation and increases dopamine biosynthesis

Speaker notes

Specifically, studies in primates and rodents have shown that many VTA dopamine neurons encode reward prediction errors. This error signal is hypothesized to direct synaptic plasticity in target neurons in the nucleus accumbens and prefrontal cortex for reinforcement-based learning. If VTA dopamine neurons signal a reward, the action or behavior that immediately preceded the reward is reinforced through dopamine modulation of downstream circuits (see Figure 10–44). Drugs of abuse bypass natural signals that activate these dopamine neurons, thus dissociating the reward system from its natural stimuli. Specifically, by increasing dopamine concentration at dopamine neurons' presynaptic terminals, drug consumption mimics dopamine neuron activation; this reinforces the preceding actions, include drug consumption itself. Thus, addictive drugs hijack the brain's reward system and exploit mechanisms that otherwise regulate learning and motivational

long-term changes addicts:

- Decreases in CREB transcription factor in NAc (and extended amygdala)
- Decreases in metabolism in orbito frontal cortex (OFC)
- Decreases in dopamine D2 receptor binding

Drugs of abuse act on endogenous neurotransmitter receptors and transporters

Drug	Endogenous ligands	Mechanism of action
Nicotine	acetylcholine	Agonist of ligand gated channels (nAChR)
THC	anandamide, 2AG	Agonist of cannabinoid receptors (GPCRs)
Opioids	enkephalin, ß-endorphin, Dynorphin	Agonist of opioid GPCRs (μ,∂,k)
Cocaine		Inhibits 5-HT transporters, DAT, NET. Increased DA, NA, 5-HT in synaptic cleft.
Amphetamine		Inhibits MAO, NET, and VMAT. Increased DA and NA in synaptic cleft.
MDMA (ecstasy)		Inhibits 5-HT transporters and VMAT. Increased DA, 5-HT, NA in synaptic cleft.

Speaker notes

Cocaine

DAT: dopamine transporter, extracellular

NET: NA transporter, extracellular

MAO: monoamine oxidase, intracellular.

- : Catalyzes oxidation of monoamines (serotonin, melatonin, norepinephrine, epinephrine (MAO-A) and dopamine, tyramine, tryptamine (MAO-A & MAO-B)
- : bound to outer membrane of mitochondria of most cell types in the body.

VMAT2: vesicular monoamine transporter, intracellular

: blocking VMAT2 can cause reverse transport direction (cytosol to synaptic cleft) for monoamine transporters. Particularly for MDMA and amphetamines

: SLC18A2 gene

: transports monoamines—particularly neurotransmitters such as dopamine, norepinephrine, serotonin, and histamine from cytosol into synaptic vesicles

-MDMA enters monoamine neurons by acting as a monoamine transporter substrate (i.e., a substrate for DAT, NET, and SERT)

Addictive drugs hijack the brain's reward system by enhancing the action of VTA dopamine neurons

- Drug addiction: compulsive drug use despite long-term negative consequences
- All drugs of abuse increase dopamine concentration at the output targets of the ventral tegmental area
- Nucleus accumbens– processes reward information
- Prefrontal cortex– goal selection and decision making

Speaker notes

23 percent of individuals who use heroin become dependent on it. Altered conscious regulation of your behavior. 1 in 5.

http://www.samhsa.gov/
number of dependent users a year after first use 2008:

- hallucinogens and sedatives 2%
- pain relievers and alcohol 3%
- heroin 13%
- crack cocaine 9%
- marijuana 6%
- stimulants 5%
- powder cocaine 4%

Key components of limbic system reward circuits

1. VTA–nucleus accumbens pathway:
    - Dopamine pathway
    - Acts as a rheostat of reward. Tells other brain centers how rewarding an activity is. The more rewarding an activity is deemed, the more likely the organism is to remember it well and repeat it
    - Neurons from ventral tegmental area (VTA) to nucleus accumbens (major neurotransmitter is dopamine)
    - Critical pathway for drug addiction
2. Amygdala:
    - Helps assess whether an experience is pleasurable or aversive and whether it should be repeated or avoided to forge connections between an experience and other cues
3. Hippocampus:
    - Recording the memories of an experience
4. Frontal cortical regions:
    - Coordinates and processes all this information and determines ultimate behavior of the individual