Neurobiology of emotions

Introduction

Emotional expression

- closely tied to the visceral motor system
- entails the activity of the central brain structures that govern preganglionic autonomic neurons in the brainstem and spinal cord

Historically

the higher order neural centers that coordinate emotional responses - limbic system

More recently

several brain regions play a pivotal role in emotional processing (amygdala and cortical areas)

WHAT IS AN EMOTION?

- ***Multiphase Process*** *(Frijda, 1986)*

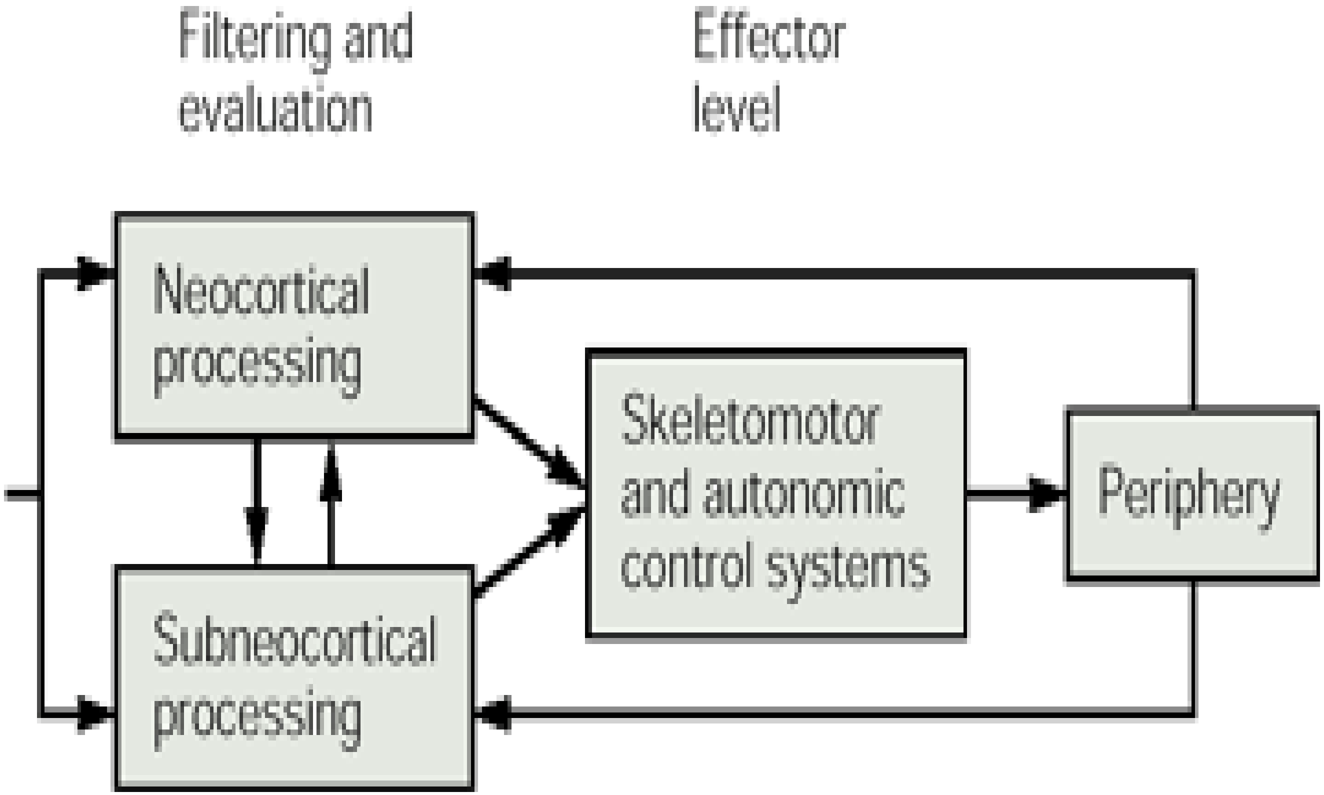
  Assessment - evaluation of context – preparing for action - physiological changes, expressions, actions

INCLUDING?

- *Specific physical changes*
  - increases or decreases in heart rate, cutaneous blood flow (blushing or turning pale), piloerection, sweating, and gastrointestinal motility - changes in activity in the sympathetic and parasympathetic components of the visceral motor system
- *Expressive movements (mime, gesture)*
- *Motor action (or at least the appearance of inner urge for action)*

Methodological approaches?

- **2 main methodological approaches:**
  - research of specific brain regions lesions consequences
  - electrical stimulation of specific brain regions



Model of the basic neural systems that control emotions

Darwin, 1872.

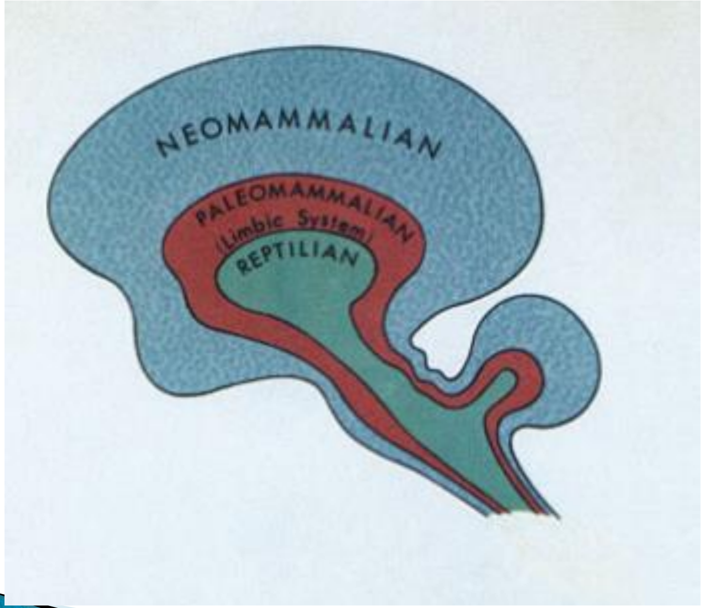
- adaptive function of emotions in the past

- emotions - psychological fossils, primitive

Evolution biologists

- functional adaptation of humans to the environment

- Survival function – phillogenetically older regions



A. the brainstem, medulla, pons, cerebellum, midbrain, globus pallidus, and olfactory bulbs
   - survival activities like breathing, heart rate, and balance

B. the amygdala, hippocampus, parahippocampal cortex, cingulate gyrus, hypothalamus, and ventral striatum/nucleus accumbens
   - emotion related to danger, reproductive and nurturance needs, and acquisition of food (early warning systems)

C. neocortex
   - complex cognitive, linguistic, motor, sensory, and social abilities

Primary emotions

– anger, fear, happiness, sadness, disgust, surprise

Secondary (social)

- shame
- jealousy
- guilt
- pride

How to measure them?

- ***How do we measure emotions****?*
  - *Facial expressions*
  - *Subjectively (first person report)*
  - *Peripheral autonomic physiology (skin conductance, facial muscle contraction, heart rate and breathing)*
  - *Functional magnetic resonance imaging (fMRI) and PET*
  - *Invasive placing of electrodes on the cortex*

- ARE EMOTIONS CROSSCULTURALLY UNIVERSAL?

Paul Ekman, 1960. – facial expressions

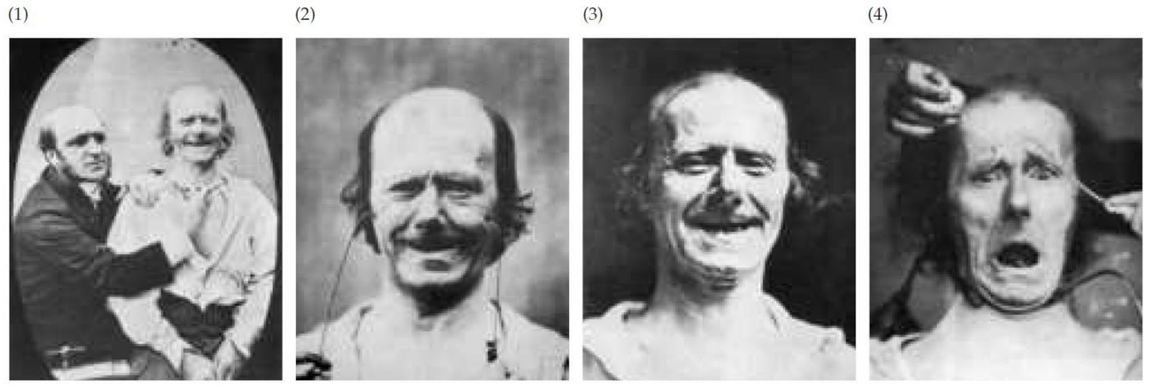
(a) show me what your face would look like if you were about to fight.

(b) show me what your face would look like if you learned your child had died.

(c) show me what your face would look like if you met friends.

Pyramidal - extrapyramidal

- Duchenne de Boulogne
  - examined the contributions of small groups of cranial muscles to the expressions of emotion
  - how the coordinated contractions of groups of muscles express distinct, pan-cultural emotional states
- **transcutaneous electrical stimulation** to activate single muscles and small groups of muscles in the face, dorsal surface of the head, and neck
- the obicularis oculi - cannot be activated voluntarily
  - the emotion-driven contraction of these muscle groups surrounding the eyes, together with the zygomaticus major, convey the genuine experience of happiness, joy and laughter
- descending motor signals from different forebrain centers onto premotor and motor neurons in the brainstem that control the facial musculature – Duchennes vs. voluntary smile (pyramidal smile)



- driven by the motor cortex, to the brainstem and spinal cord via the pyramidal tracts

Smile of volition (“pyramidal smile”)

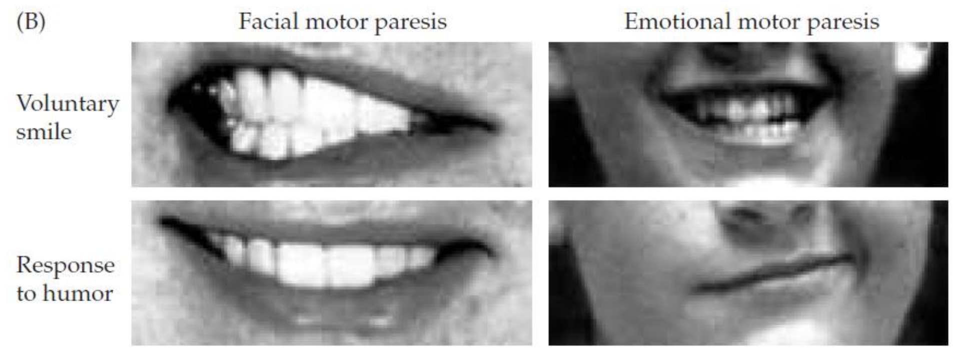
- accessory motor areas in the prefrontal cortex and ventral parts of the basal ganglia that access brainstem nuclei via multisynaptic “extrapyramidal” pathways through the brainstem reticular formation
-

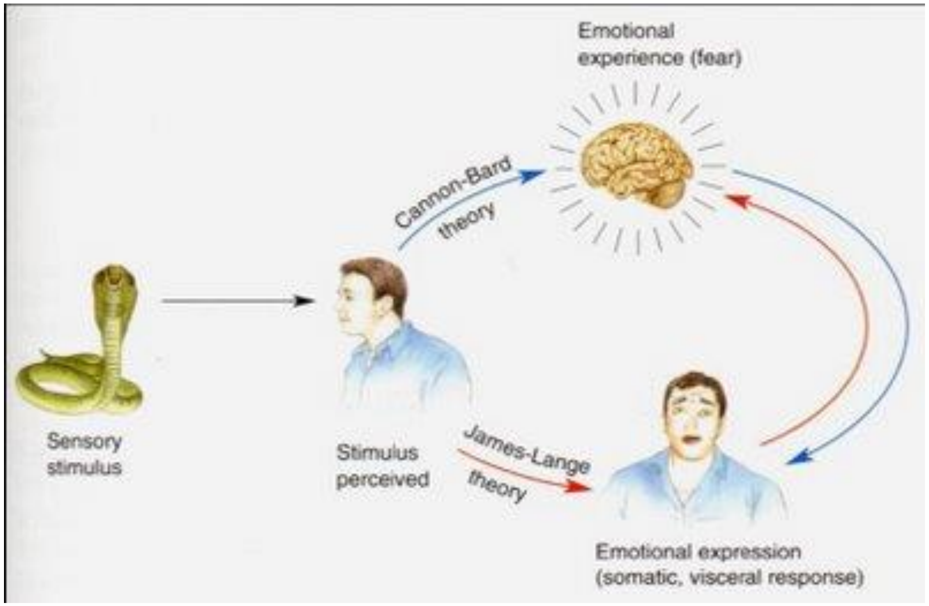
The Duchenne smile

Studies of patients with specific neurological injury to these separate descending systems of control

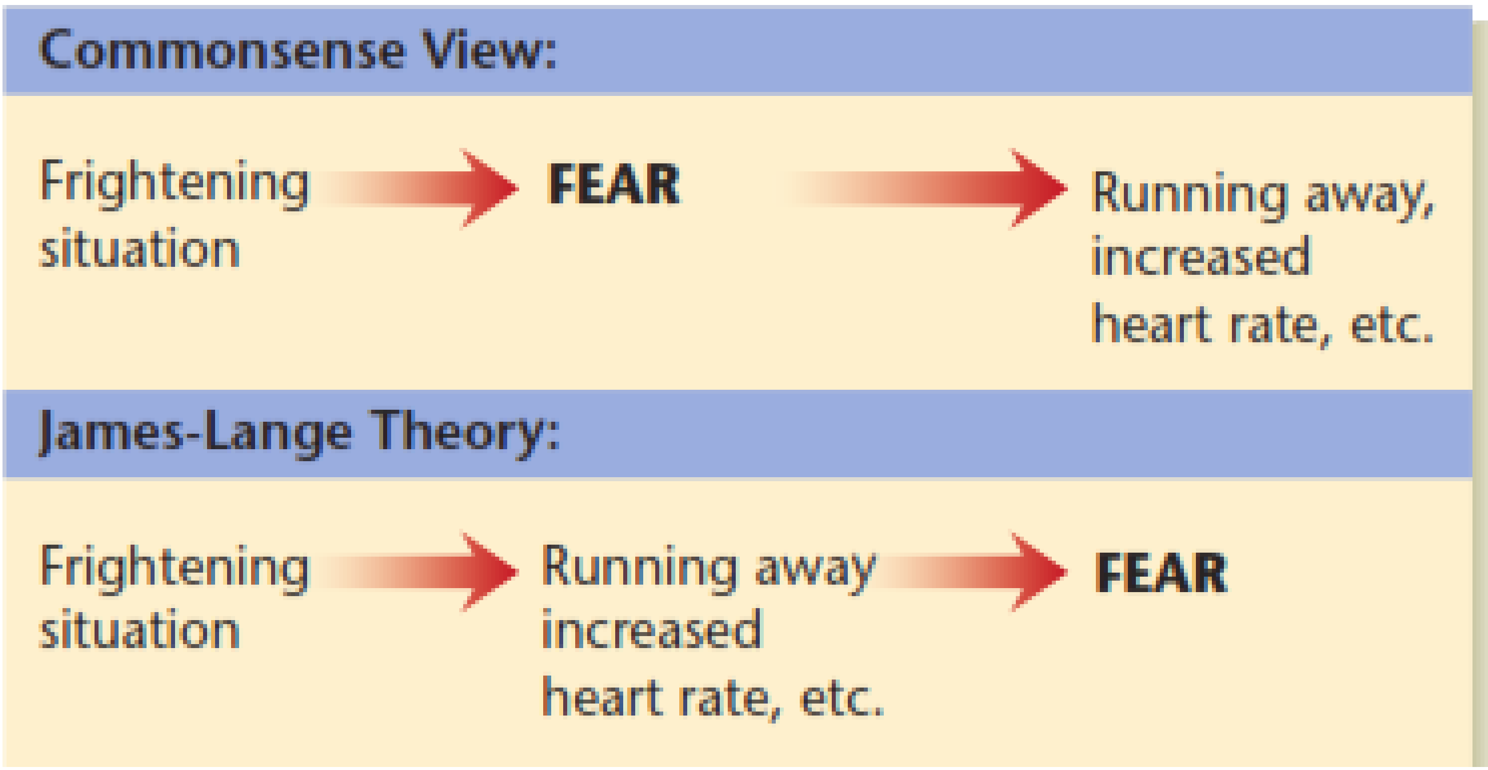
- **unilateral facial paralysis**
  - damage of descending pathways from the motor cortex (upper motor neuron syndrome), voluntary facial paresis
  - pathways from regions of the forebrain other than the classical motor cortex in the posterior frontal lobe remain available to activate facial movements in response to stimuli with emotional significance

- **emotional facial paresis**
  - able to produce symmetrical pyramidal smiles, but fail to display spontaneous emotional expressions involving the facial musculature contralateral to the lesion




Emotional
experience (fear)
Cannon-Bard
theory
Sensory
stimulus
Stimulus
perceived
James-Lange
theory
Emotional expression
(somatic, visceral response)

When does the fear appear?



J-L theory of emotions (From Kandel, Schwartz i Jessell, 2000)

JAMES LANGE - emotions are cognitive responses to information from the periphery

- the conscious experience of emotion, occurs *after* the cortex receives signals about changes in our physiological state
- feelings are preceded by physiological changes
  - an increase or decrease in blood pressure, heart rate, muscular tension
  - "We feel sorry because we cry, angry because we strike, afraid because we tremble and not that we cry, strike or tremble because we are sorry, angry or fearful as the case may be."
- EVIDENCE?

- Streck, Martin i Stepper (1988)

  (*the pen experiment*)

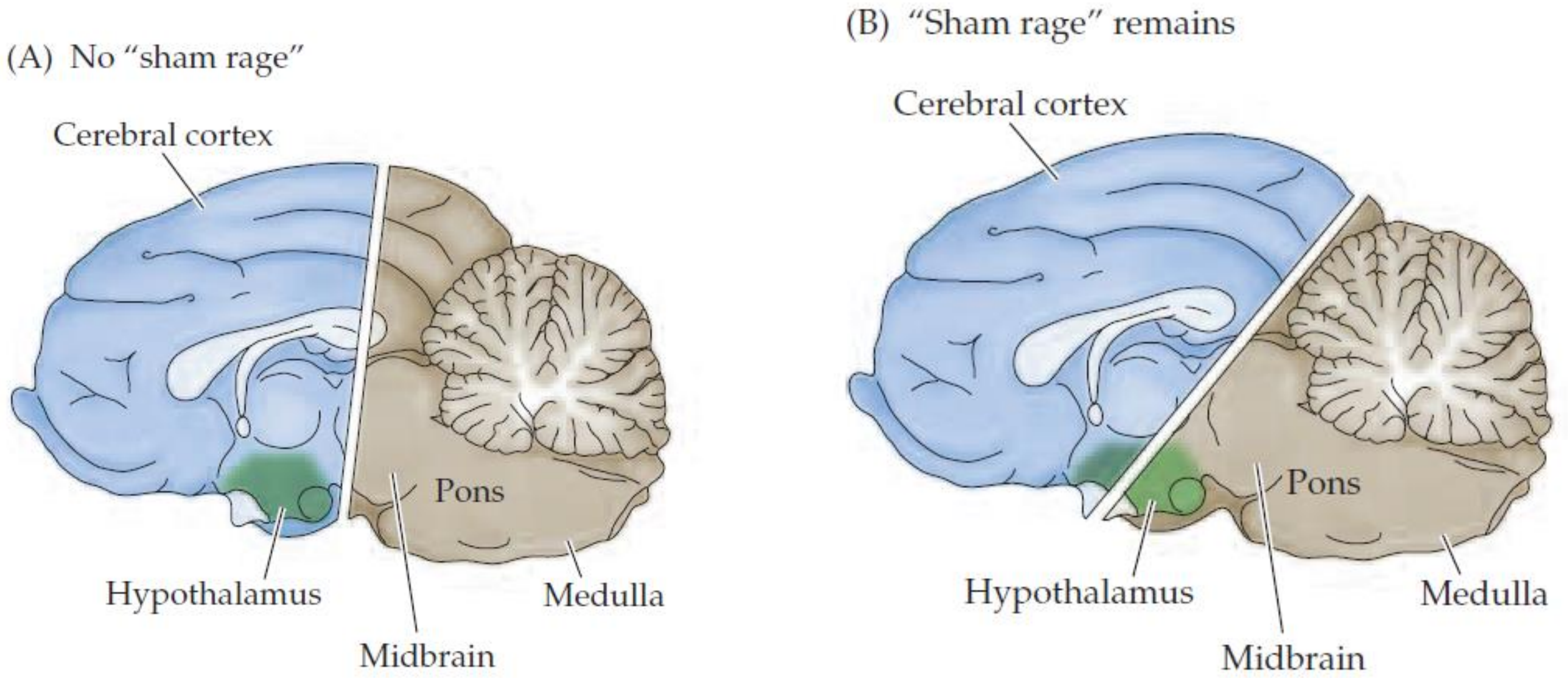
- *Mobius syndrome*
  - The facial expression of emotion is not crucial to the feeling of happiness

Mobius syndrome

Walter Cannon – Phillip Bard (1928.-1937.)

- two subcortical structures, the **hypothalamus and the thalamus**, have a key role in mediating emotions
- Studies: cats in which the whole cerebral cortex had been removed: they retain fully integrated emotional responses **SHAM RAGE**
  - differences from genuine rage

  - progressive transections - the coordinated response disappeared, leaving only isolated elements of the response, when the hypothalamus was included in the ablation



The midsagittal section of the cat brain (From Kandel, Schwartz i Jessell, 2000)

- the subjective experience of emotion might depend on an intact **cerebral cortex**
- the expression of coordinated emotional behaviors **does not necessarily entail** cortical processes
- emotional behaviors are often directed toward self-preservation - the involvement of **phylogenetically older parts of the nervous system**

Walter Hess – Nobel prize 1949.

Different parts of the hypothalamus produce characteristic **constellations of reactions** (parts of organized responses characteristic of specific emotional states)

- animals with lesions in the lateral hypothalamus become placid, whereas animals with lesions of the medial hypothalamus are highly excitable and easily become aggressive

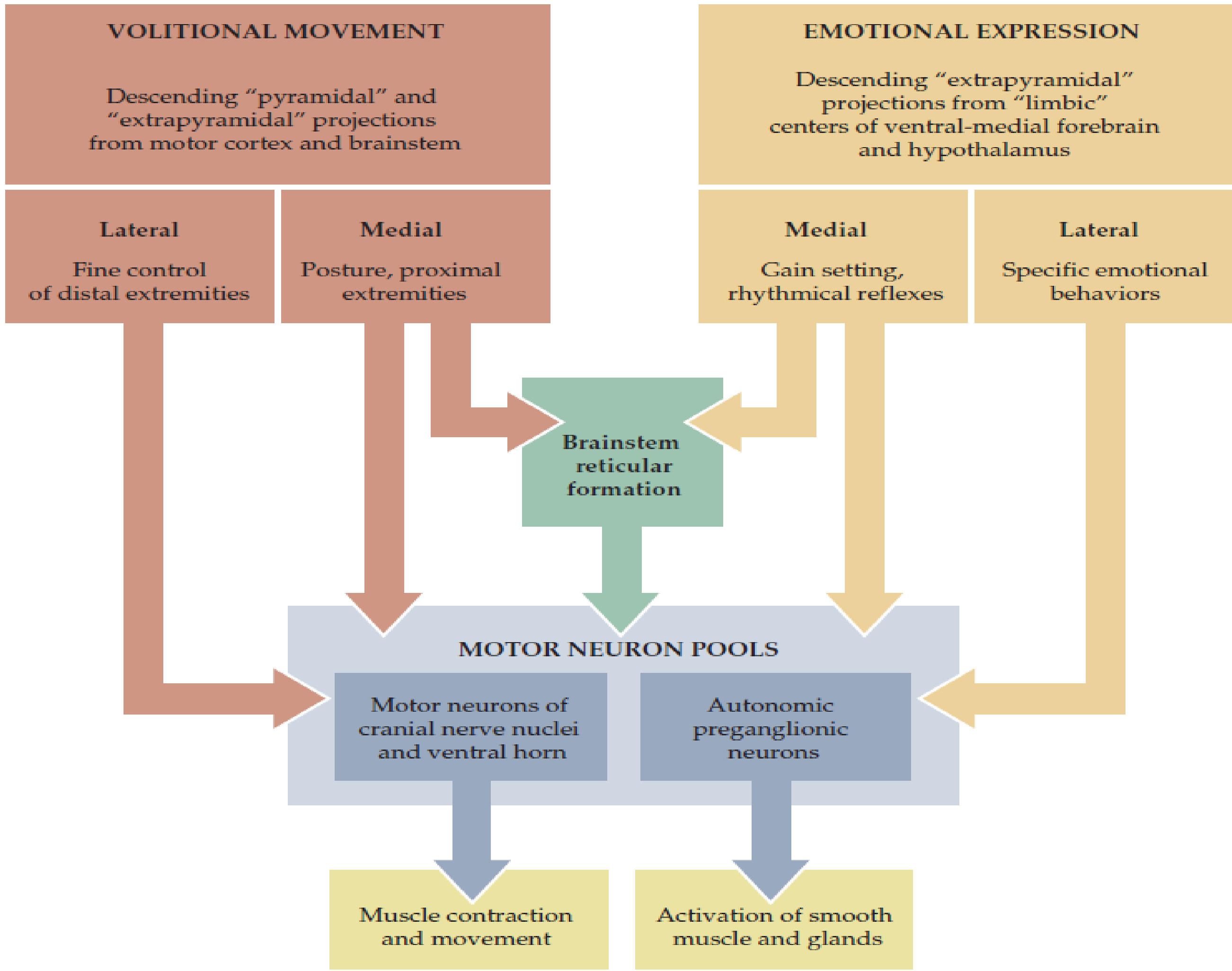
Bard and Hess

- The basic circuits for organized behaviors accompanied by emotion are in the **diencephalon and the brainstem structures** connected to it
  - the control of the involuntary motor system is not entirely separable from the control of the voluntary pathways, an important consideration in understanding the motor aspects of emotion

- The hypothalamus and other forebrain structures influence the visceral and somatic motor systems through complex pathways
  - The major targets of the hypothalamus lie in the **reticular formation**
  - **Visceral motor and somatic motor responses**

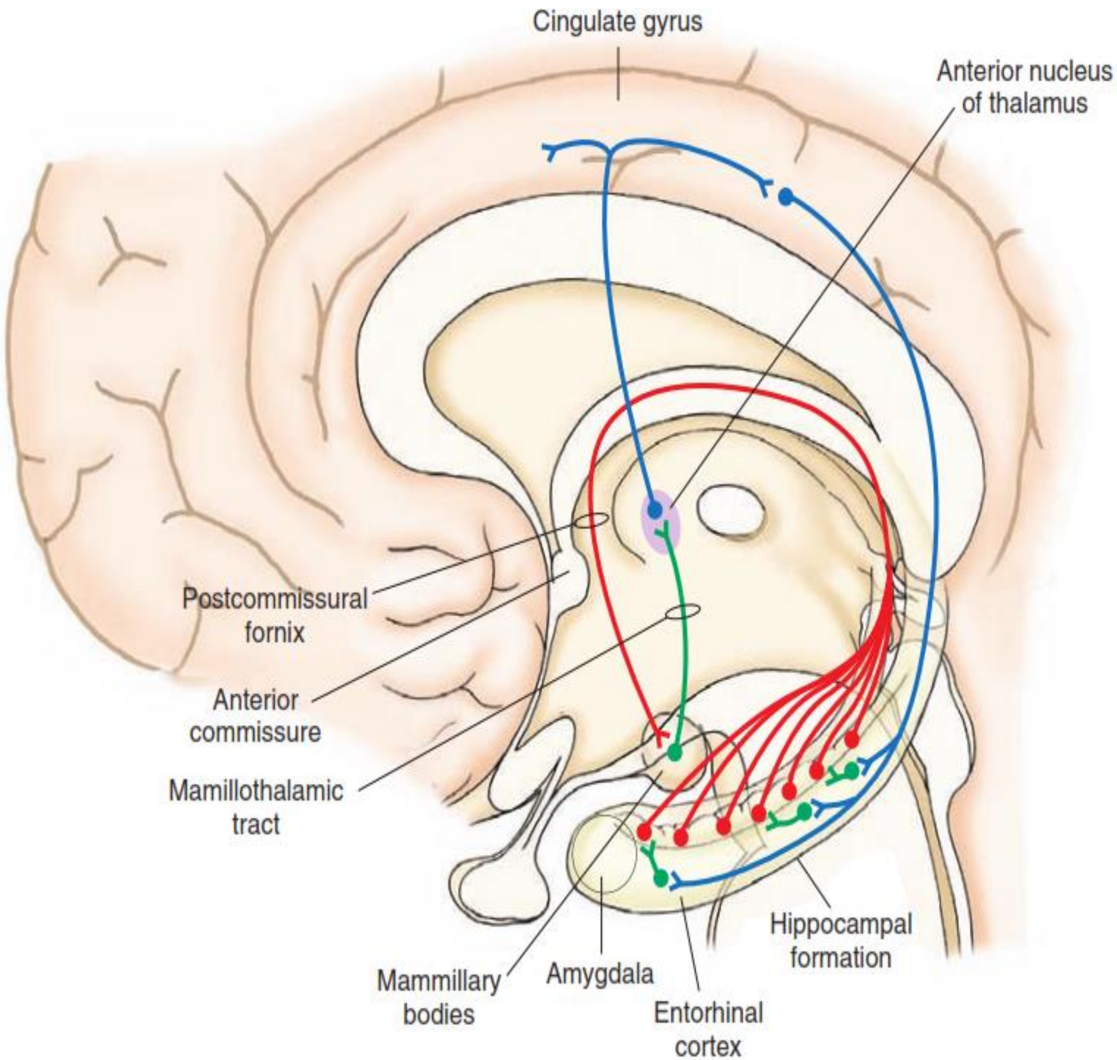
- In addition to the hypothalamus, other sources of descending projections from the forebrain to the brainstem reticular formation contribute to the expression of emotional behavior - **limbic system**

- The descending control of emotional expression entails **two parallel systems that are anatomically and functionally distinct**


VOLITIONAL MOVEMENT
Descending "pyramidal" and "extrapyramidal" projections from motor cortex and brainstem
Lateral
Fine control of distal extremities
Medial
Posture, proximal extremities
EMOTIONAL EXPRESSION
Descending "extrapyramidal" projections from "limbic" centers of ventral-medial forebrain and hypothalamus
Medial
Gain setting, rhythmical reflexes
Lateral
Specific emotional behaviors
Brainstem reticular formation
MOTOR NEURON POOLS
Motor neurons of cranial nerve nuclei and ventral horn
Autonomic preganglionic neurons
Muscle contraction and movement
Activation of smooth muscle and glands

James Papez, 1937.

- **The limbic lobe**
  - the cingulate gyrus, the parahippocampal gyrus (which is the anterior and inferior continuation of the cingulate gyrus), and the hippocampal formation (the hippocampus proper, the dentate gyrus, and the subiculum)
  - patients who have been infected with the rabies virus (which characteristically attacks the hippocampus)
    - show profound changes in emotional state, including bouts of terror and rage

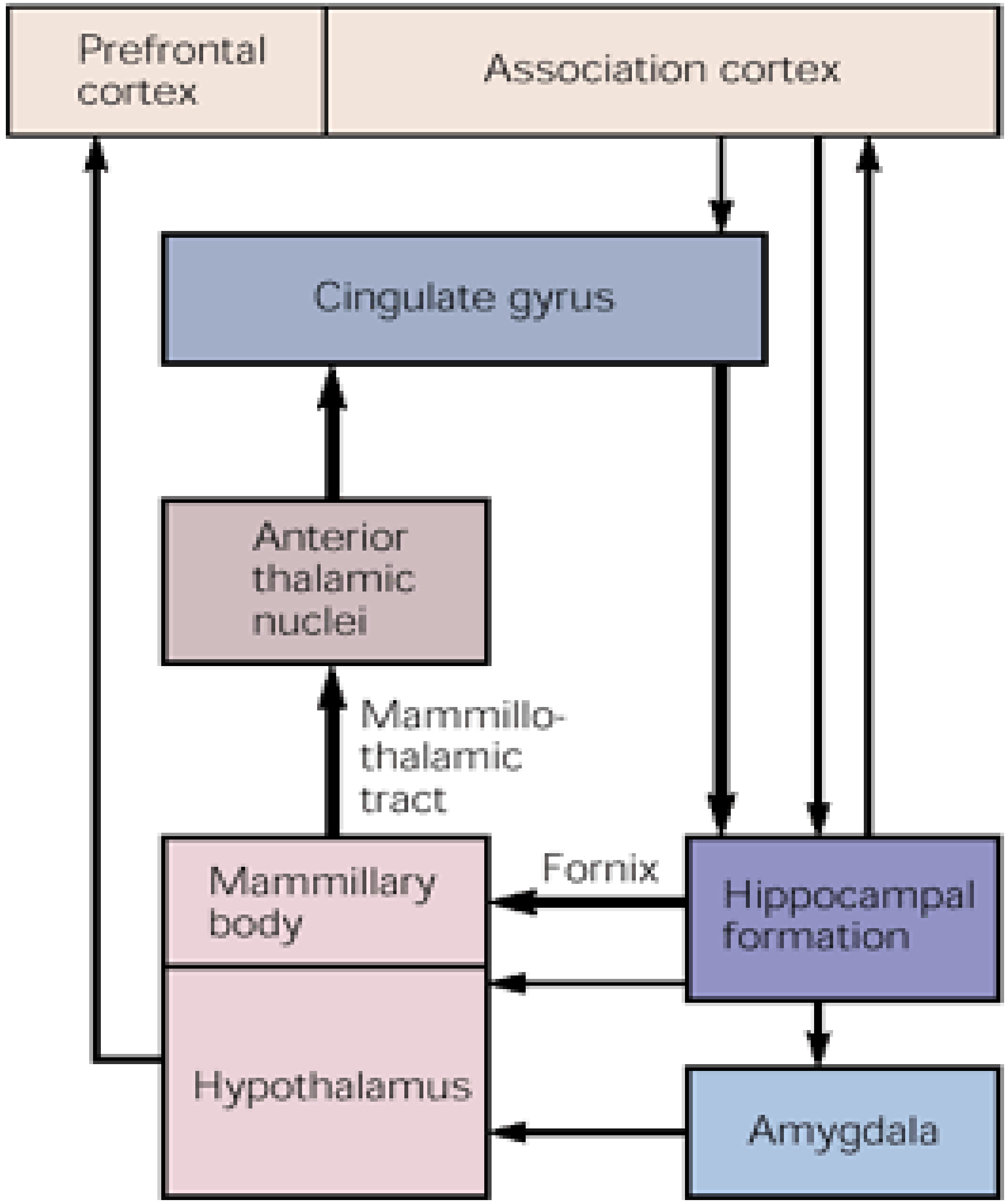


Papez circuit (From Siegel and Sapru, 2011)

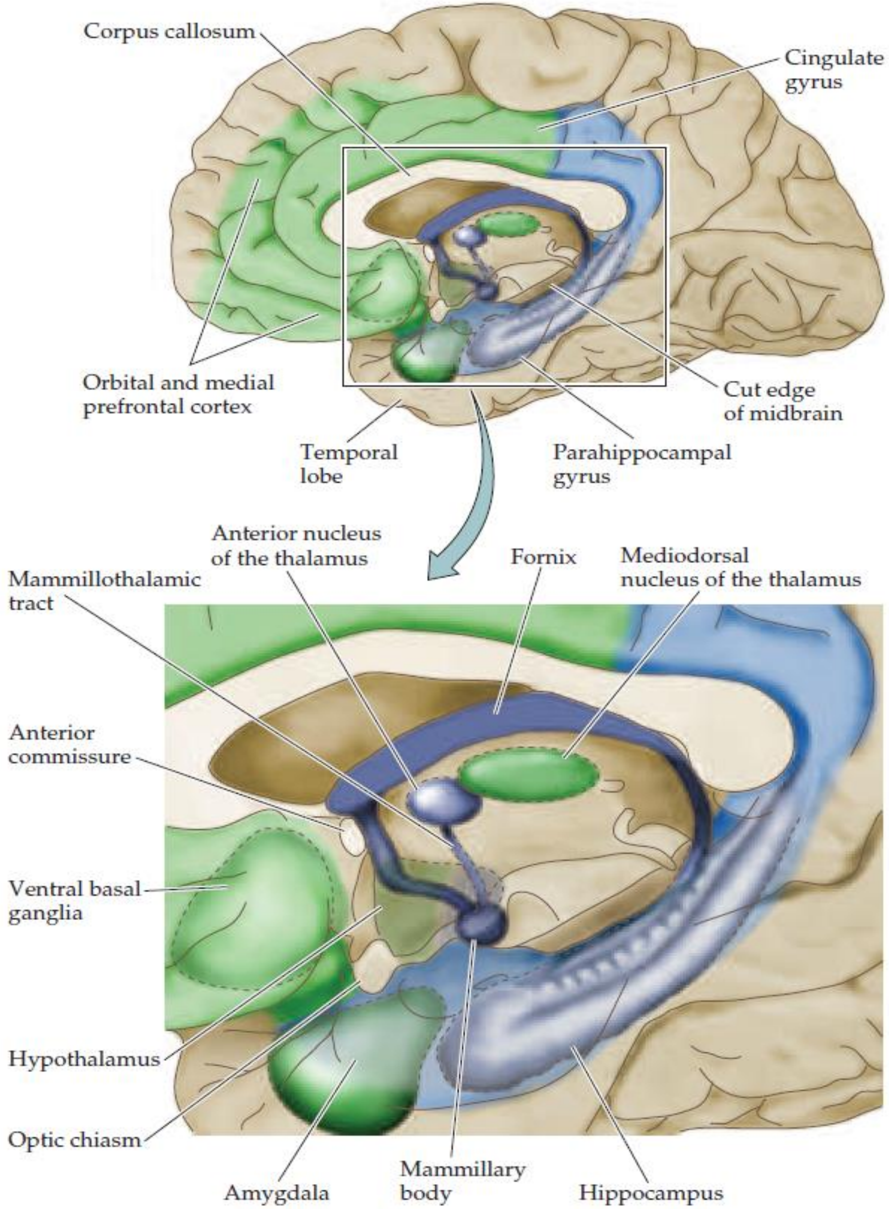
Paul McLean

- later **expanded** the concept of limbic system
  - parts of the hypothalamus, the septal area, the nucleus accumbens (a part of the striatum), neocortical areas - the orbitofrontal cortex and medial prefrontal cortex, and the amygdala

- direct connections between neocortical areas, the hippocampal formation, and the amygdala



Prefrontal cortex
Association cortex
Cingulate gyrus
Anterior thalamic nuclei
Mammillo-thalamic tract
Fornix
Mammillary body
Hypothalamus
Hippocampal formation
Amygdala


Corpus callosum
Cingulate gyrus
Orbital and medial prefrontal cortex
Cut edge of midbrain
Temporal lobe
Parahippocampal gyrus
Anterior nucleus of the thalamus
Fornix
Mediodorsal nucleus of the thalamus
Mammillothalamic tract
Anterior commissure
Ventral basal ganglia
Hypothalamus
Optic chiasm
Amygdala
Mammillary body
Hippocampus

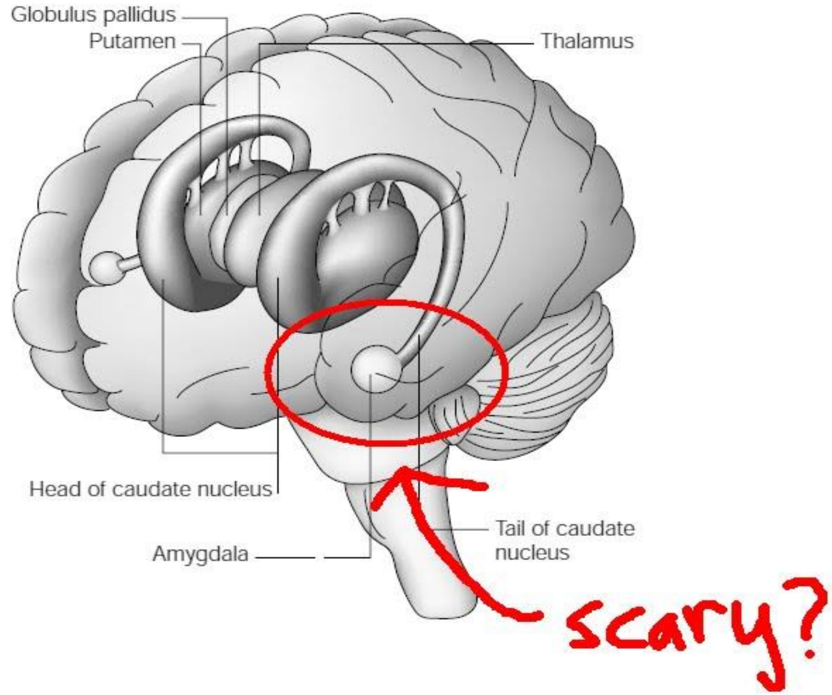
- **the amygdala** (rather than the hippocampus)
  - intervenes between the regions concerned with the somatic expression of emotion (the hypothalamus and the brain stem nuclei) and the neocortical areas concerned with conscious feeling (fear-the cingulate, parahippocampal, and prefrontal cortices)

Differentiation of emotions – neural studies
Joseph LeDoux, Michael Davis, and Michael Fanslow

- the **unconscious evaluation of the emotional significance of a stimulus begins before the conscious processing of the stimulus**

- Memory of emotional states as autonomic and somatic responses involves implicit memory storage. Memory of feelings involves explicit memory storage.
  - Damage to the **amygdala** disrupts the ability of an emotionally charged stimulus to elicit an unconscious emotional response
  - Damage to the **hippocampus** (the core of the medial temporal lobe system concerned with conscious memory) interferes with remembering the cognitive features of fear—where the fear-provoking stimulus was and in what context it occurred

Learned Emotional Responses Are Processed in the Amygdala



Amygdala

- The major groups of nuclei: *lateral*, *basal*, *medial*, *anterior*, *central*, and *cortical nuclei*.

- The amygdaloid complex has two components (functionally):
  - **Basolateral and corticomedial group of nuclei**

- **Afferent fibers**
  - direct inputs from the olfactory bulb
  - indirect inputs from the pyriform lobe
  - direct and indirect inputs from the solitary nucleus
  - auditory signals from the temporal neocortex and integrative signals from the prefrontal cortex
  - the ventromedial hypothalamus, substantia innominata, nuclei of the diagonal band of Broca, and medial thalamus

- **Efferent fibers**
  - the hypothalamus, BNST, and midbrain PAG

- AMYGDALA
  - mediates both inborn and acquired emotional responses – it is were UR and CR (through LTP) are paired

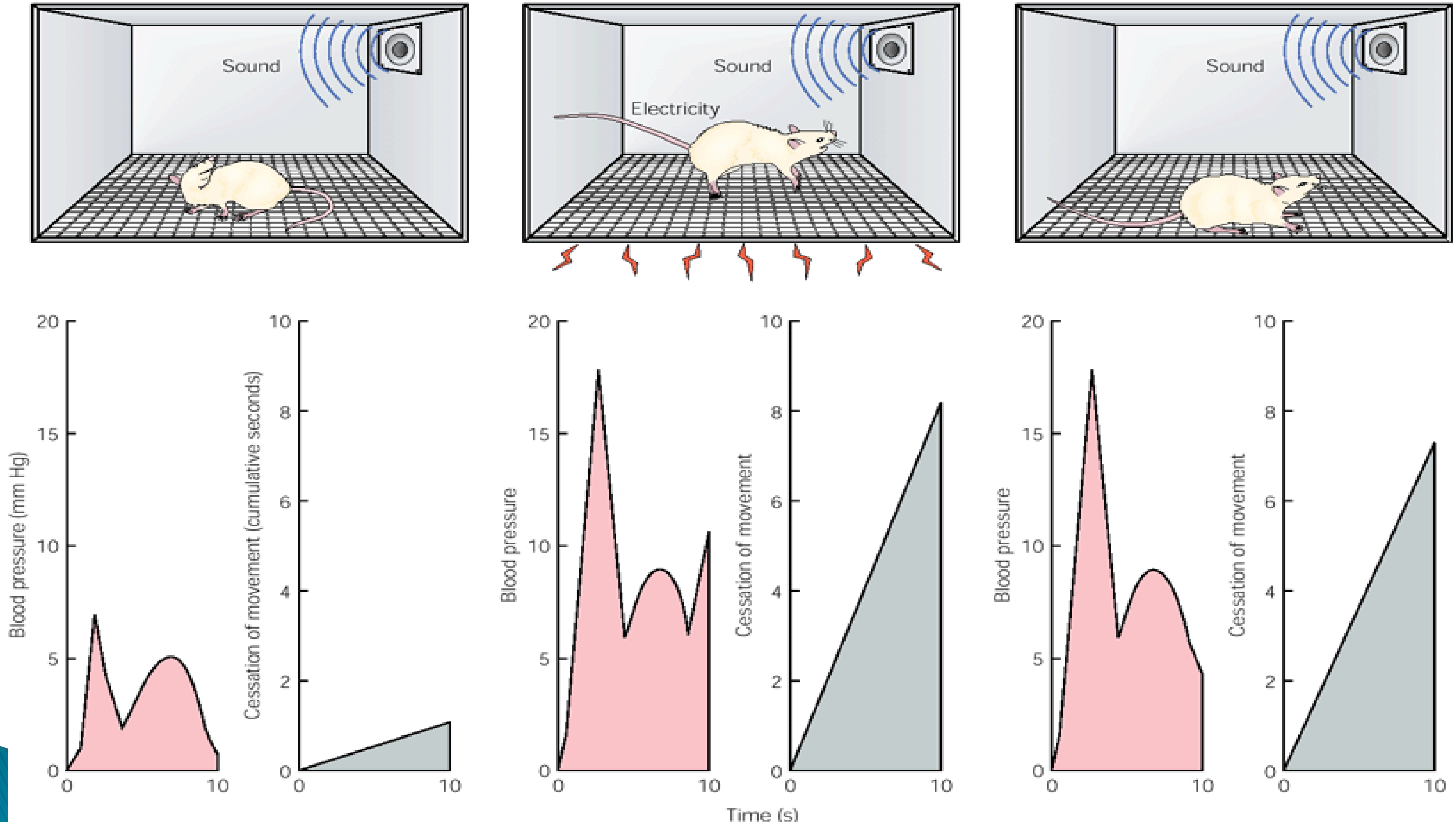
Classical conditioning of fear

- the best studied example of a learned emotional state

- **Ivan Pavlov**
  - classical conditioning of fear; expanded form of learning in which an association is established between the stimulus and its consequences

Ivan Pavlov in experimental setting

US – UR
US + CS= association
CS – CR

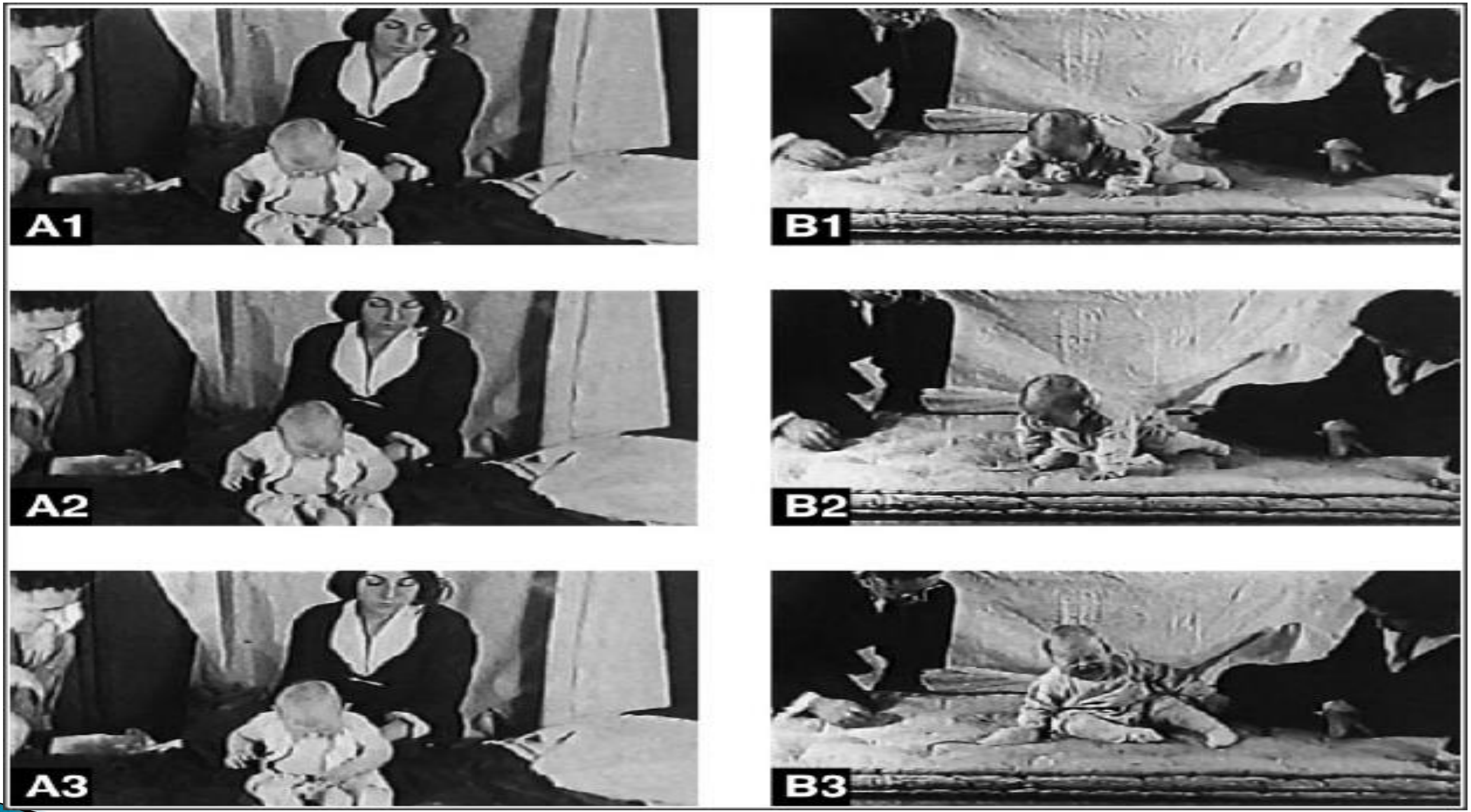


An example of classical conditioning (From Kandel, Schwartz i Jessell, 2000)

CHANGES:

A. somatomotoric immobility
B. sudden increase in the degree of excitation
C. decreasing the reflex threshold
D. hypoalgesia
E. sympathetic activation (tachycardia, hypertension, peripheral vasoconstriction, cessation of peristalsis)
F. release of glucocorticoids

WATSON AND RAYNER (1920.)



fear-potentiated startle

- people and experimental animals will startle more powerfully in response to a loud noise when they are frightened than if they are relaxed

- Bilateral destruction of the amygdala - eliminates this form of learned fear.
  1. emotional memories of learned fear are directly stored in the amygdala itself
  2. other emotional memories are not stored in the amygdala directly but are stored in the cingulate and parahippocampal cortices, with which the amygdala is interconnected

The sensory information about sound is conveyed to the basolateral complex **from two sources**:

- directly and rapidly from the auditory sensory nucleus in the thalamus
- indirectly and more slowly from the primary sensory areas of the cortex

- Information from the thalamus to the amygdala **can initiate short-latency, primitive emotional** responses

Prepare the amygdala to receive more highly processed information from cortical centers

- projections mainly into the basolateral nuclei
- stimulation of either thalamic or cortical pathways produces (LTP) in the basolateral complex

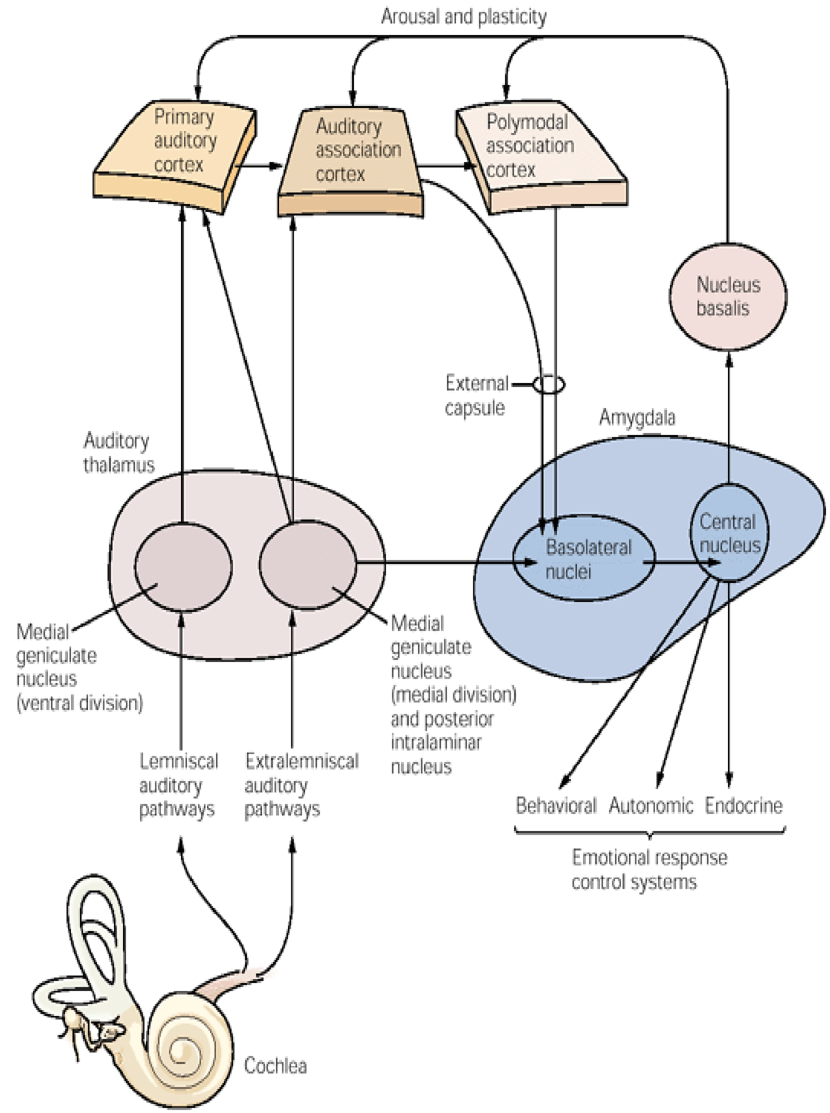


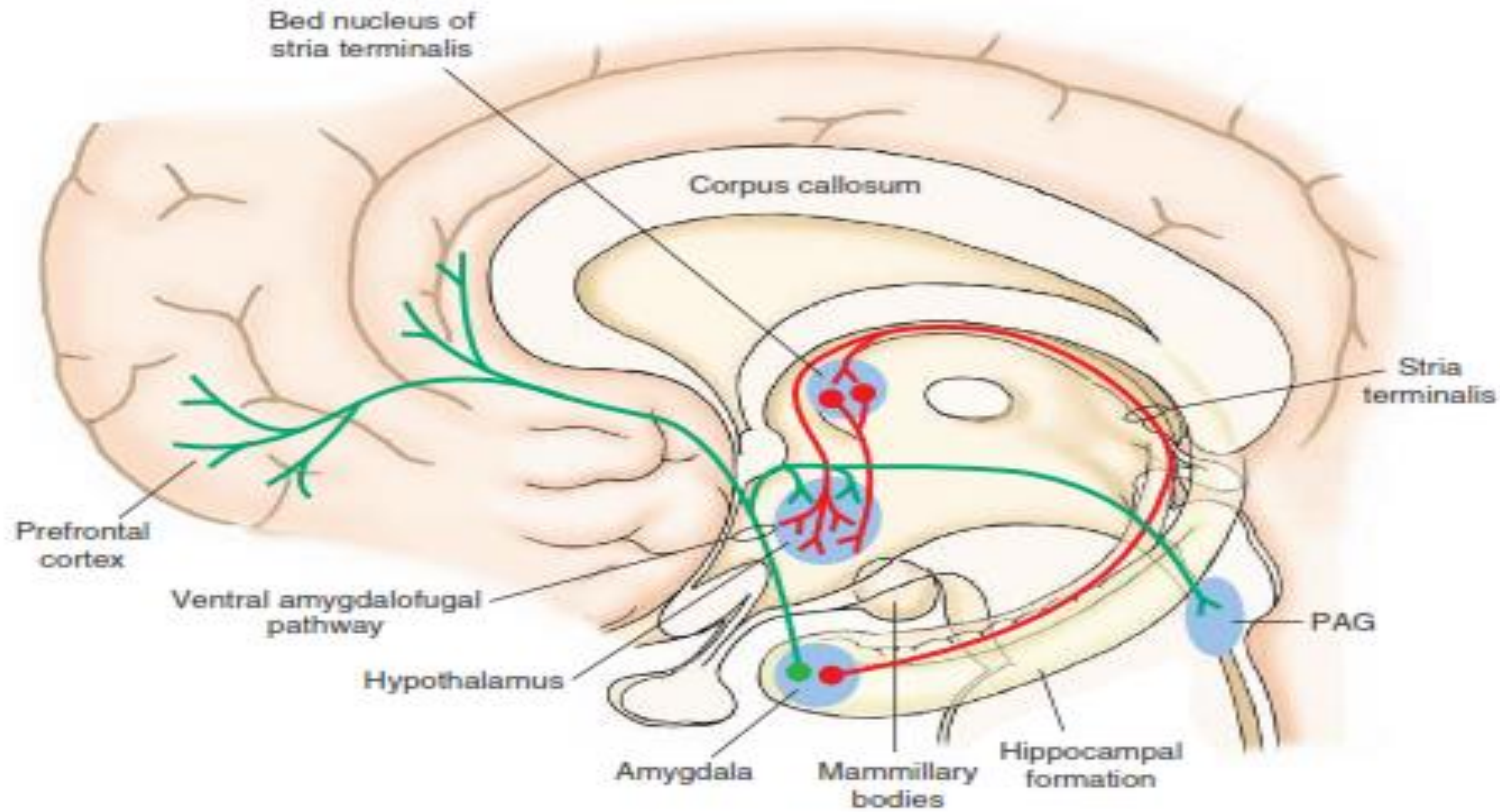
Figure 15. Pathways involved in the processing of emotional information
(From Kandel, Schwartz i Jessell, 2000)

- responses to a once-neutral sound - resembles human anxiety states
    - subjects presented repeatedly with a neutral sound together with an offensively loud noise - sweating hands, dry mouth, and facial perspiration to the neutral sound alone
- <u>patients with damage to the amygdala do not learn to fear the neutral sound</u>
    - consciously aware that the neutral sound and the offensive noise were paired together

Autonomic expressions of emotional states - mediated by the amygdala

- influence of the amygdala on conscious feeling - mediated by its projections to the cingulate gyrus and prefrontal cortex

- the nuclei of the amygdala - reciprocally connected to the lateral hypothalamus, brain stem, hippocampus, thalamus, and neocortex



Efferent projections of the amygdala (From Siegel and Sapru, 2011)

- **The stria terminalis**
  - projects to the bed nucleus of the stria terminalis and to the rostrocaudal extent of the medial hypothalamus
  - fibers from the bed nucleus also supply similar regions of the hypothalamus
- **The ventral amygdalofugal pathway**
  - projects to the hypothalamus and midbrain periaqueductal gray matter (PAG)
  - other fibers pass rostrally from the amygdala to the prefrontal cortex

BL and CM nuclei of the amygdala

Efferent projections from basolateral and corticomedial amygdala target the lateral and medial regions of hypothalamus (and midbrain PAG) - differentially modulate the various visceral functions normally associated with the hypothalamus

	Corticomedial	Basolateral
Feeding and drinking behaviour	Inhibit	Facilitate
Endocrine function	Facilitate	Inhibit
Growth hormone release	Inhibit	Facilitate
ACTH release	Inhibit	Facilitate

- Consequences differ:
  - Amygdala lesions in monkeys
  - Amygdala lesions in humans

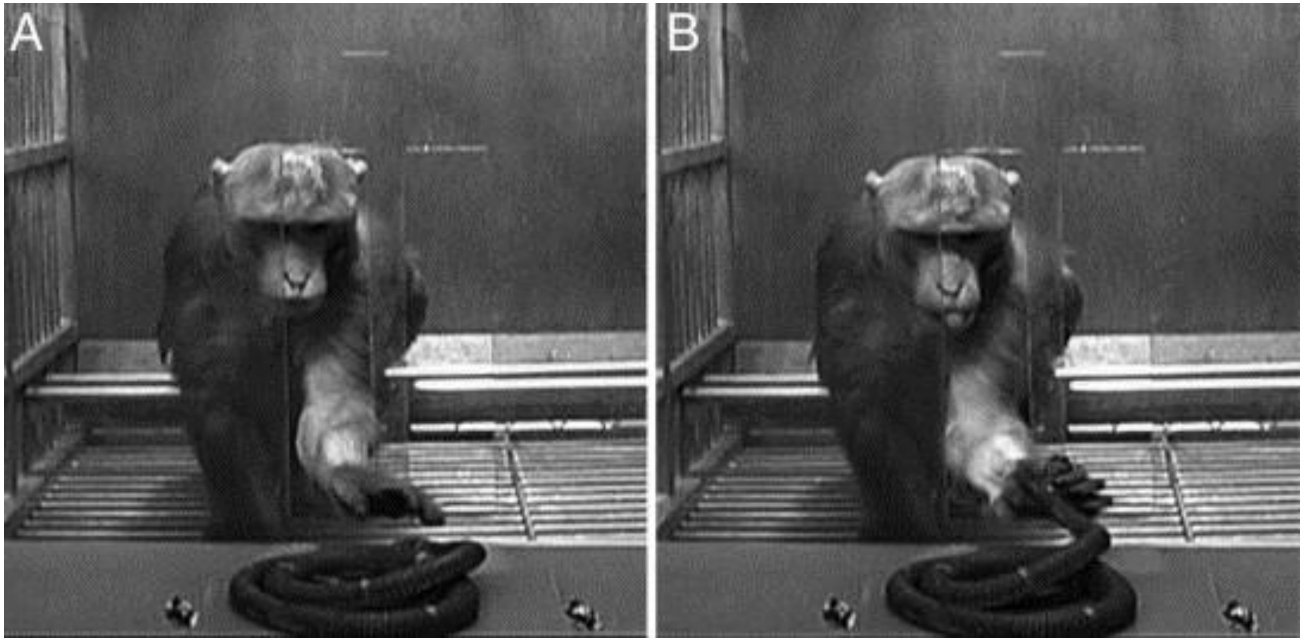
Kluver Bucy syndrome (1937.)

- bilateral removal of the temporal lobes in monkeys (including the amygdala and the hippocampal formation) and nonlimbic temporal cortex — a dramatic behavioral syndrome
  - monkeys - tame and fearless and their emotions flattened
  - for some years ascribed largely to the limbic system

- the syndrome can be **fractionated** - only some components involve the limbic system
  - For example, the visual deficits in Klüver-Bucy syndrome are mostly due to damage to the visual association areas of the inferior temporal cortex, the area concerned with the recognition of faces and other complex visual forms

- The hippocampus, the mammillary bodies, and anterior thalamic nuclei - found **not** to be involved in emotion but are critical for **cognitive** forms of memory storage

Kluver Bucy syndrome monkeys



Kluver Bucy syndrome monkeys

The woman who knows no fear

17 Dec 94

Patient S.M. Urbach Wieth disease

*These results, says Damasio, indicate that the **amygdala has a pivotal role in linking frightening signals from the environment with the body's fear responses**. Fear is universally important for survival in animals, Damasio notes, so it is reasonable that a special brain system has evolved to deal with it. The amygdala also seems to help us respond correctly to complex mixtures of negative emotions expressed by other people. Because she often fails to recognise criticism or aggression, S.M. has difficulty interacting socially. Positive emotions seem to be processed in another region of the brain. Just where is a mystery. **"We've never seen a patient who can 't recognise a happy face,"** says Adolphs.*

JENNIFER ALTMAN From New Scientist magazine, vol 144 issue 1956, 17/12/1994,

TWO **anatomically separate neural systems**

1. involved in the explicit memory of facial identity

2. concerned with the implicit memory of the appropriate cues that signal emotions expressed by faces

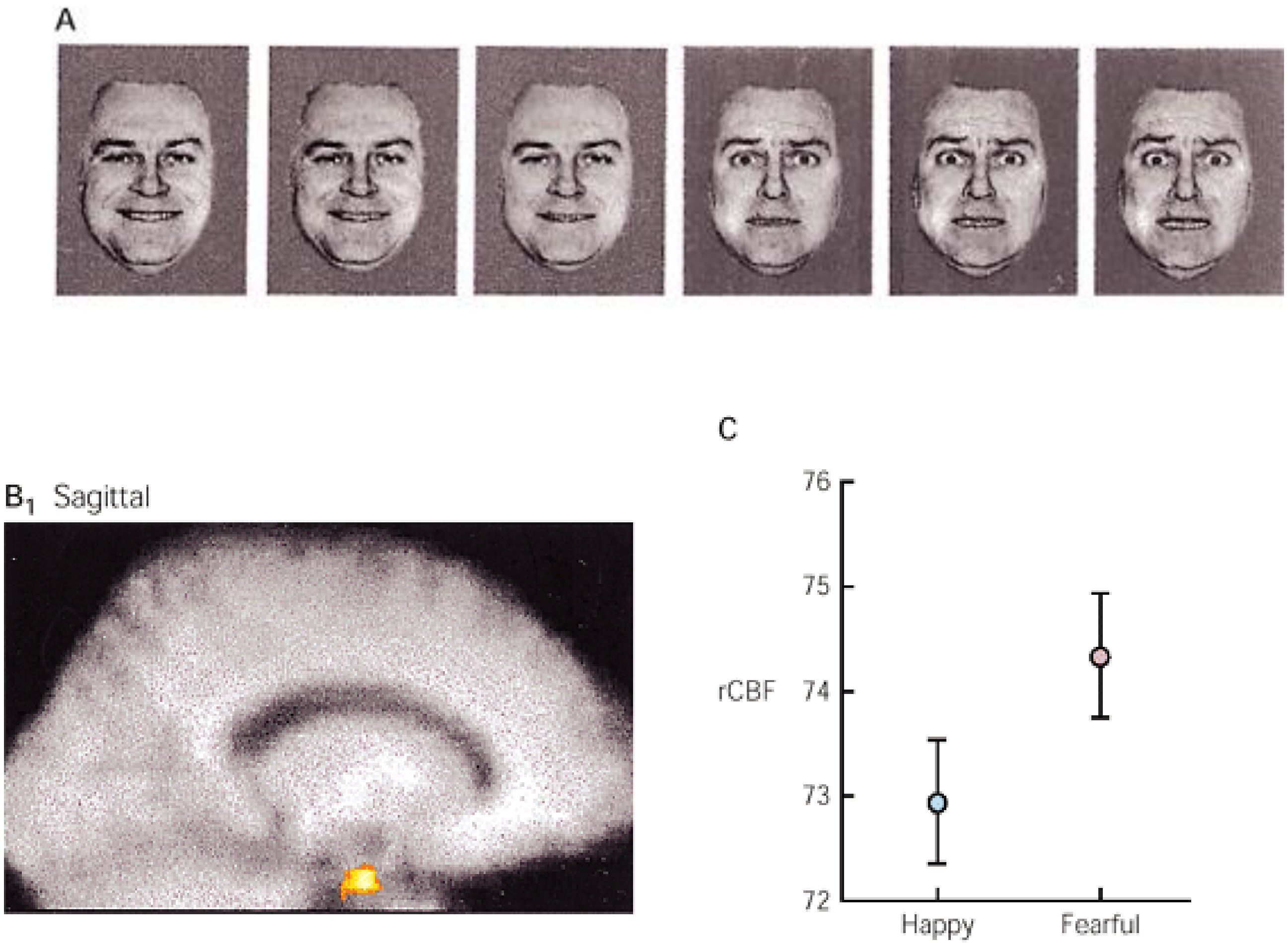


Figure 12 (From Kandel, Schwartz i Jessell, 2000)

- The mean regional cerebral blood flow (**rCBF**) for the predominantly happy and predominantly fearful expressions (Morris et al. 1996.)

CORTICES INVOLVED IN EMOTIONS

RESEARCH

1935 John Fulton and Carlyle Jacobsen

- the frontal cortex (*lobotomy*) in chimpanzees – calming effect

Egas Moniz

- isolating the orbital frontal cortex in humans – reducing anxiety
- 1935 psychosurgery – first attempt
- 1936 report on first 20 patients (sch, depr, anx)
- follow-up : few days

Moniz's first patient was less agitated and less overtly paranoid than she had been before, although she was also more apathetic and in fact duller than Moniz had hoped. She had a few physical side effects such as nausea and disorientation, but overall struck Moniz as much improved.

Moniz won the Nobel Prize in physiology/medicine for his contribution

Cerebral components – main limbic components

Prefrontal cortex

- receives afferent fibers from all regions of the cortex
- inputs from all brainstem monoaminergic systems and limbic-related structures
  - the mediodorsal thalamic nucleus
  - lateral hypothalamus
  - nuclei of the diagonal band of Broca basolateral
  - amygdala
  - subicular cortex

Efferent fibers

  - temporal neocortex
  - deep temporal lobe structures (amygdala and subicular cortex)
  - hypothalamus (direct and indirect routes)
    - mediodorsal thalamic nucleus – midline thalamic nuclei - prefrontal cortex

Cerebral components – main limbic components

Anterior cingulate gyrus

Input:

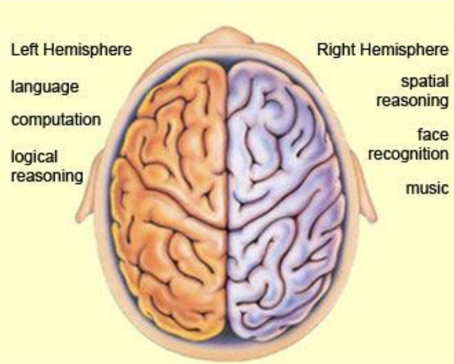
- the anterior thalamic nucleus,
- ventral tegmental area (dopaminergic fibers)
- the diagonal band of Broca

Efferent fibers:

- the mediodorsal thalamic nucleus (mediodorsal thalamic nucleus → midline thalamic nuclei → anterior lateral hypothalamus)
- the subicular cortex
  - through the cingulum bundle to the hippocampal formation, forming a component of the Papez circuit

EMOTIONAL DOMINANCE OF THE RIGHT HEMISPHERE

- difficulty in recognizing emotional facial expression after lesions
- recognition of emotionally important events in patients with severed corpus callosum only from the left visual field
- emotionally expressive facial movements more pronounced on the left side of the face
- recognition of emotional facial expressions in photos shown in left visual field



LEFT H	RIGHT H
Positive emotion	Negative emotion
Lesions in the left cerebral hemisphere often lead to depression	Lesions in the right cerebral hemisphere more often lead to manic behaviour
Positive emotions ◊ EEG activity L prefrontal and temporal cortex	Negative emotions ◊ EEG activity R prefrontal and temporal cortex
Depression ◊ decreased activity in the L ventral and dorsolateral prefrontal cortex	OCD ◊ increased activity in the R medial prefrontal cortex
L and R lesions of the ventromedial prefrontal cortex – patients not able to cognitively predict the consequences of their actions (positive and negative)	

Specific neuroanatomical sex differences

Specific Sex Differences in the Brain

The sexually dimorphic nucleus of the preoptic area (SDN-POA)

The interstitial nucleus of the anterior hypothalmus-3 (INAH-3)

- larger in men than women

Certain sex differences in cognitive performance

- men perform better than women on most visuospatial tasks
- M vs W 13:1 in advanced mathematical reasoning ability
- women perform better than men on verbal tasks
- brain function in men is more lateralized than in women
  - observed in a clinical setting; women are more likely than men to recover speech after a stroke that damages cortical speech areas

SDN –POA (Hofman and Schwab, 1991)

- Regulation of LH, FSH and prolactine
- Max number of neurons in 2-4 years
- Sexual dimorphism visible after 4th year
  - F- reduction in neuron numbers SDN POA
  - M- increase of neurons up to 50 years
- Programmed cell death
  - 2.2 times larger in males than in females
  - 2 times more neurons

- Hofman, MA, & Swaab, DF (1991). Sexual dimorphism of the human brain: Myth and reality.Experimental Clinical Endocrinology,98, 161–170.

Genetic and Anatomical Basis for sexual orientation?

Three structural differences

- <u>The suprachiasmatic nucleus</u>
  - larger in volume and contains more neurons in homosexual men than in a reference group of heterosexuals
- <u>The hypothalamic nucleus INAH-3</u>
  - larger in heterosexual than in homosexual men
- <u>The midsagittal cross-sectional area of the anterior commissure</u>
  - larger in a group of homosexual men than in a reference group of heterosexuals

The concordance rate among twins—the occurrence of homosexuality in both twins of a pair

- much higher among identical twins than among nonidentical twins
- even smaller for adopted siblings of homosexual individuals

Table 57-5 Concordance for Homosexuality in Twins

	Males[a]	Females[b]
Monozygotic twins	(29/56) 52%	(34/71) 48%
Dizygotic twins	(12/54) 22%	(6/37) 16%
Adopted same-sex siblings	(6/57) 11%	(2/35) 6%
	Males[c]	**Females[c]**
Monozygotic twins	(22/34) 65%	(3/4) 75%
Dizygotic twins		
Male/male	(4/14) 29%	
Male/female	(3/9) 33%	

[a]Bailey and Pillard 1991. [b]Bailey et al. 1993. [c]Whitman, Diamond, and Martin, 1993.

Figure 18. Concordance for homosexuality in twins (From Kandel, Schwartz i Jessell, 2000)

A gene-linkage analysis of the X chromosome in 40 pairs of homosexual brothers Using pedigree analysis (Dean Hamer and colleagues)

- 33 pairs had inherited the same chromosomal markers of a region at one tip of the X chromosome labeled Xq28
- there may be one or more genes within Xq28 that predispose an individual to male homosexuality

The debate - the causes of homosexuality in terms of nature versus nurture: *both* are involved

- a complex behavioral trait such as sexual orientation - unlikely to be caused by a single gene, a single hormone-induced alteration in brain structure, or a single experience in life

The etiology of homosexuality and heterosexuality - **multifactorial**.

Literature

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- Siegel and Sapru (2012) Essential neuroscience. Lippincott Williams & Wilkins.