Neural bases of learning and memory

Lecture 2/7

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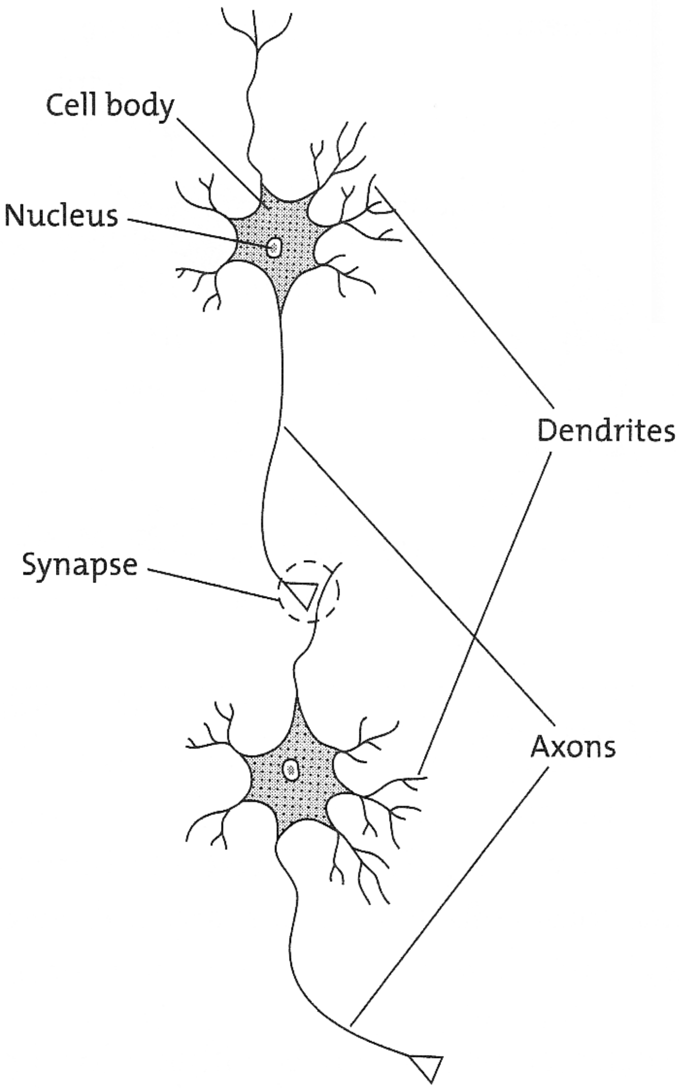
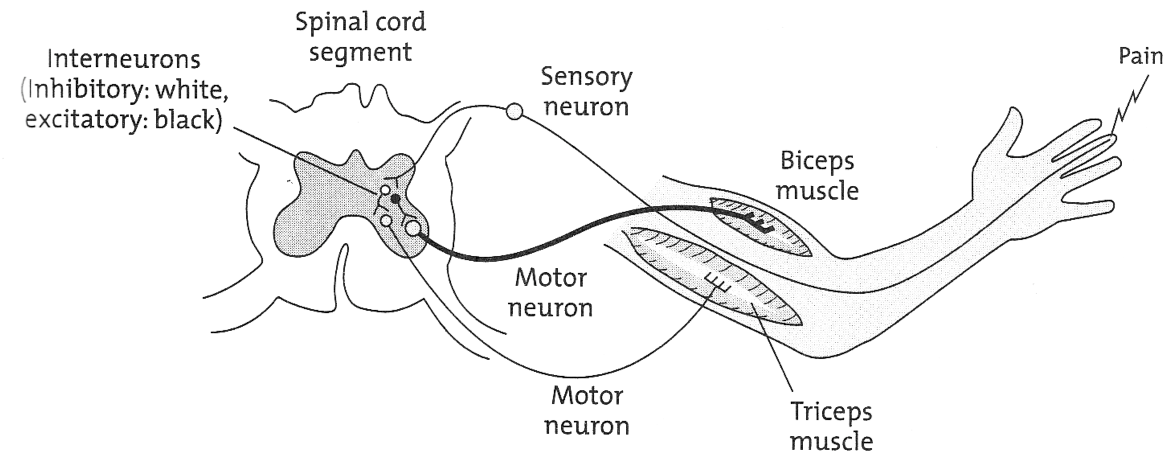
Agenda

- Overview of the neuroscience of memory/learning
- Basic concepts and ideas that will be useful for thinking about later findings.

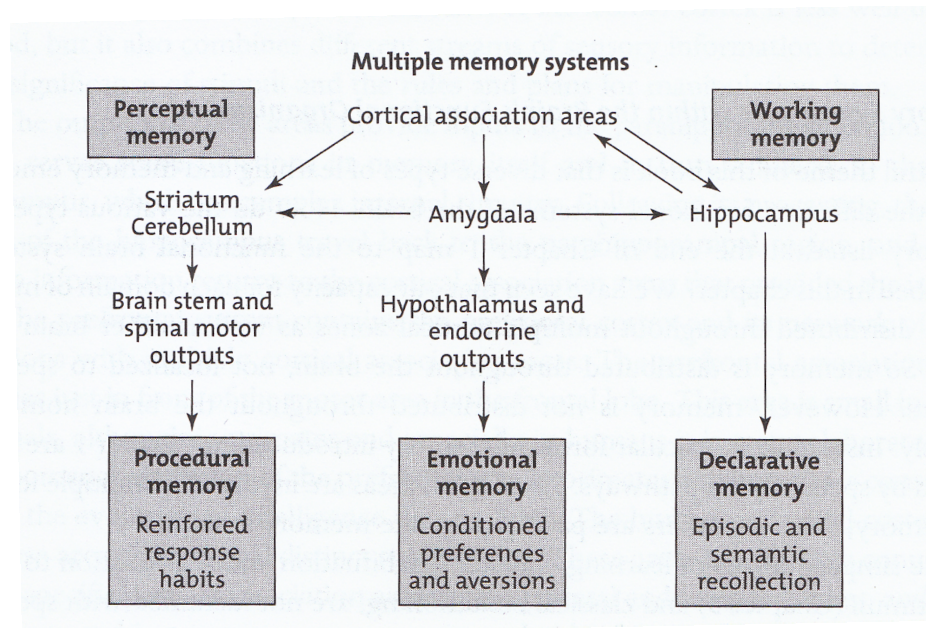
1 *Cells*



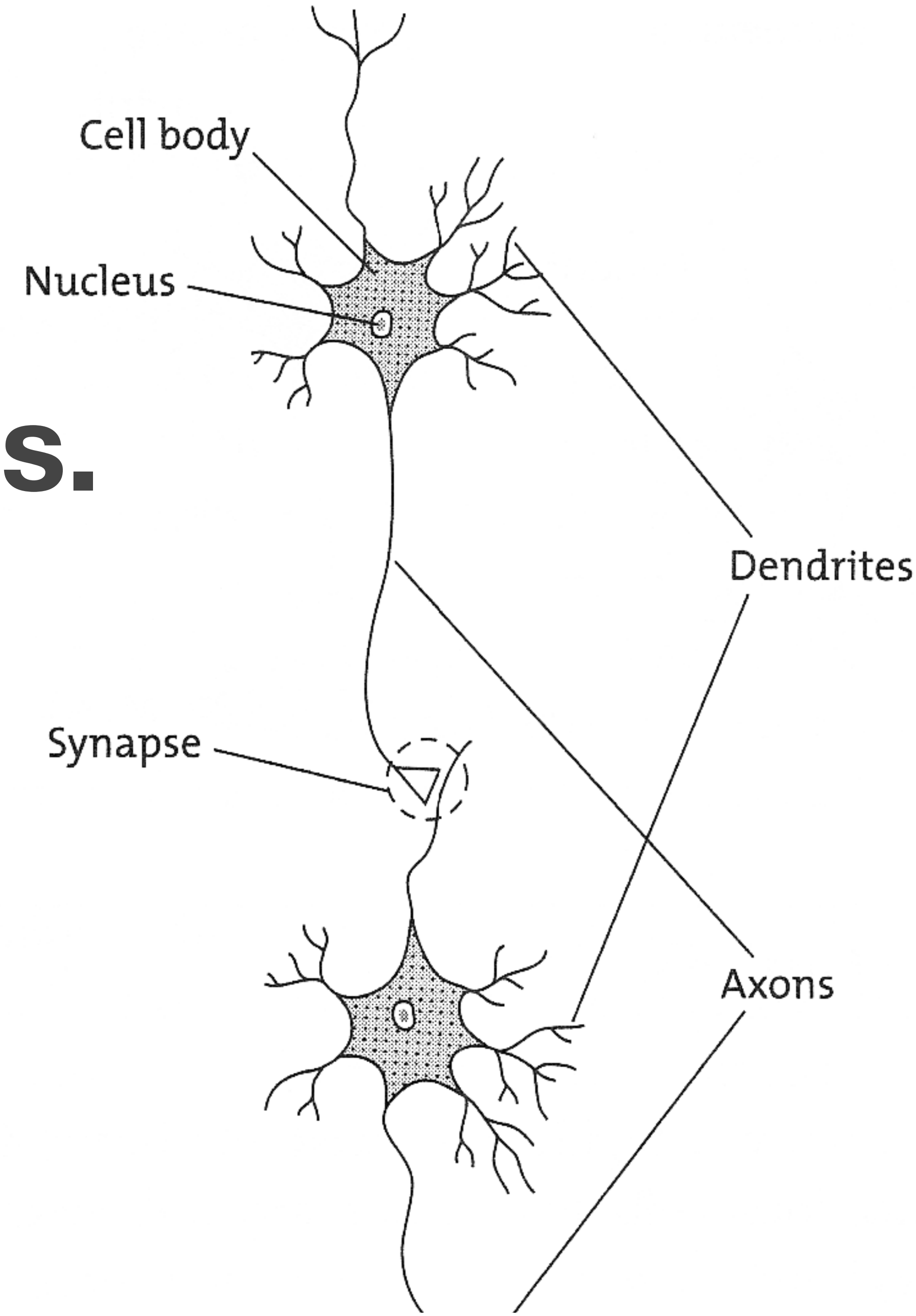
2 *Circuits*



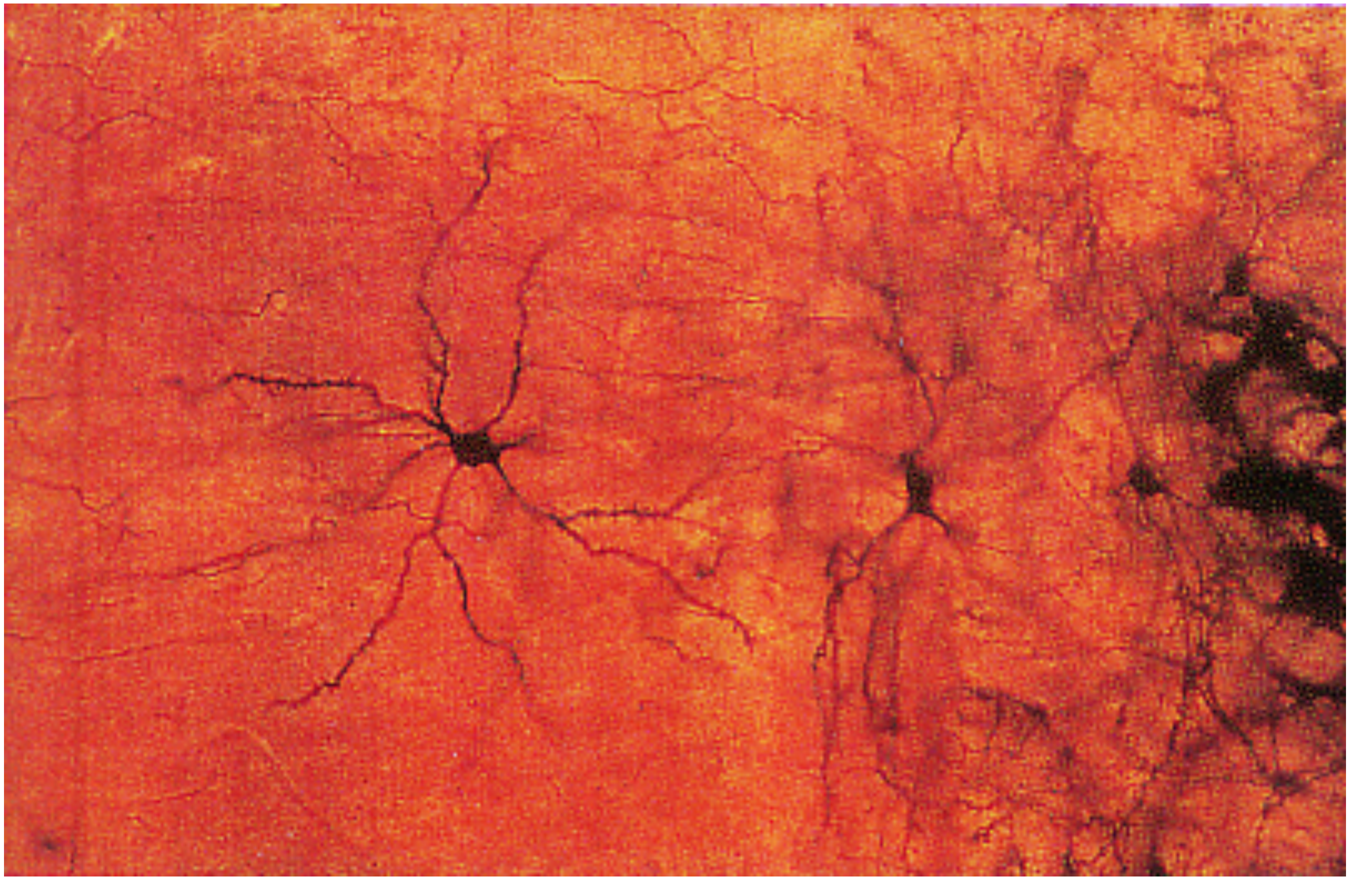
3 *Systems*



1 Cells. Neurons.



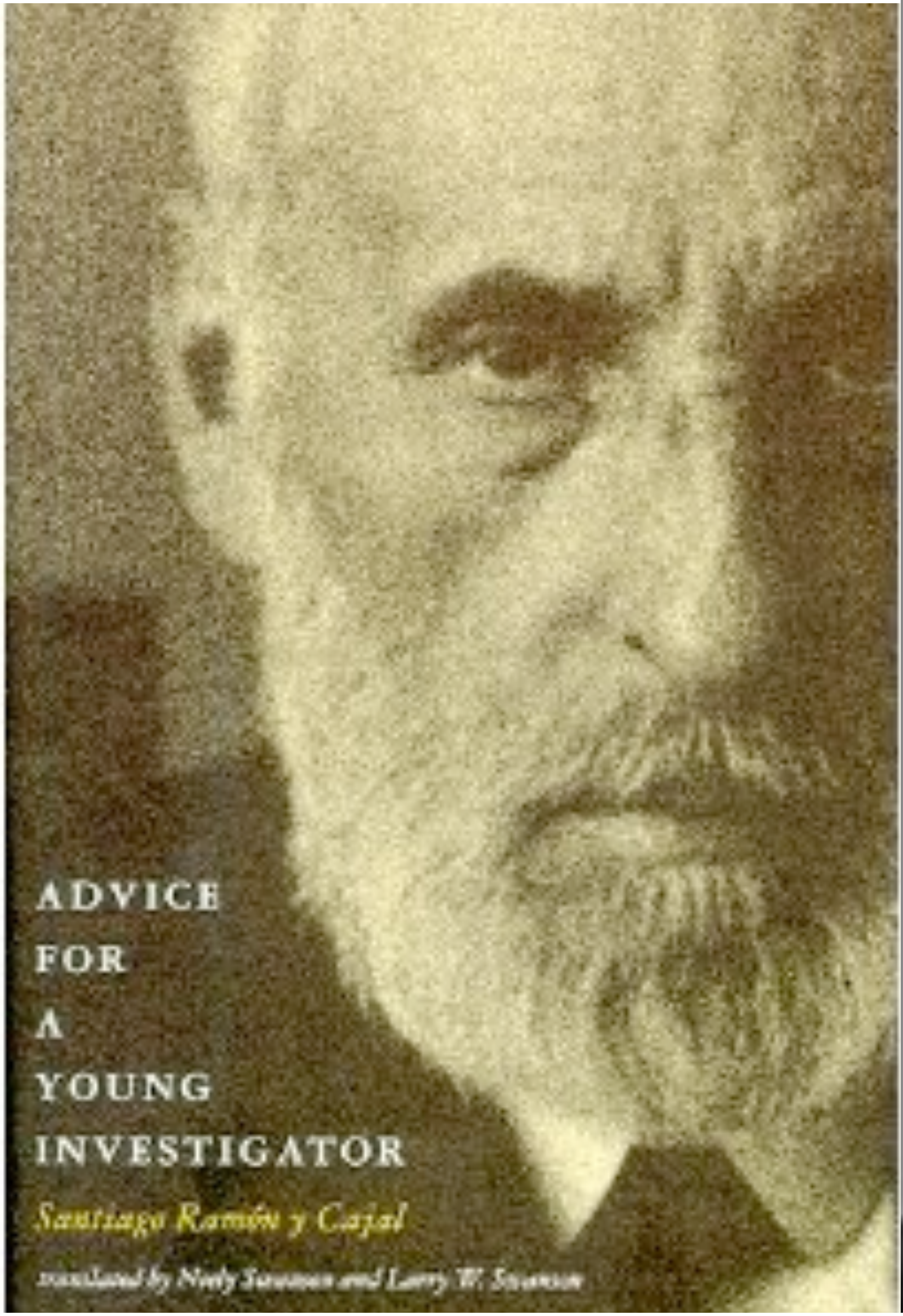
Golgi Stain (Camillo Golgi)

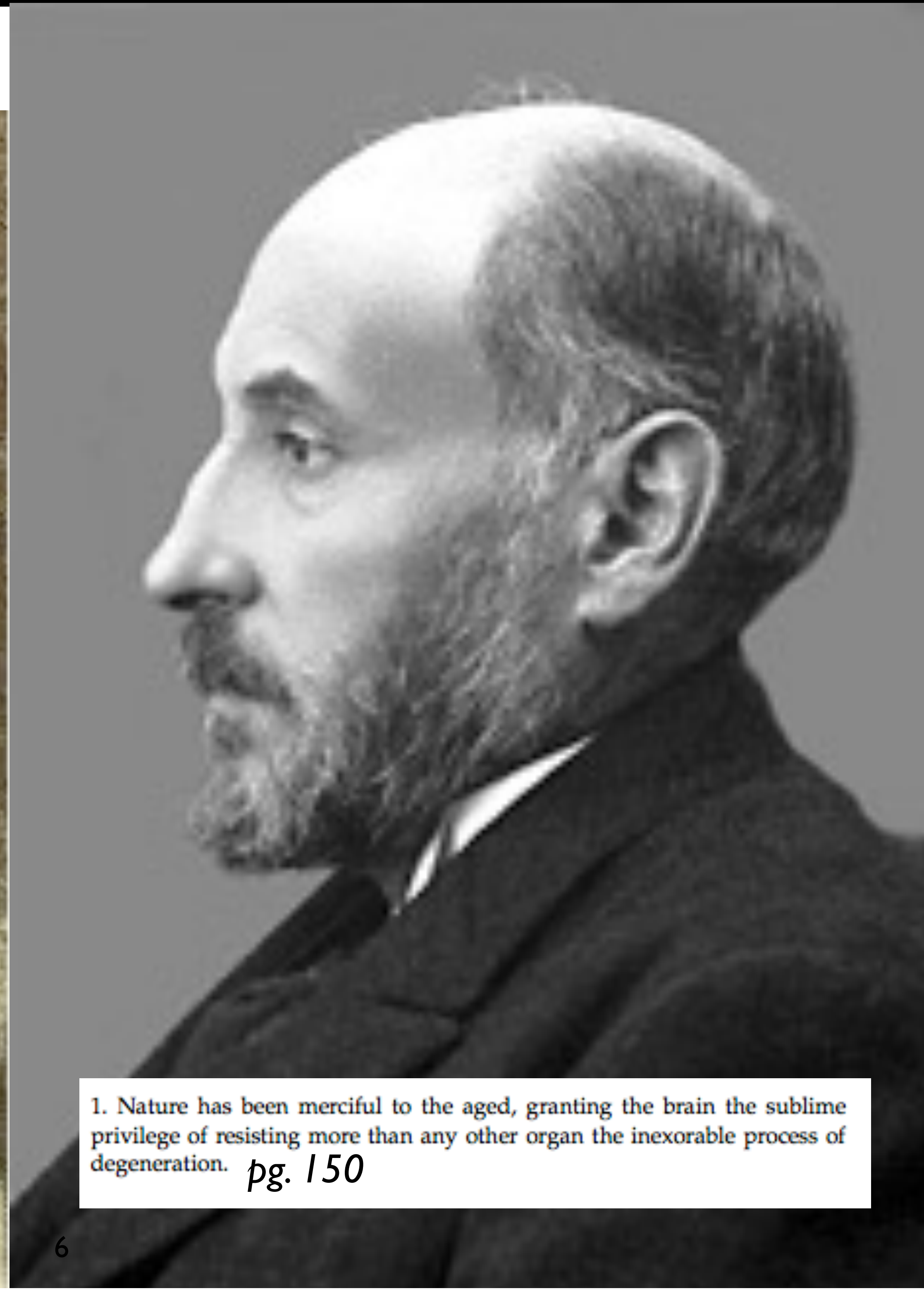


1873: developed a silver stain that allowed visualization of individual neurons

Reticular theory: brain a continuous network of cells

Santiago Ramon y Cajal





1. Nature has been merciful to the aged, granting the brain the sublime privilege of resisting more than any other organ the inexorable process of degeneration. *pg. 150*

Neuron as discrete individual cells

- **Santiago Ramon y Cajal** refined Golgi's staining method, which (for still unknown reasons) only stains *some* cells and not others

Drawing of a Purkinje cell in the cerebellum cortex done by Santiago Ramón y Cajal, clearly demonstrating the power of Golgi's staining method to reveal fine detail

Neuron as discrete individual cells

- This staining method revealed fine structure of **dendrites** and the single **axon** which left the cell body

- Staining didn't flow from one cell to the next suggesting the neurons communicate indirectly (there are gaps)

- **Neuron Doctrine** - that the nervous system is composed of individual cells that interact and are the basic units of information processing/computation.

- Golgi and Cajal shared the 1906 Nobel Prize in Physiology

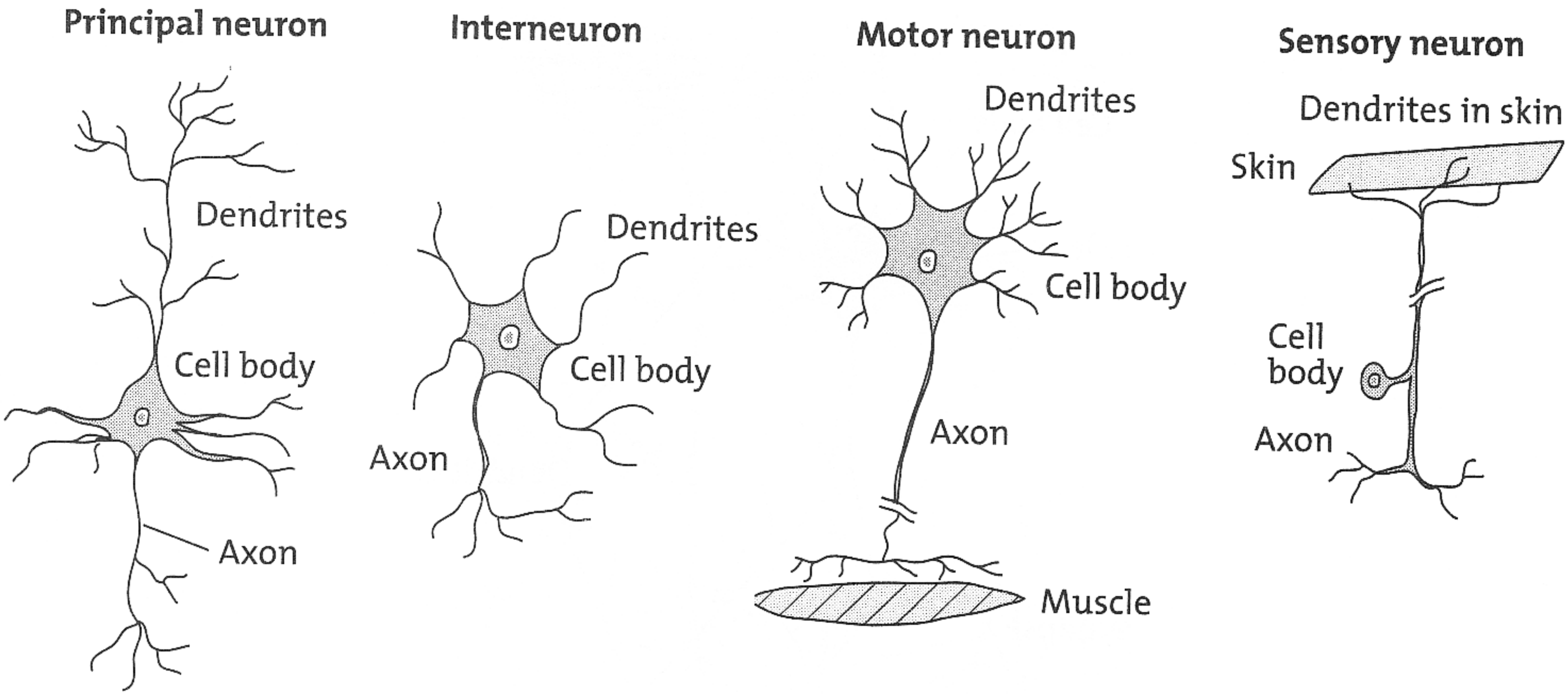
Drawing of a Purkinje cell in the cerebellum cortex done by Santiago Ramón y Cajal, clearly demonstrating the power of Golgi's staining method to reveal fine detail

Neuron as discrete individual cells

information flow

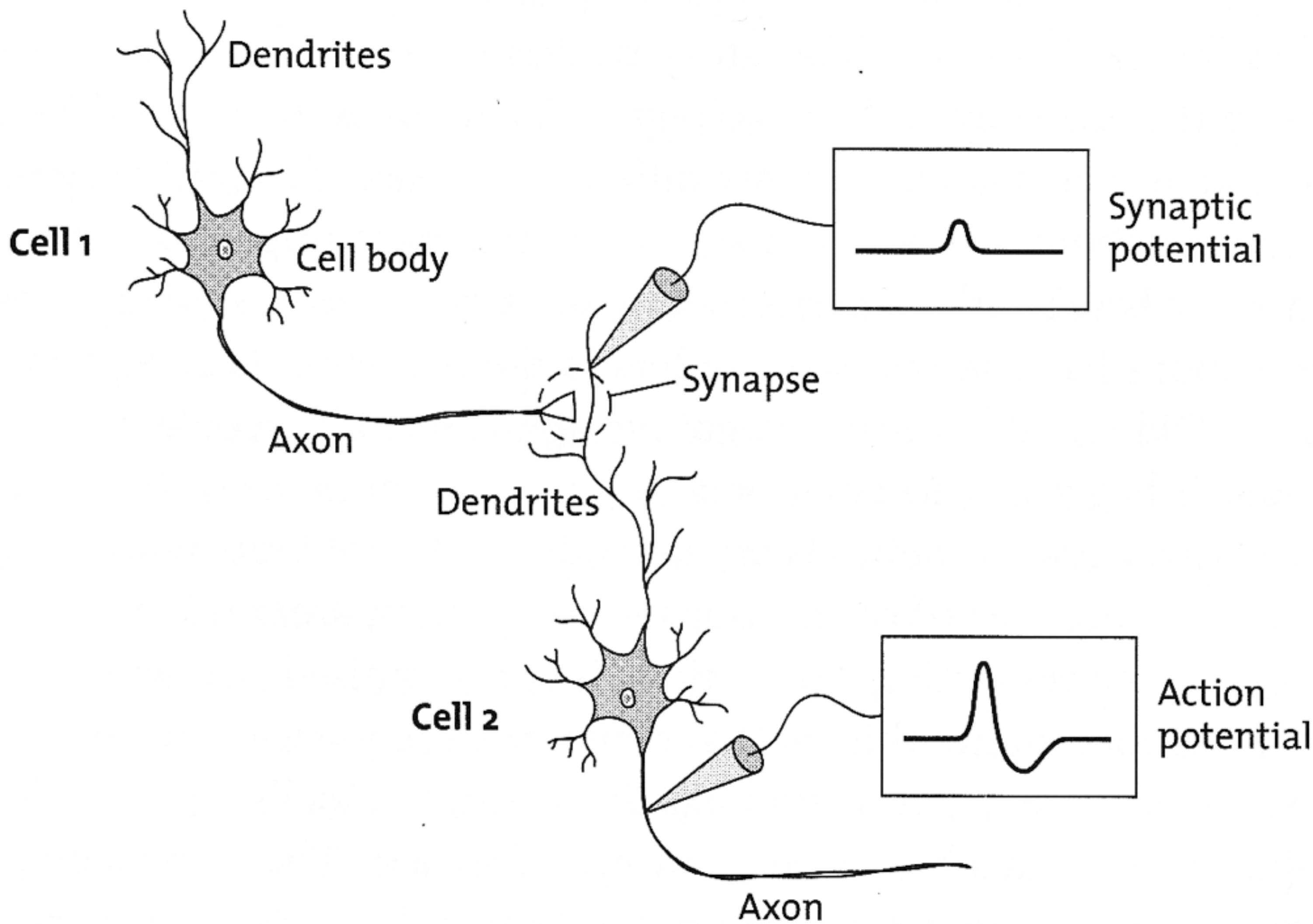
(Cajal deduced this from orientation of neurons in sensory areas)

Neuron as discrete individual cells

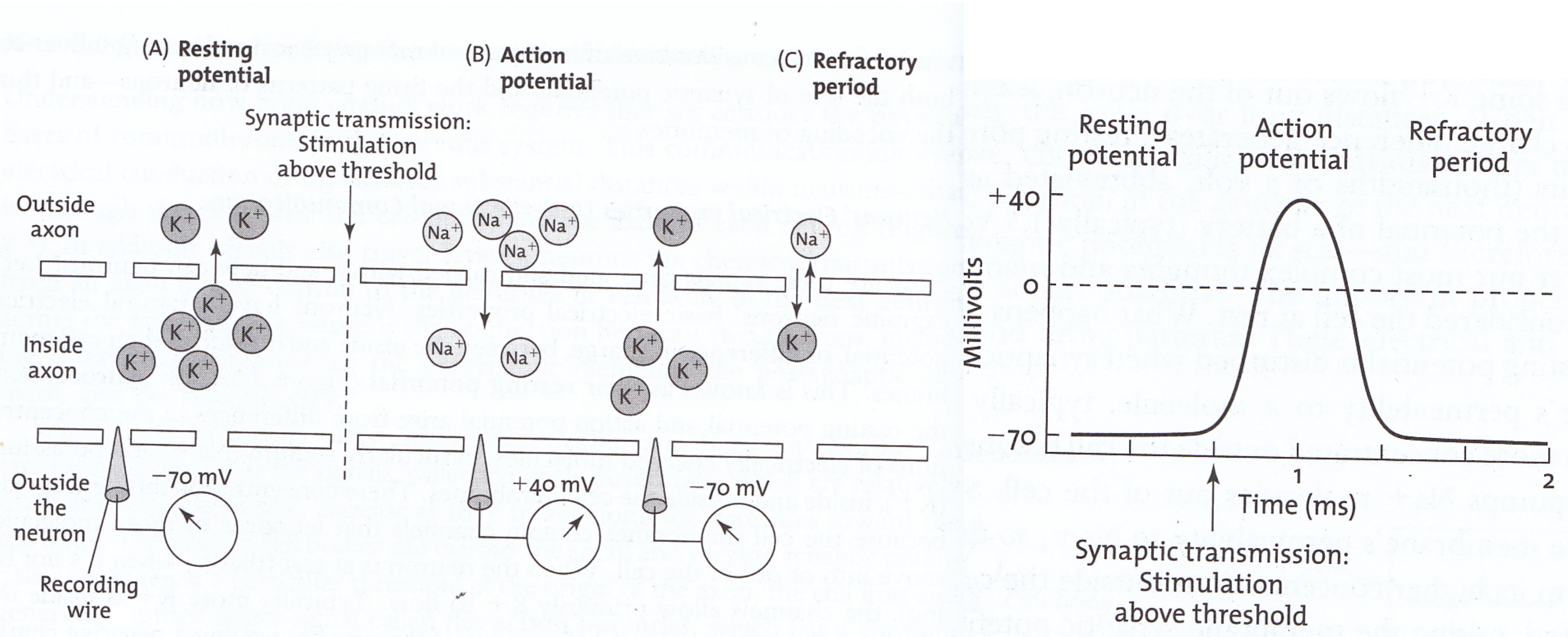


There are many types of neurons, each with different structure/ connectivity patterns, and the patterns of connectivity (across species) predict complexity of behavior.

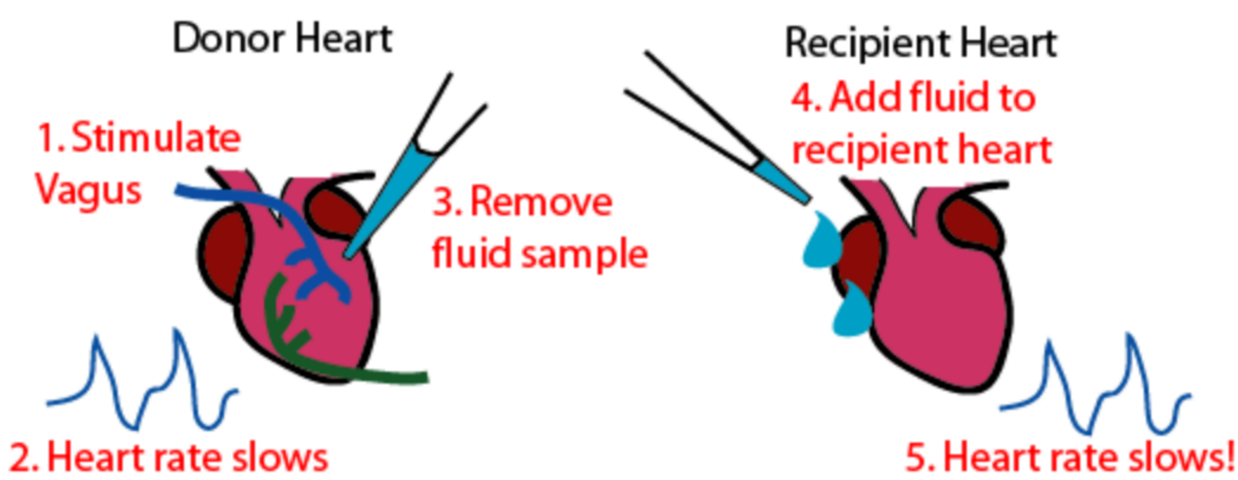
How do they work?



Electrical properties of neurons and potentials



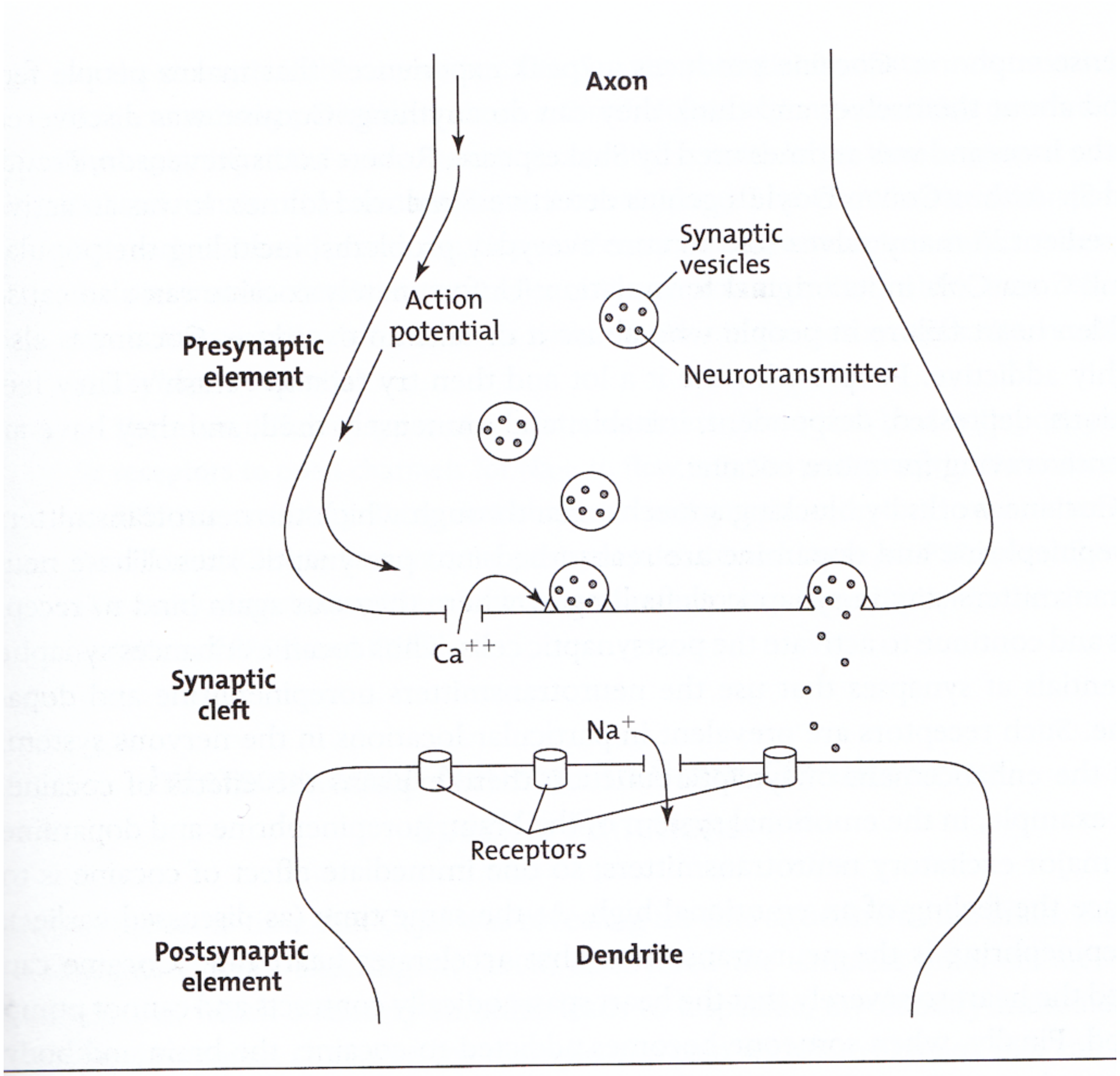
The synapse: Where the sidewalk (or neuron) ends



Chemical signaling?

Otto Loewi's famous frog heart experiment (1921)

The synapse: Where the sidewalk (or neuron) ends



Receptive Fields and the Selectivity of Neural Response

Primary Visual Ctx

Somatosensory Ctx

Inferotemporal Ctx

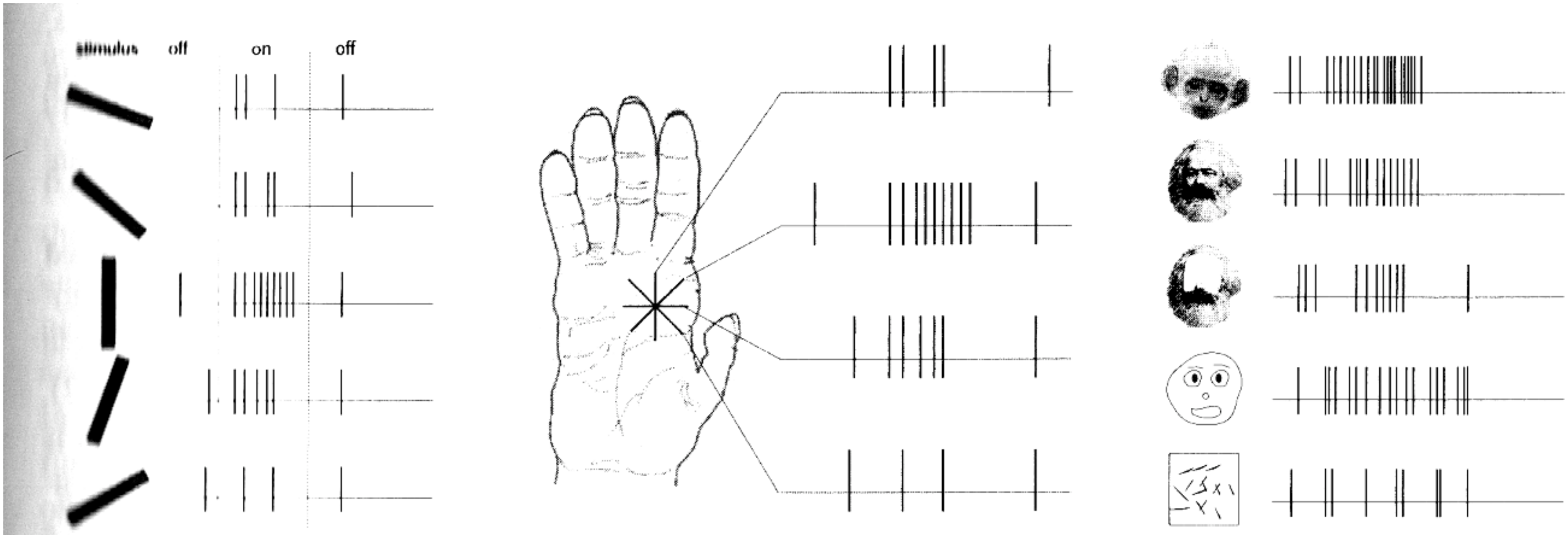
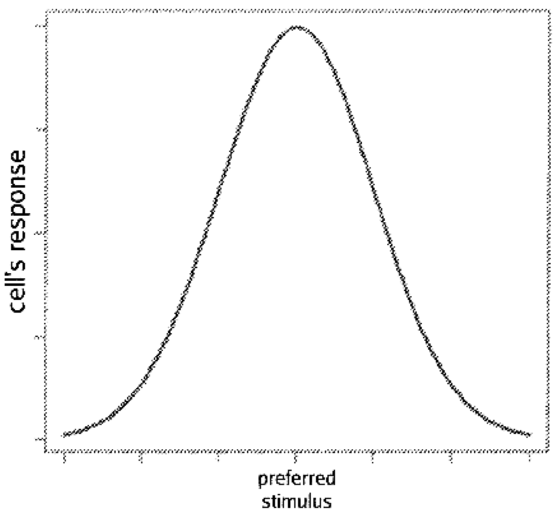


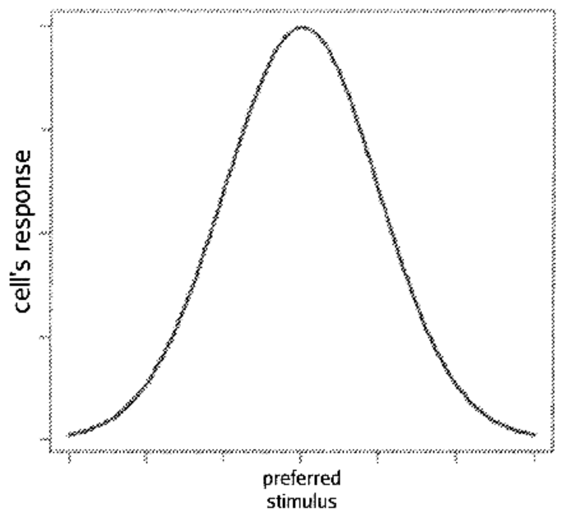
Figure 3.2 — RECEPTIVE FIELDS of sensory neurons. *Left:* a typical tuning profile of a neuron in the primary visual cortex of a cat, which responds selectively to a line segment of a particular orientation, appearing at a particular location in the visual field. The neuron's responses are shown alongside the stimuli that evoked them. *Middle:* the receptive field of a monkey's somatosensory neuron, plotted on the skin of the hand; also shown are the spike trains evoked by straight-edge stimuli of different orientations. *Right:* the responses of a face-tuned neuron in the inferotemporal cortex of a monkey to various stimuli (many such neurons were described by Perrett, Mistlin, and Chitty, 1987).

Receptive Fields and the Selectivity of Neural Response



A typical TUNING CURVE of a sensory neuron is smooth, graded, and compact, reflecting moderate selectivity in the space of possible stimuli. One of the many computational benefits of this property of neuronal response tuning is hyperacuity, discussed in section 5.1.

Receptive Fields and the Selectivity of Neural Response



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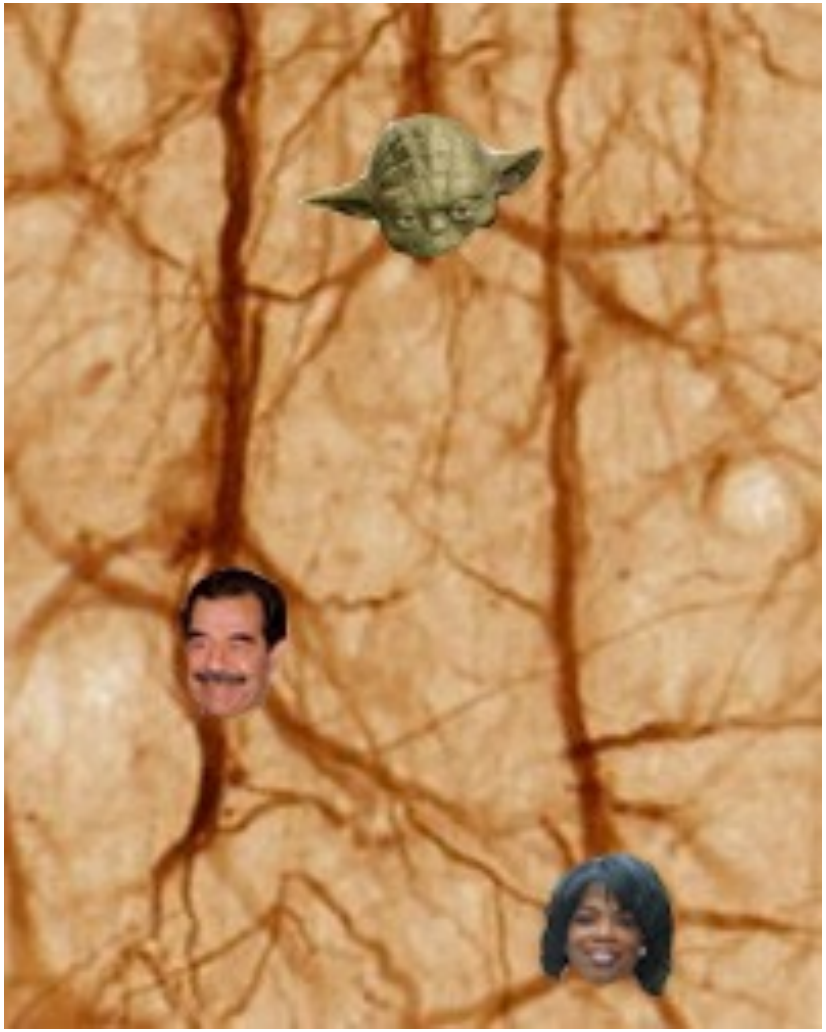
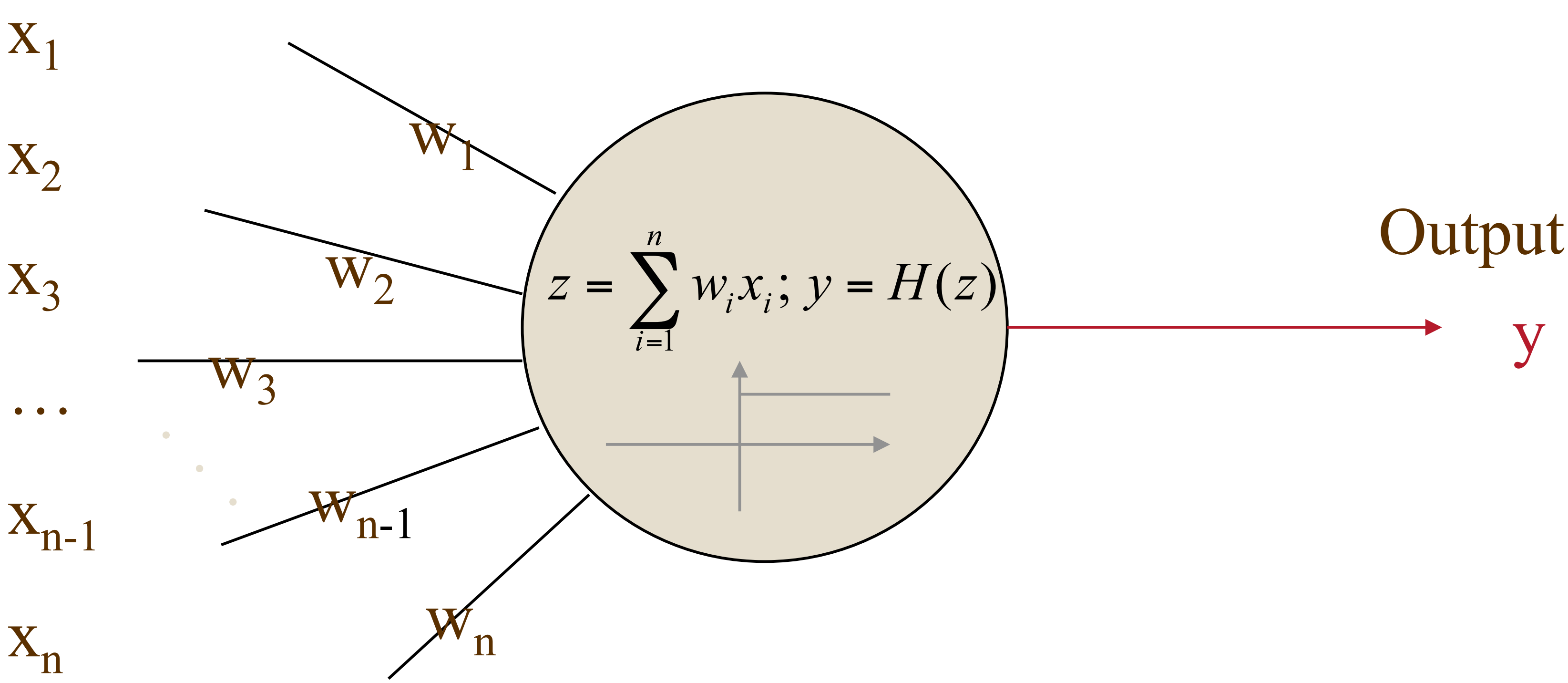


Neurons form the basic computational units of information processing in the brain.

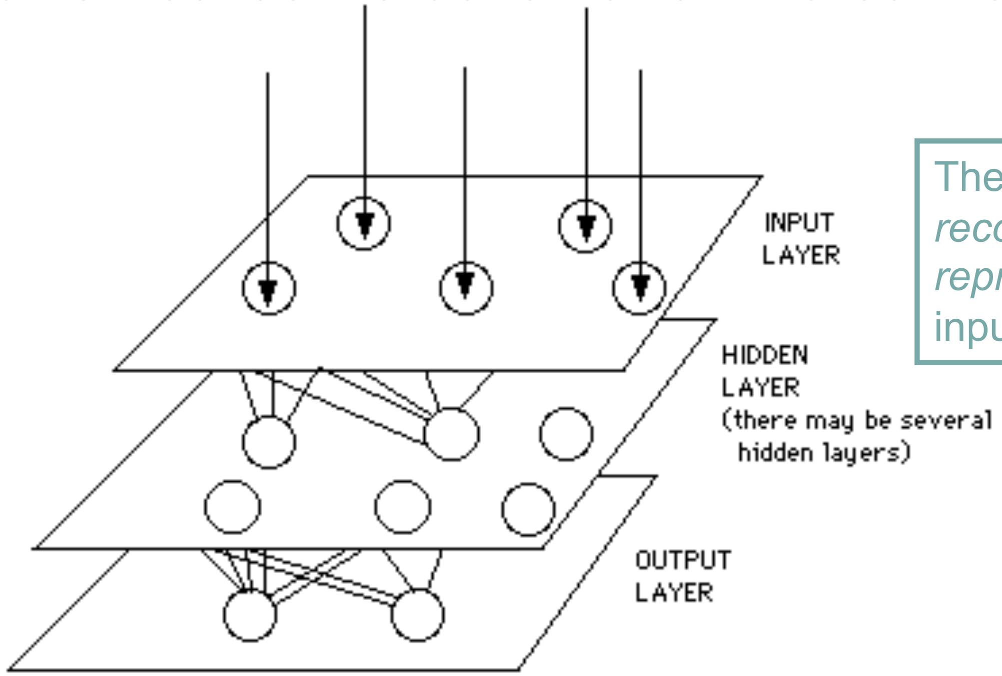


The McCullogh-Pitts model

Neurons form the basic computational units of information processing in the brain.

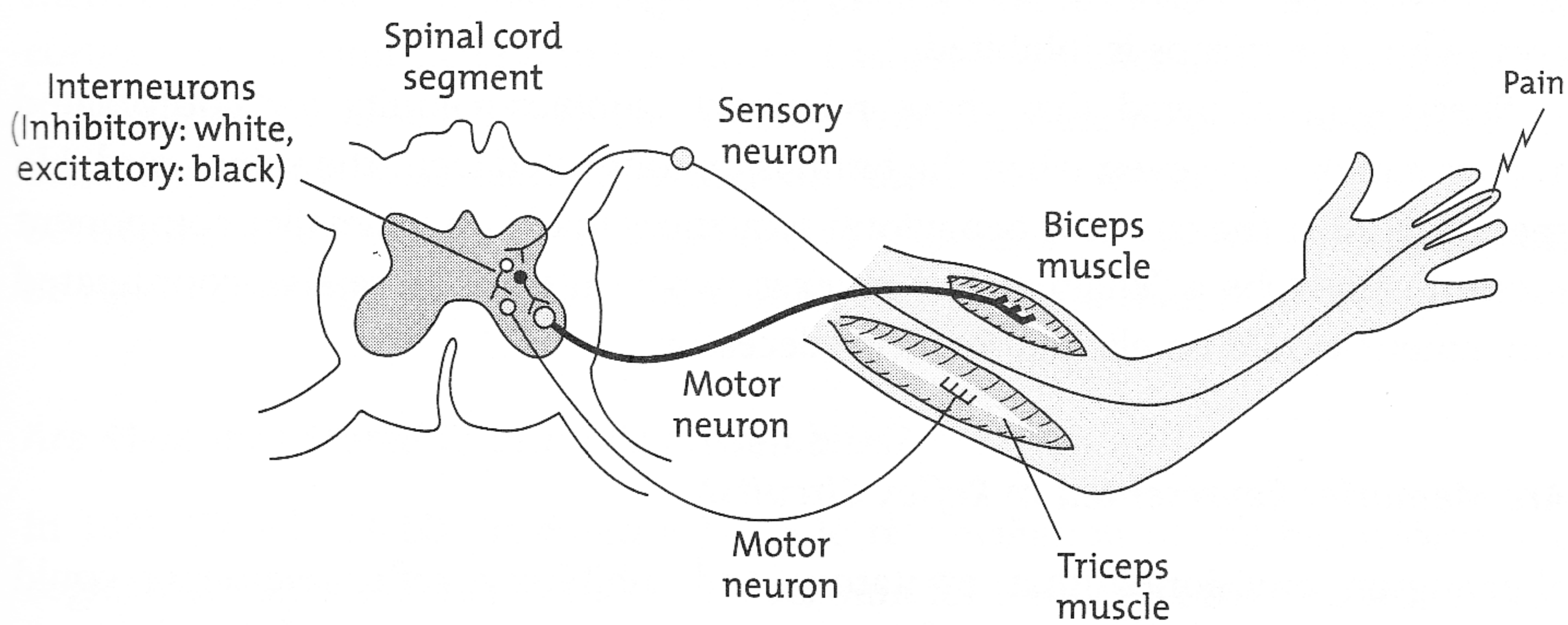
Adaptive interaction between individual neurons

Power: collective behavior of interconnected neurons

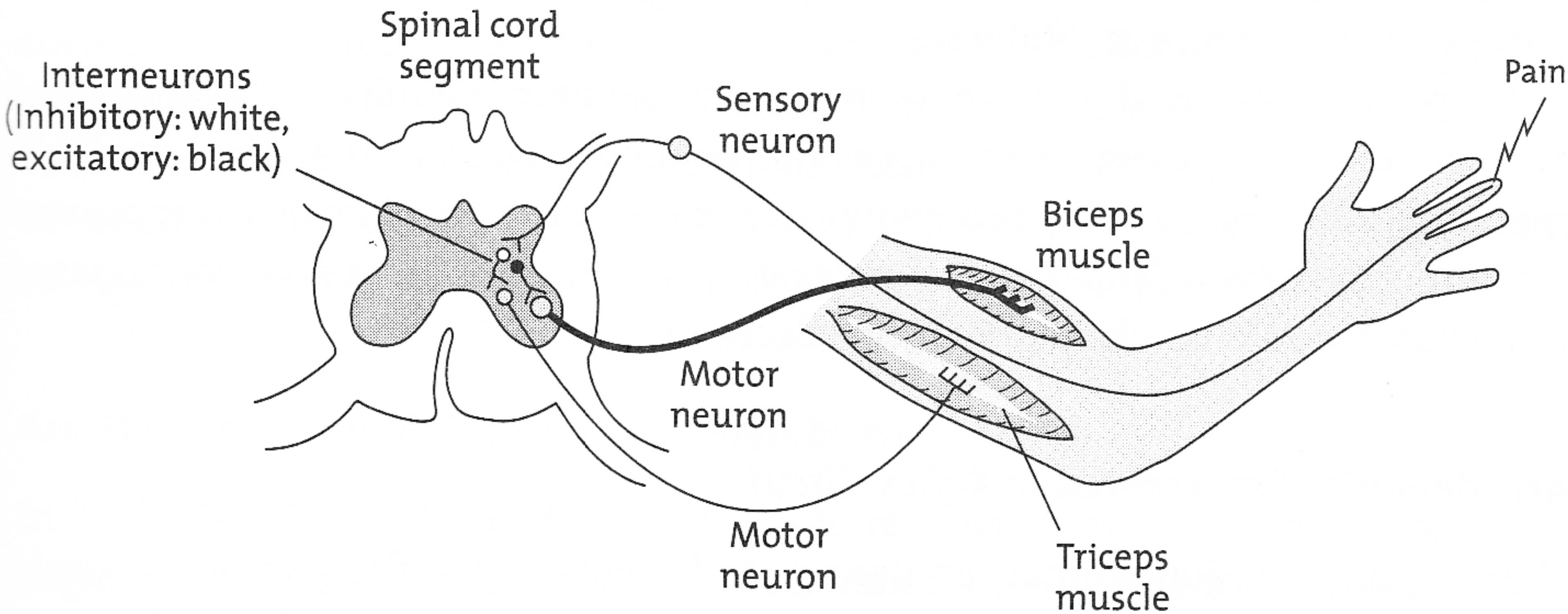


The hidden layer learns to *recode* (or to *provide a representation* of) the inputs: associative mapping

2 Circuits.


Spinal cord segment
Interneurons (Inhibitory: white, excitatory: black)
Sensory neuron
Pain
Biceps muscle
Motor neuron
Motor neuron
Triceps muscle

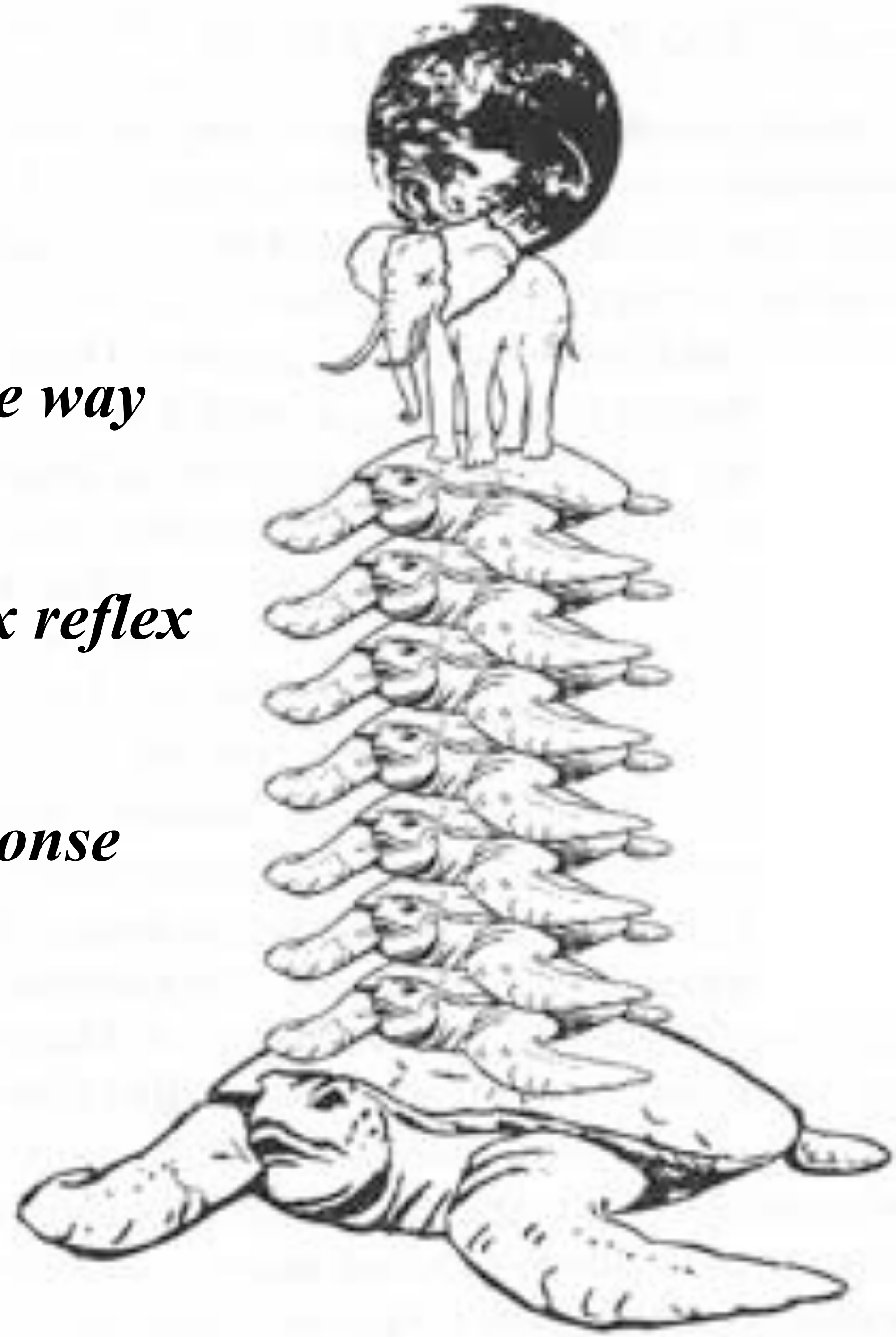
Sherrington and the "Reflex" arc



It is reflexes (or turtles) all the way down?

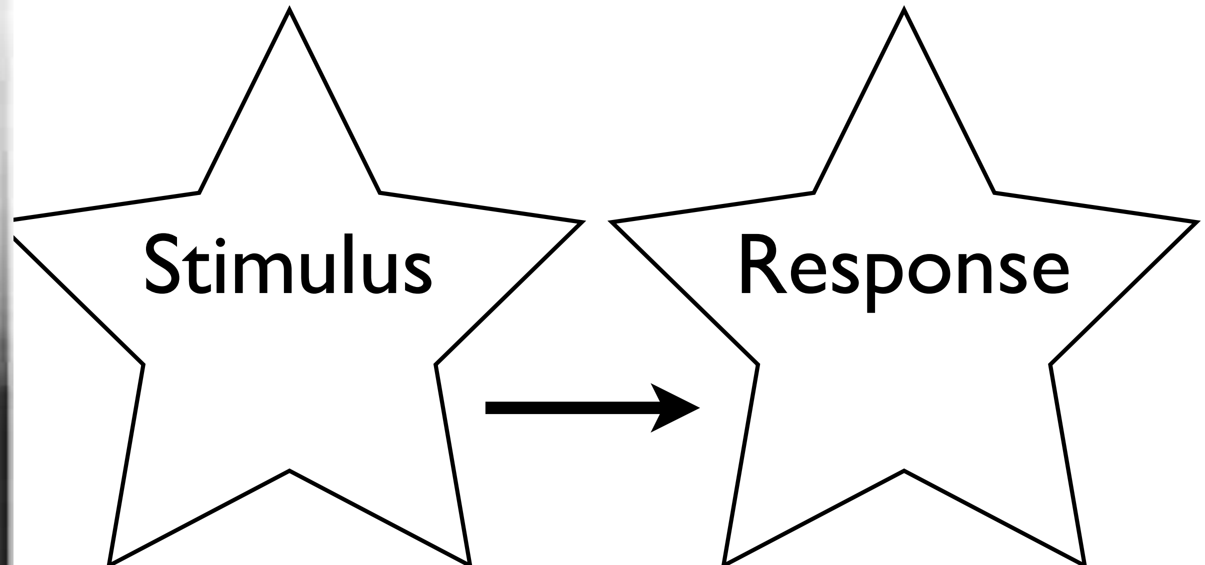
Is everything just more complex reflex arcs in cortex?

Is all behavior stimulus-response relationships?



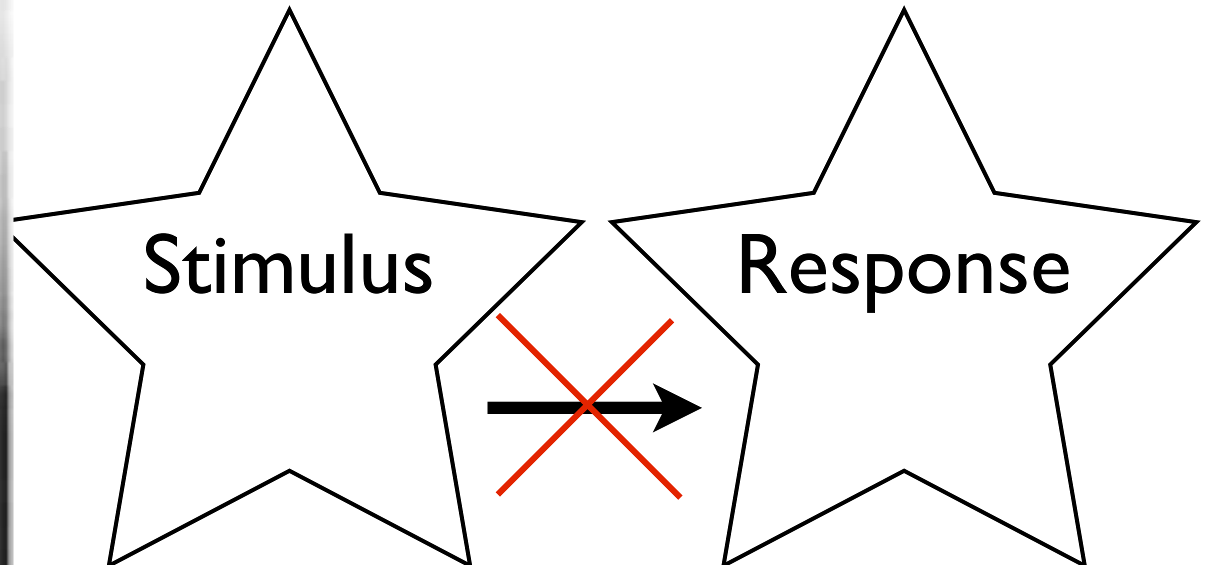
"In Search of the Engram"

Karl Lashley



Karl Lashley

“In Search of the Engram”



"In Search of the Engram"

Motor Cortex?

"Snip"

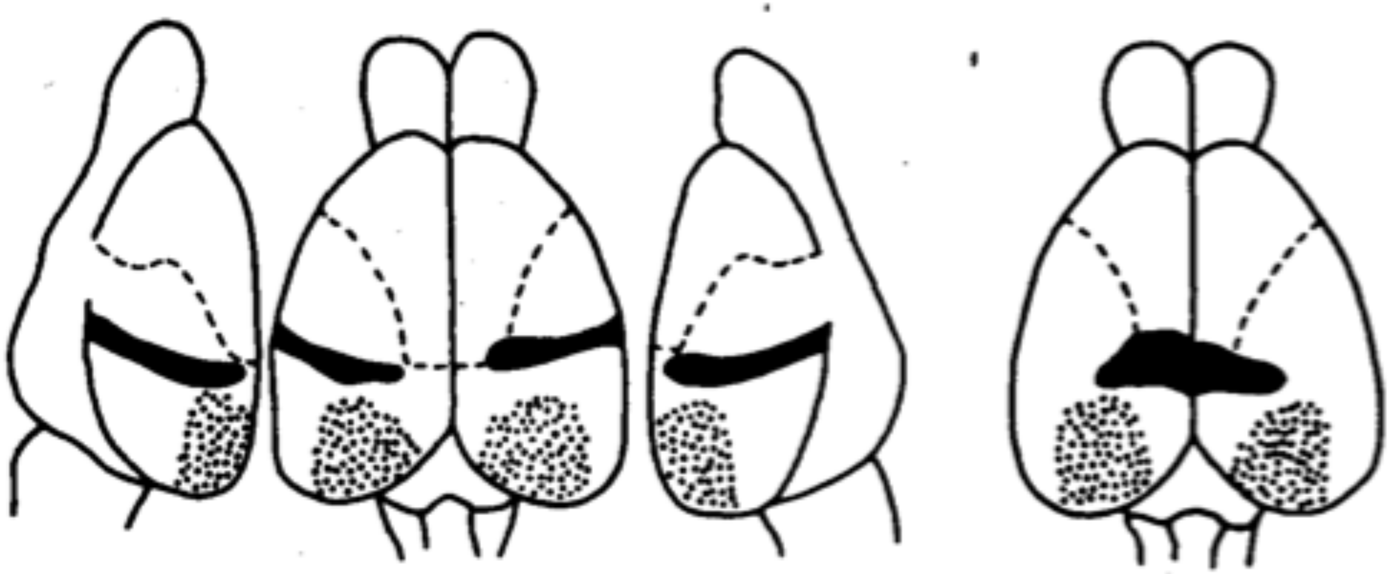


Figure 3. **Lesions partially separating the visual area (stippled) from the motor areas (outlined by dashes) of the rat's brain without disturbing visual learning**

"In Search of the Engram"

Motor Cortex?

"Snip"

Figure 4. Extent of cortical lesion which did not abolish latch-box habits. The lesion is bounded caudally by the central fissure and extends forward to include the arcuate sulcus

"In Search of the Engram"

Transcortical conduction?

"Snip"

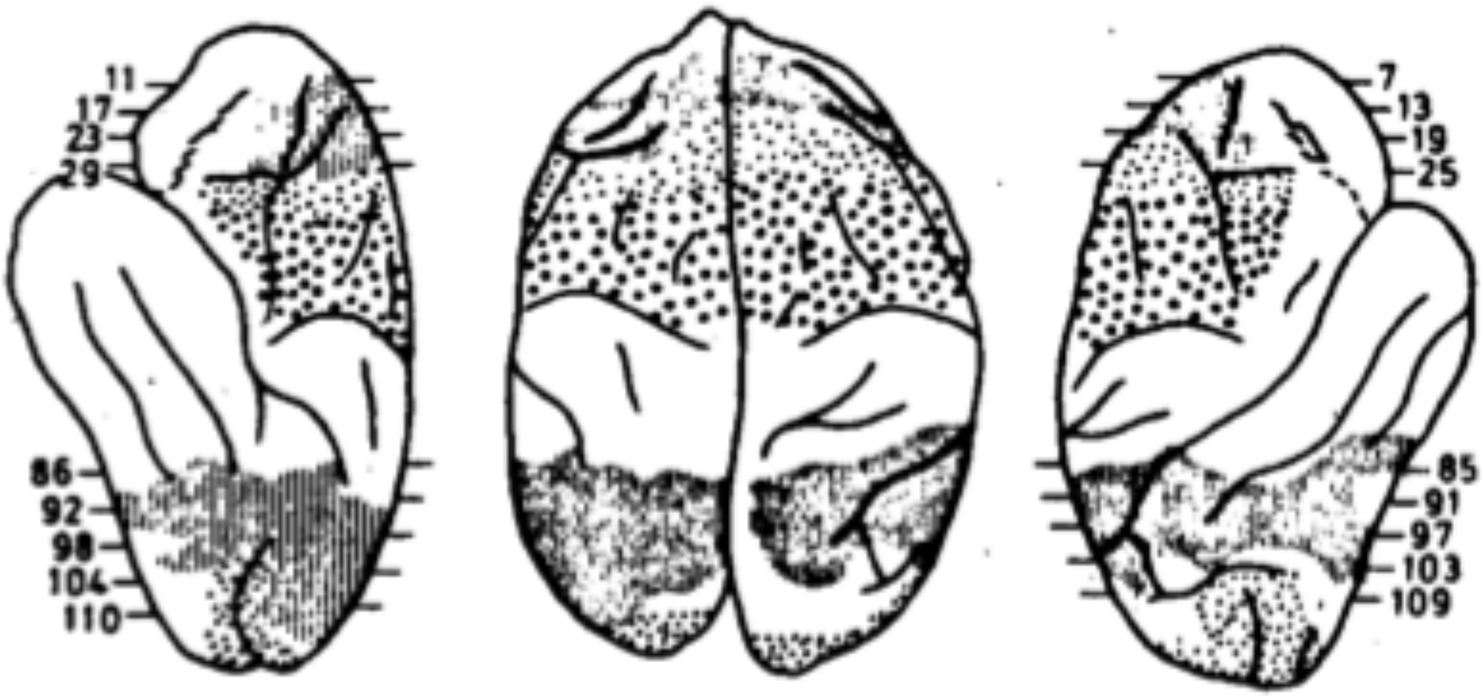
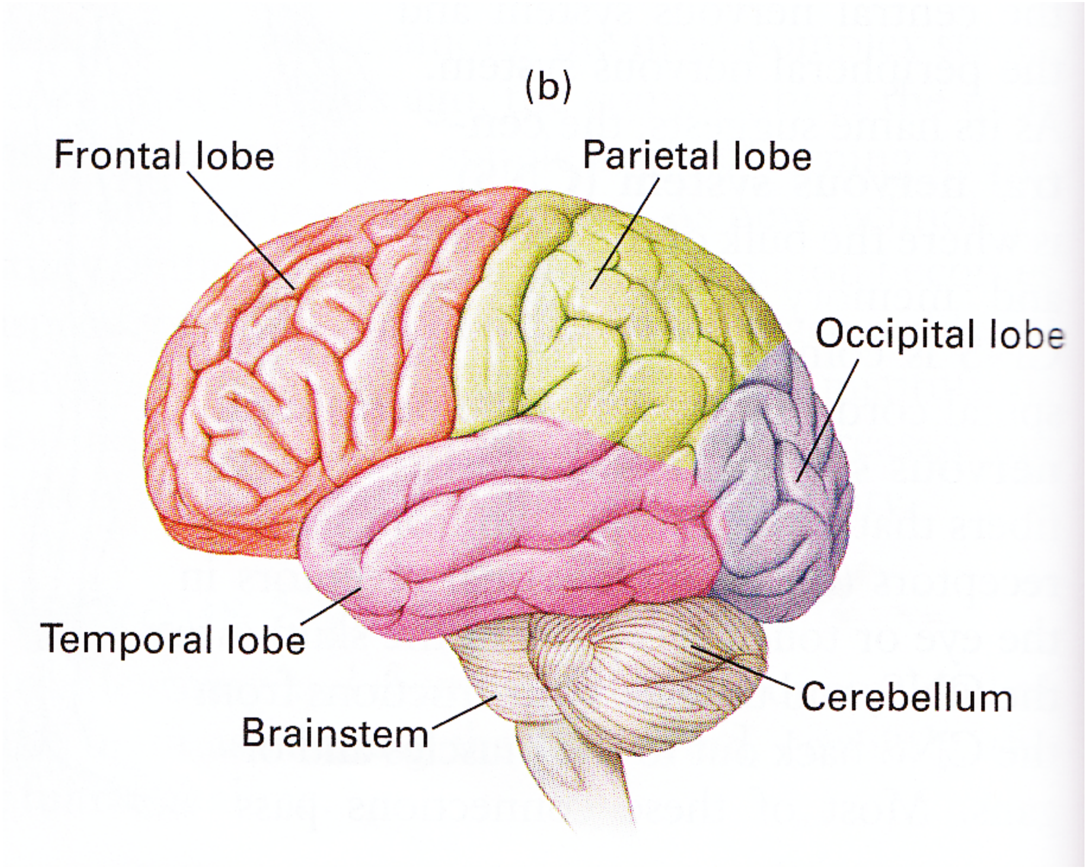


Figure 5. Lesions, marked by hatching, which destroyed the greater part of the so-called visual associative areas in a monkey without affecting visual functions

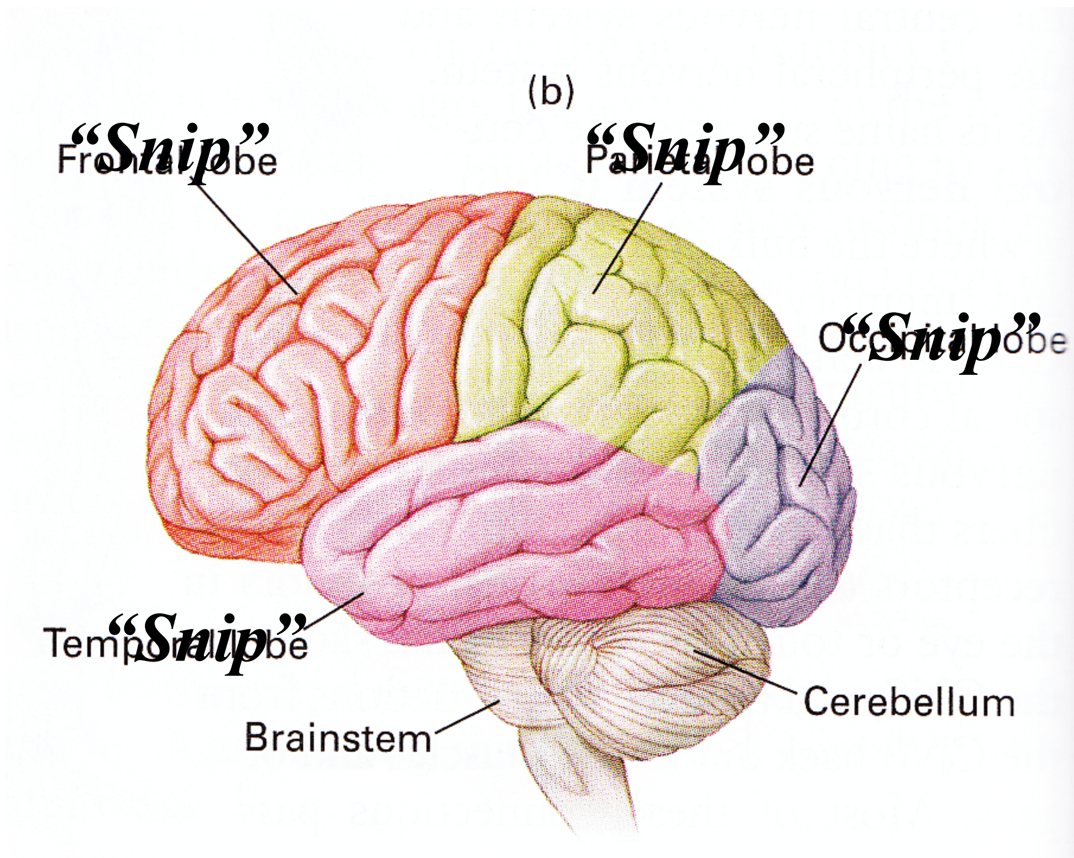
"In Search of the Engram"

Association areas (occipital lobe, frontal, parietal, temporal)



“In Search of the Engram”

Association areas (occipital lobe, frontal, parietal, temporal)



“In Search of the Engram”

A number of experiments with the rat have shown that habits of visual discrimination survive the destruction of any part of the cerebral cortex except the primary visual projection area. (page 12)

"In Search of the Engram"

Memory disturbances of simple sensory habits follow only upon very extensive experimental destruction, including almost the entire associative cortex (page 12)

“In Search of the Engram”

Adult chimpanzees, trained in such complicated tasks as choosing an object, like a model shown, retain the habits after removal of the entire prefrontal cortex (page 13)

"In Search of the Engram"

When rats are trained in a habit based on the discrimination of intensities of light, to choose a brightly lighted alley and avoid a dimly lighted one, the removal of the striate cortex completely abolishes the habit (page 14)

"In Search of the Engram"

The psychological studies, like the more limited direct experiments on the brain, point to the conclusion that the memory trace is located in all parts of the functional areas; that various parts are equipotential for its maintenance and activation (page 17)

"In Search of the Engram"

I sometimes feel, in reviewing the evidence on the localization of the memory trace, that the necessary conclusion is that learning just is not possible. It is difficult to conceive of a mechanism which can satisfy the condition set for it. Nevertheless, in spite of such evidence against it, learning does sometimes occur. (page 17)

“In Search of the Engram”

Theory of Mass Action or Equipotentiality

Mass Action Described: Cell Assemblies, Donald Hebb, and Hebbian Learning

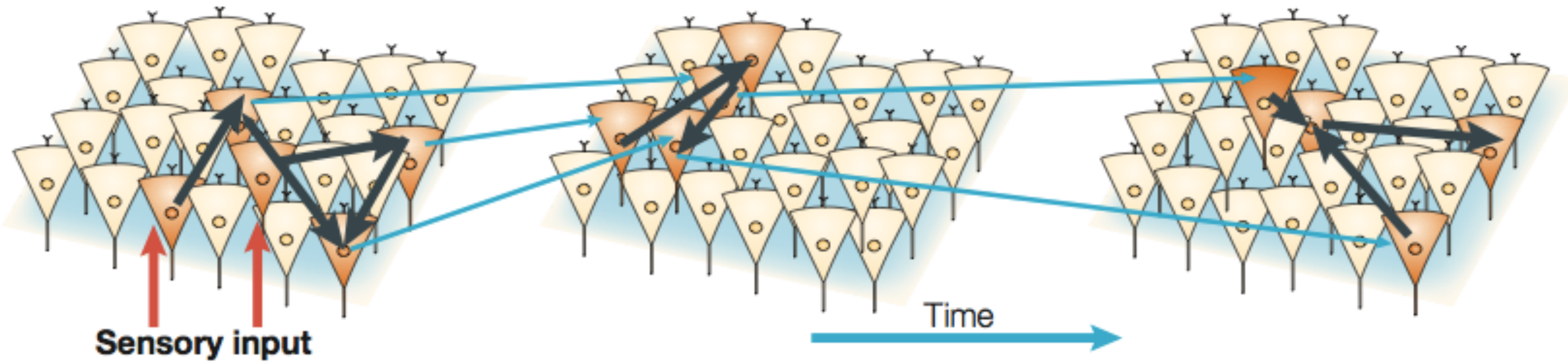


Figure 1 | **The cell assembly hypothesis.** Sensory input (red arrows) drives certain neurons to fire. Thereafter, activity evolves owing to intrinsic cortical dynamics. Strengthened recurrent connections between members of a single assembly (black arrows) transiently stabilize assembly firing through mutual excitation. As the excitability of this assembly fades, inter-assembly connections (blue arrows) lead to subsequent activation of a new assembly. The resulting 'phase sequence' evolves through network dynamics and is not strictly determined by the time series of sensory inputs. The evolution of this phase sequence is the hypothesized substrate of internal cognitive processes (see also BOX 1).

Cell Assemblies, Donald Hebb, and Hebbian Learning

"When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased"

(The organization of behavior, p. 62)

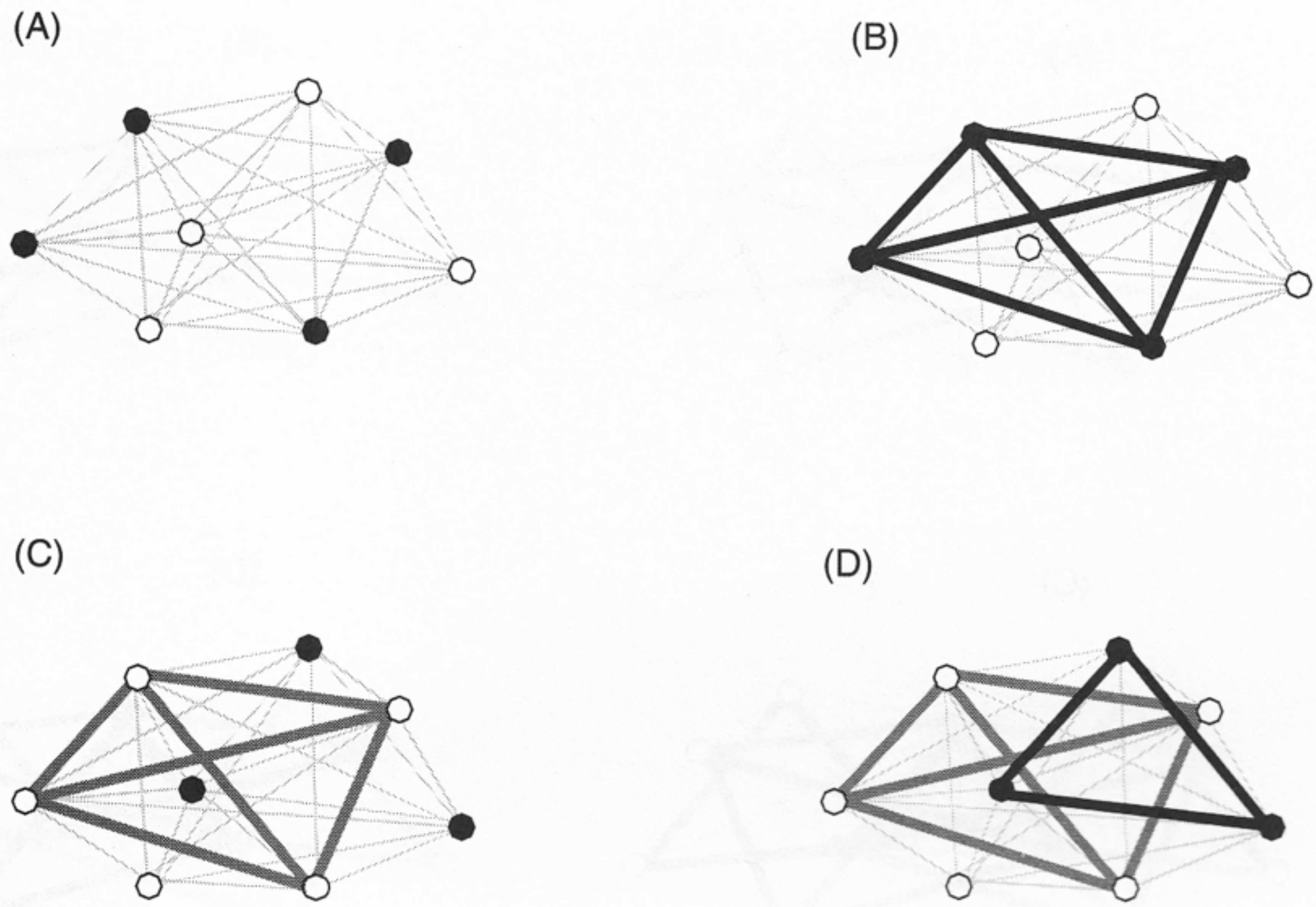


Figure 5.2 Simplified example of an autoassociative network, consisting of a group of nodes (circles). (A) External inputs (not shown) evoke a pattern of activity over the network, resulting in the activation of a subset of nodes (solid circles). (B) Weighted connections develop between

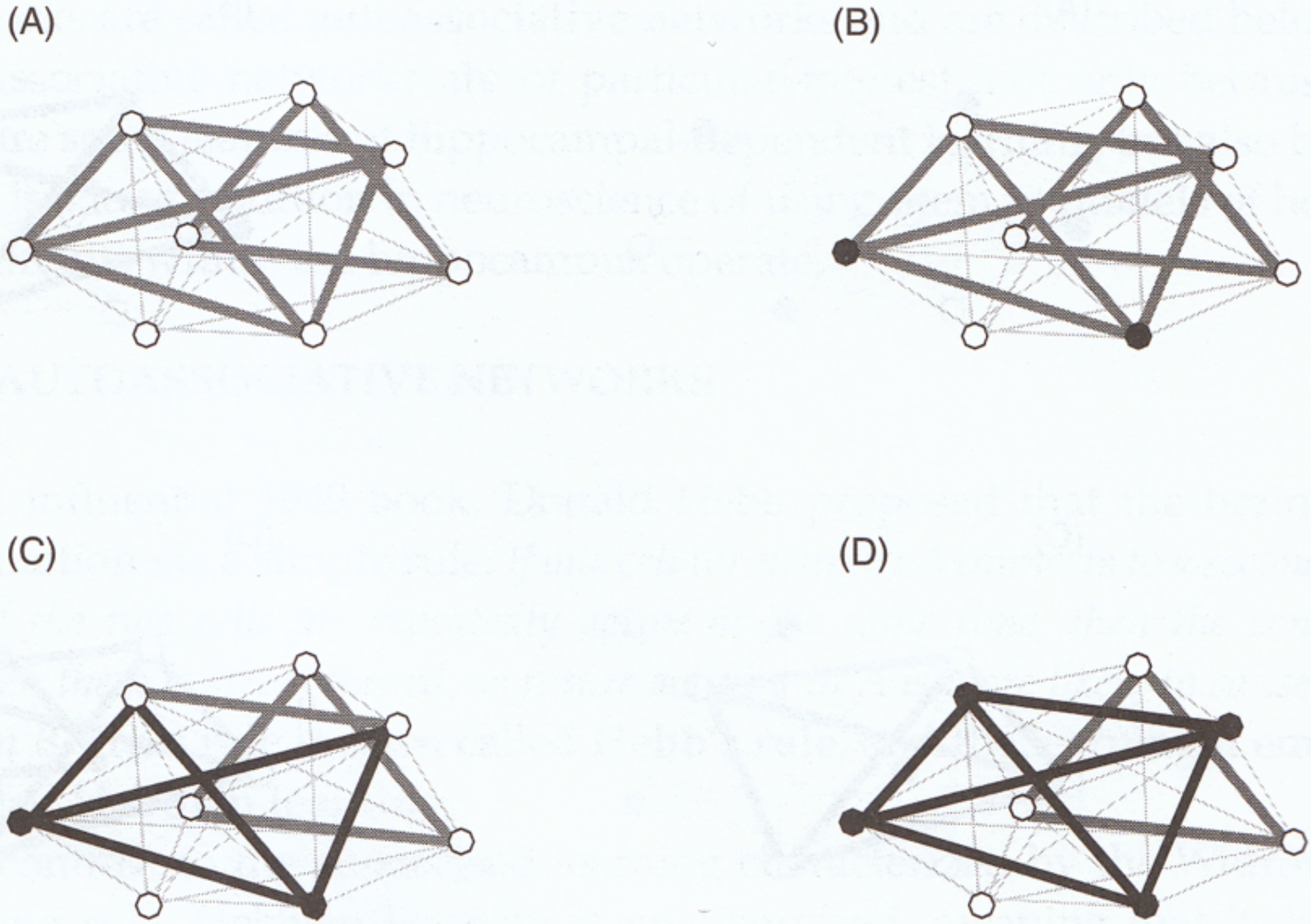


Figure 5.3 Pattern completion in an autoassociative network. (A) The network has stored two patterns by strengthening the weights between nodes that are coactive in each pattern. (B) A partial version of one pattern is presented, which activates a subset of the nodes (solid circles).

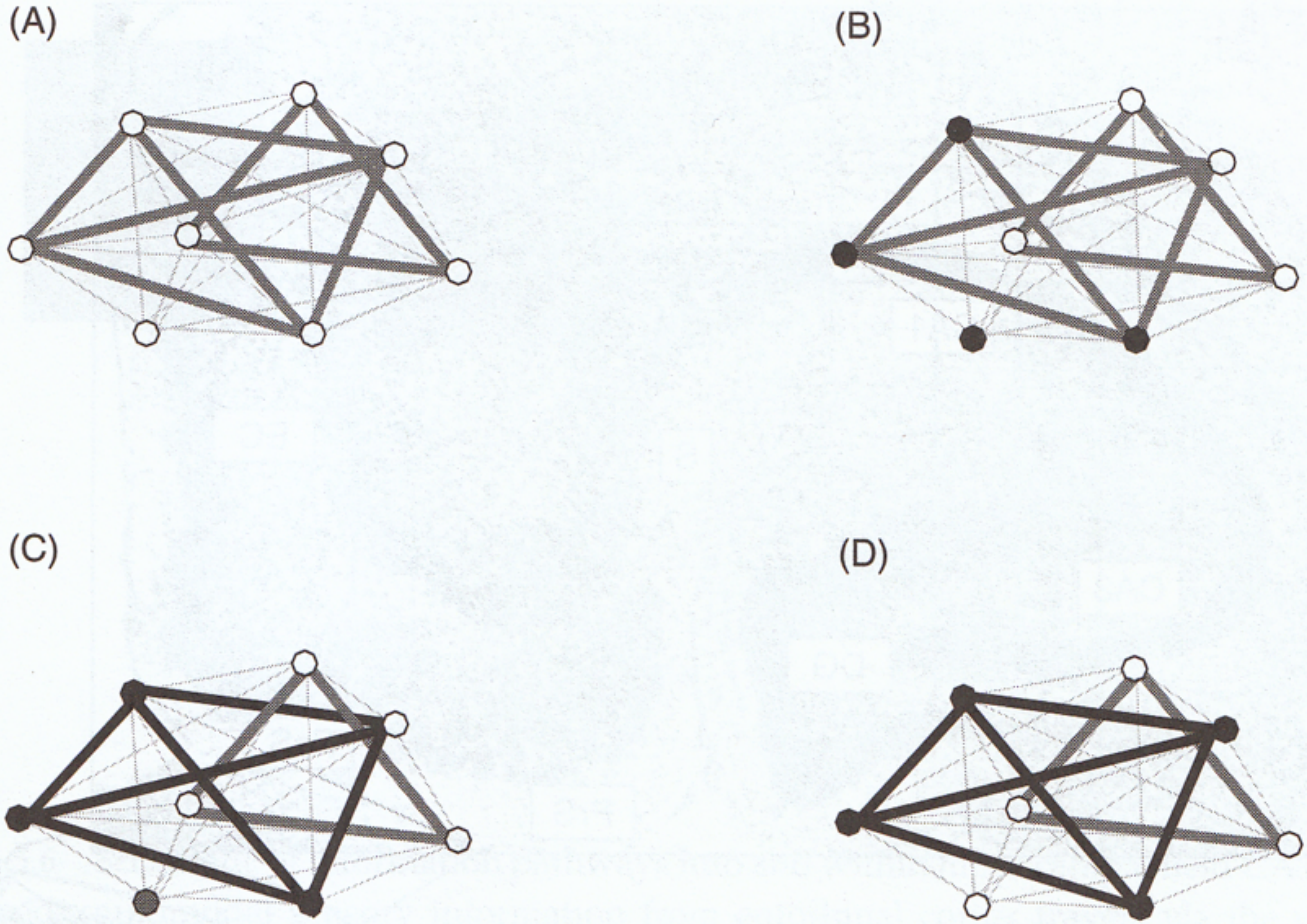


Figure 5.4 Pattern recognition in an autoassociative network. (A) The network has stored two patterns by strengthening the weights between nodes that are coactive in each pattern. (B) External inputs activate nodes (solid circles), some of which are part of a previously stored

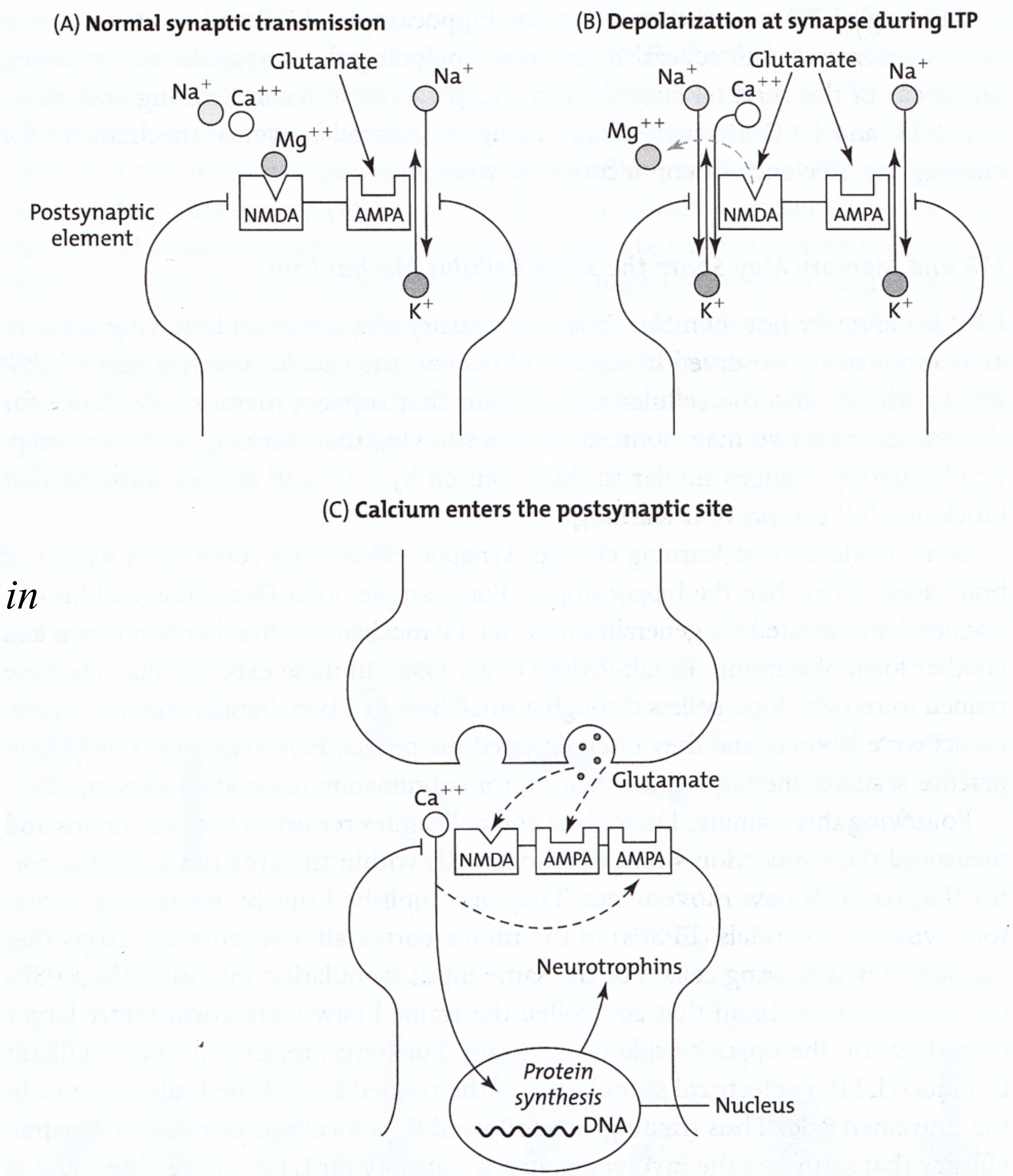
It happens!

Bliss & Lomo (1973) found evidence of long-term potentiation (LTP)!

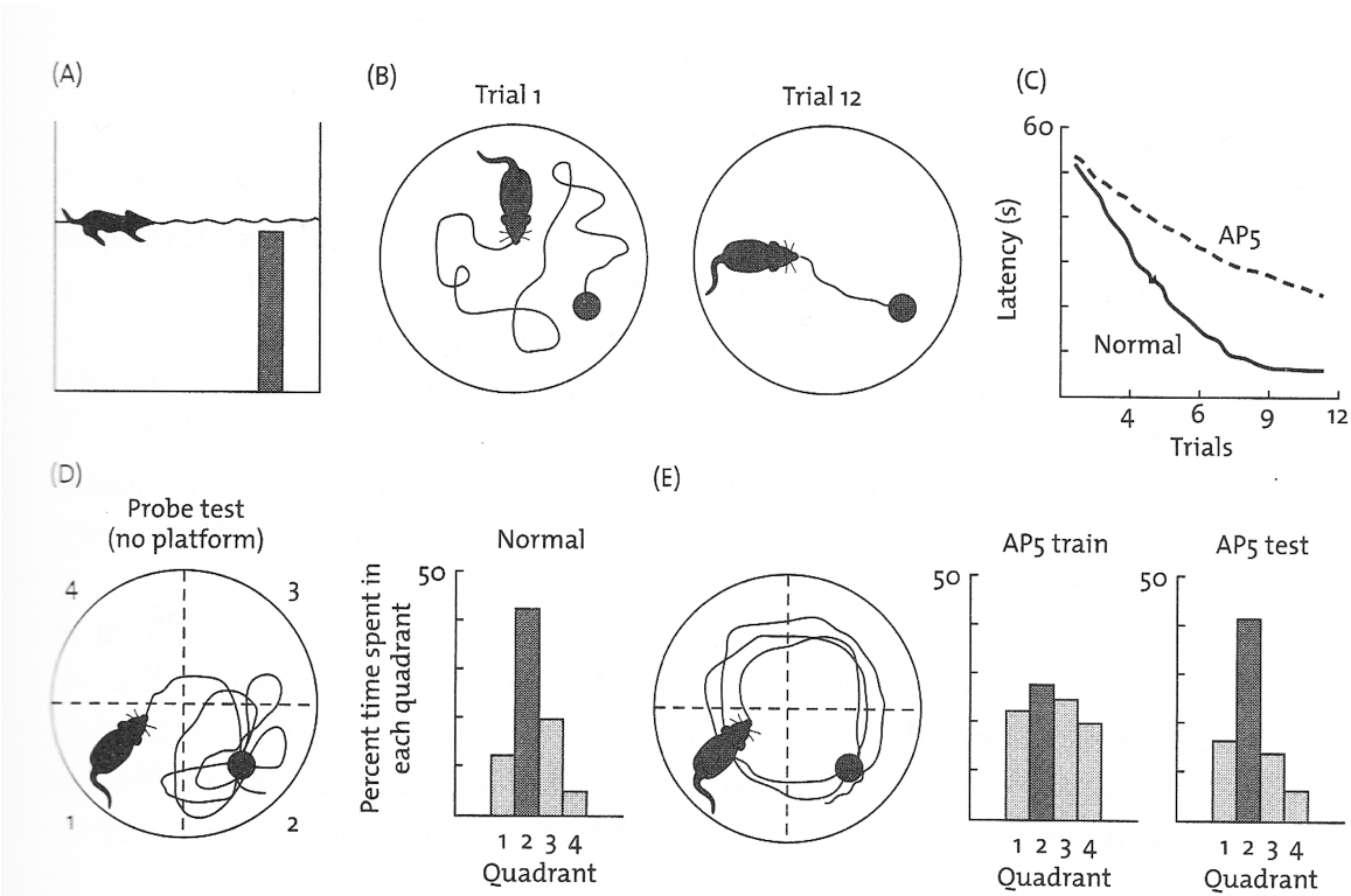
1. Repeatedly stimulate a single pathway in slice of hippocampus.

2. Afterwards, new stimulation caused greater excitatory synaptic potential

3. This is long-lasting



A possible causal link between LTP and new memory formation (Steele & Morris, 1999)



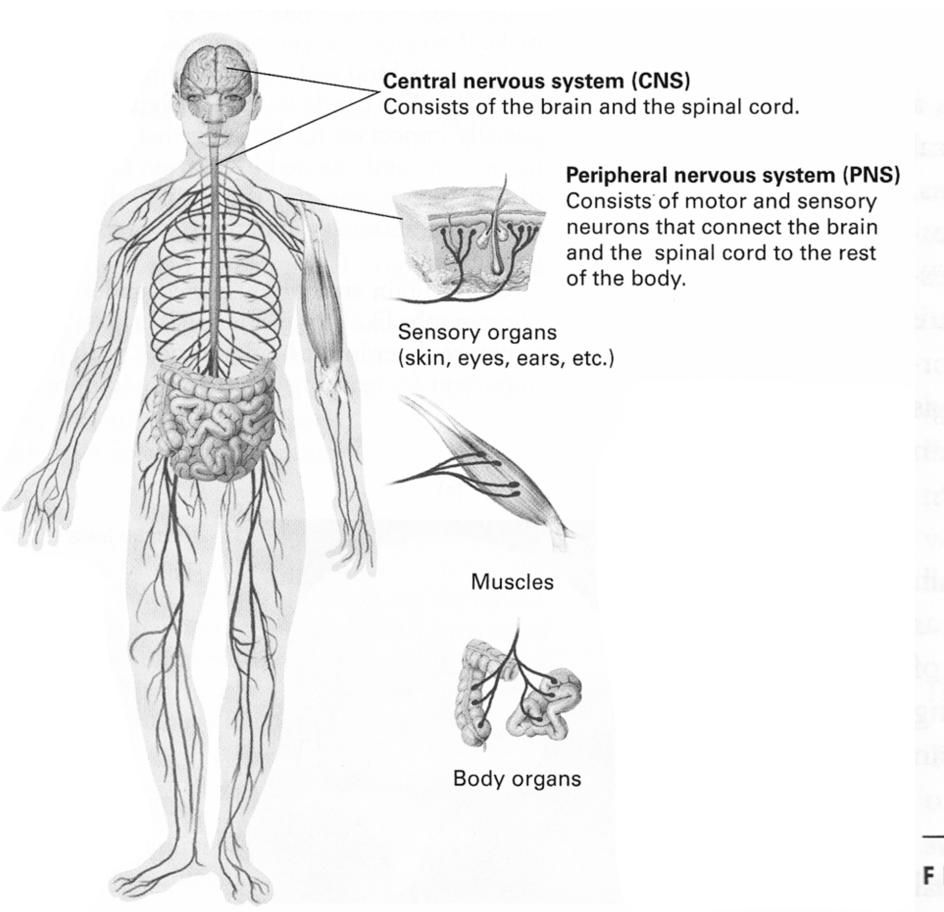
Does the theory of mass action imply that the cortex is a large undifferentiated mass of self-organized cell assemblies?

Does the theory of mass action imply that the cortex is a large undifferentiated mass of self-organized cell assemblies?

No. Like most things in life, it is someplace in between.

3 Systems.

The organization of the nervous system



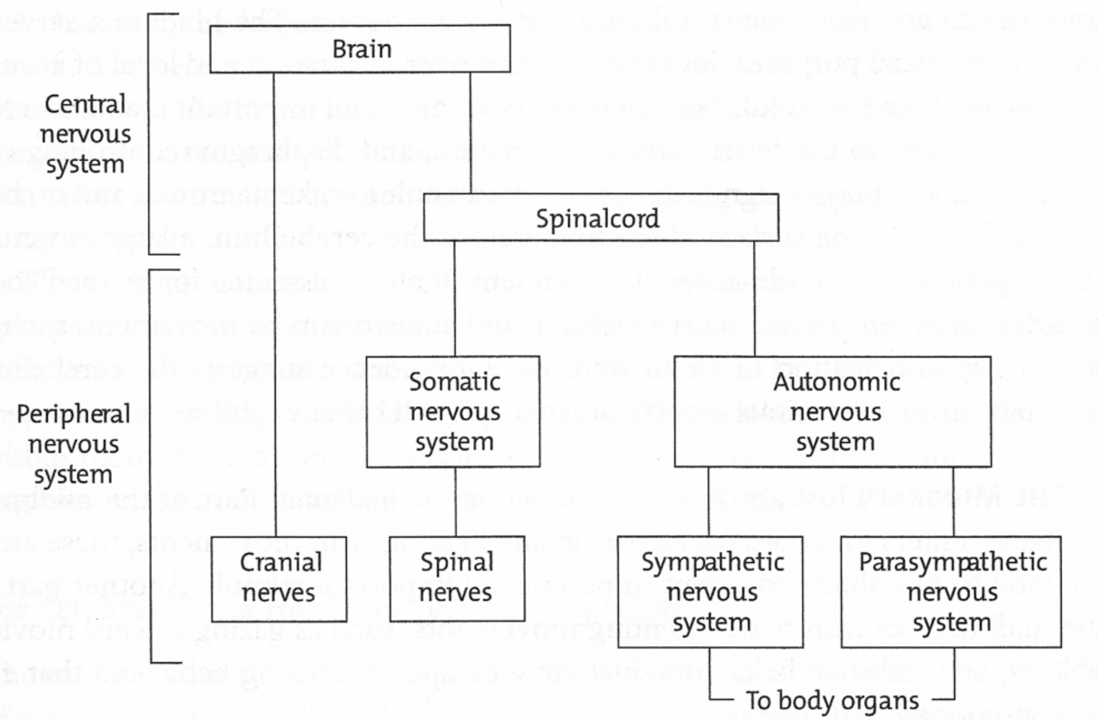


FIGURE 2.12 Hierarchy of nervous system components and their connections.

The organization of the nervous system

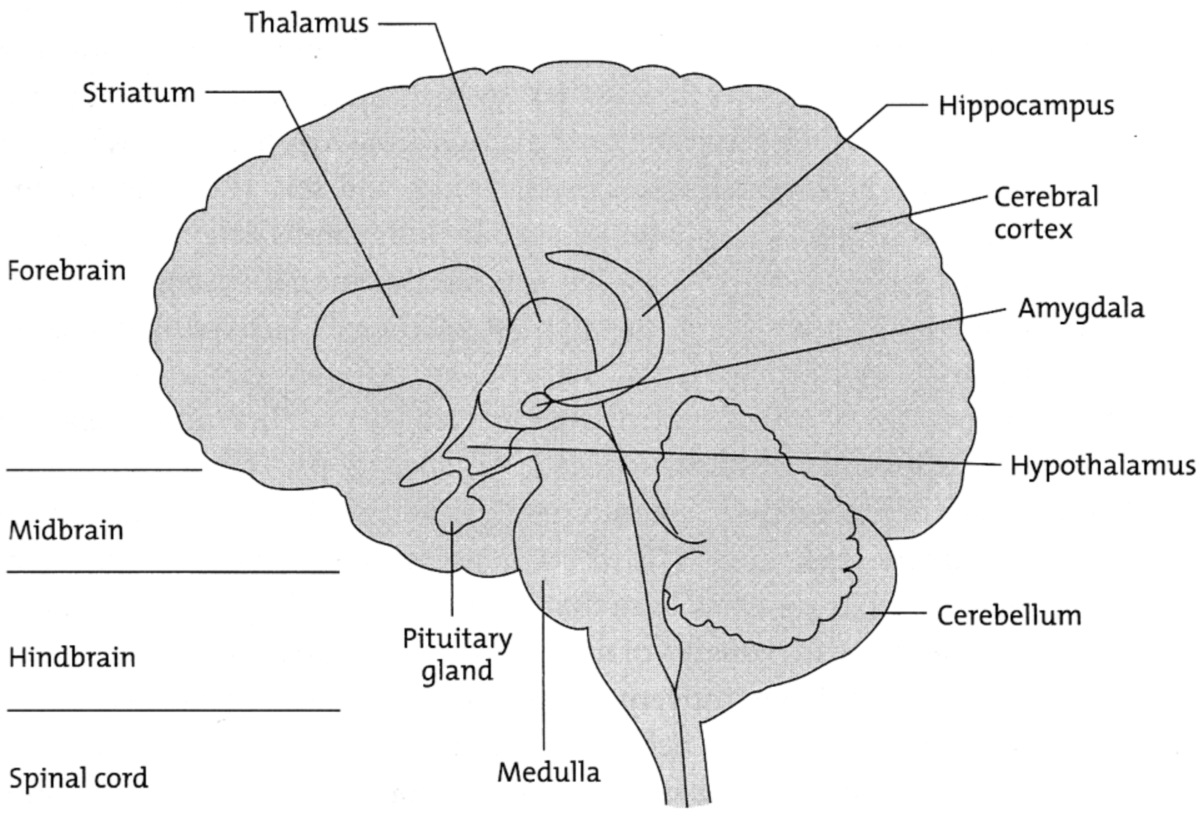


FIGURE 2.13 Levels of the brain and major structures.

Hindbrain

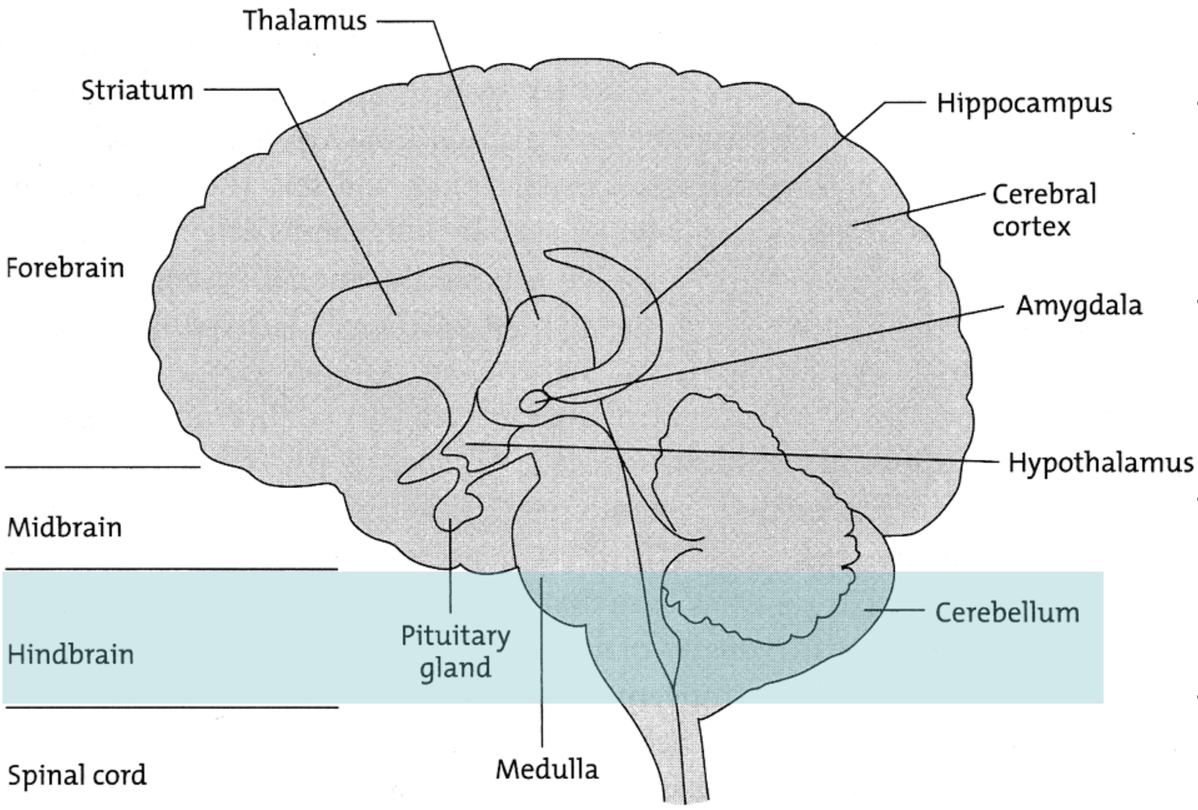


FIGURE 2.13 Levels of the brain and major structures.

- Includes spinal cord and cranial nerves
- Control over respiration, sleep/wake, heartbeat, etc..
- Composed of several nuclei with specific function
- The surface includes the cerebellum which supports the control of fine movement, learning the specific timing of predictive sensorimotor events, etc...

The organization of the nervous system

Midbrain

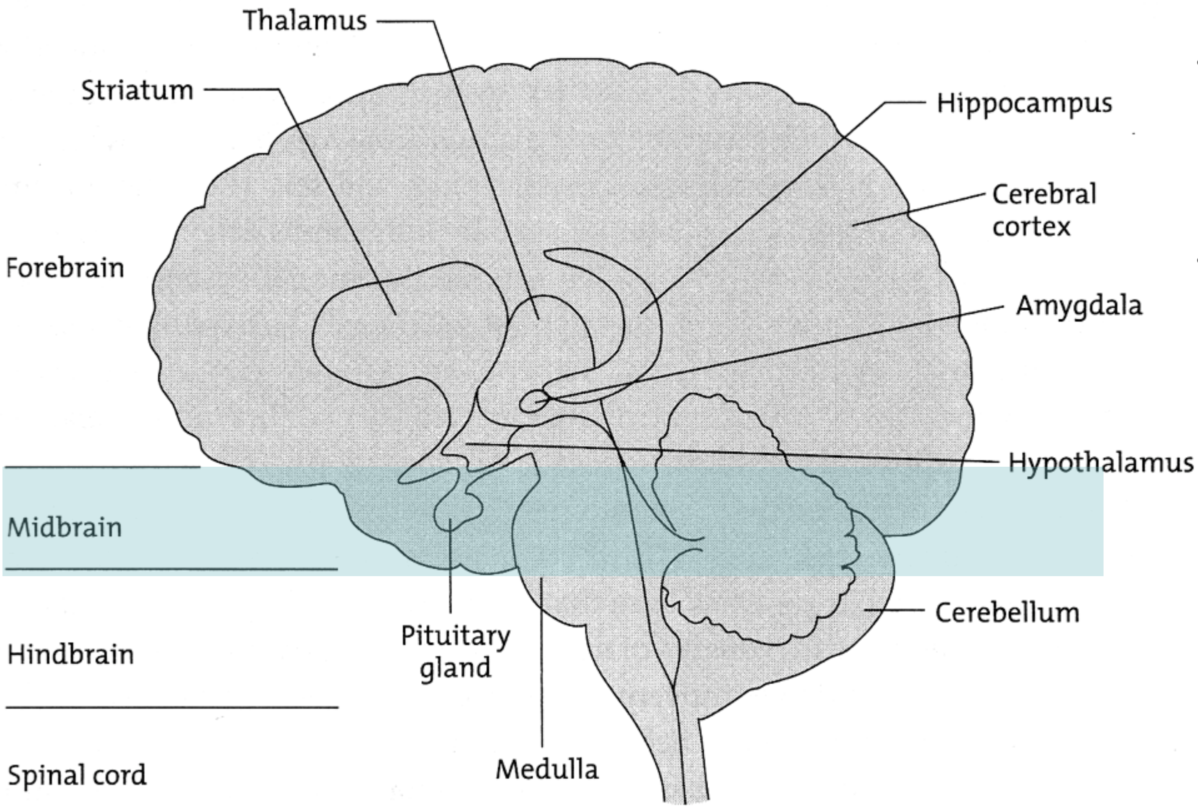


FIGURE 2.13 Levels of the brain and major structures.

- Coordinates vision, hearing, and movement
- Basic orienting movements and reflexive behaviors

Forebrain

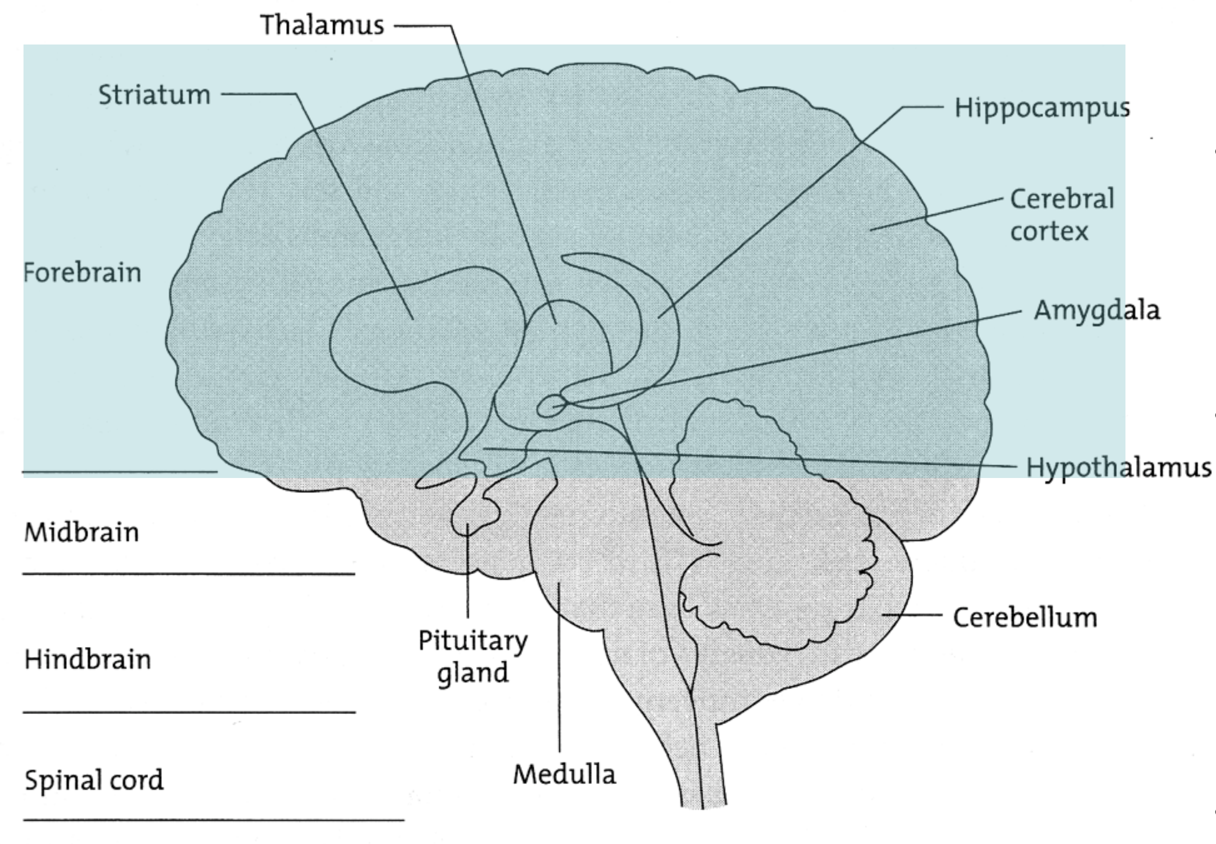
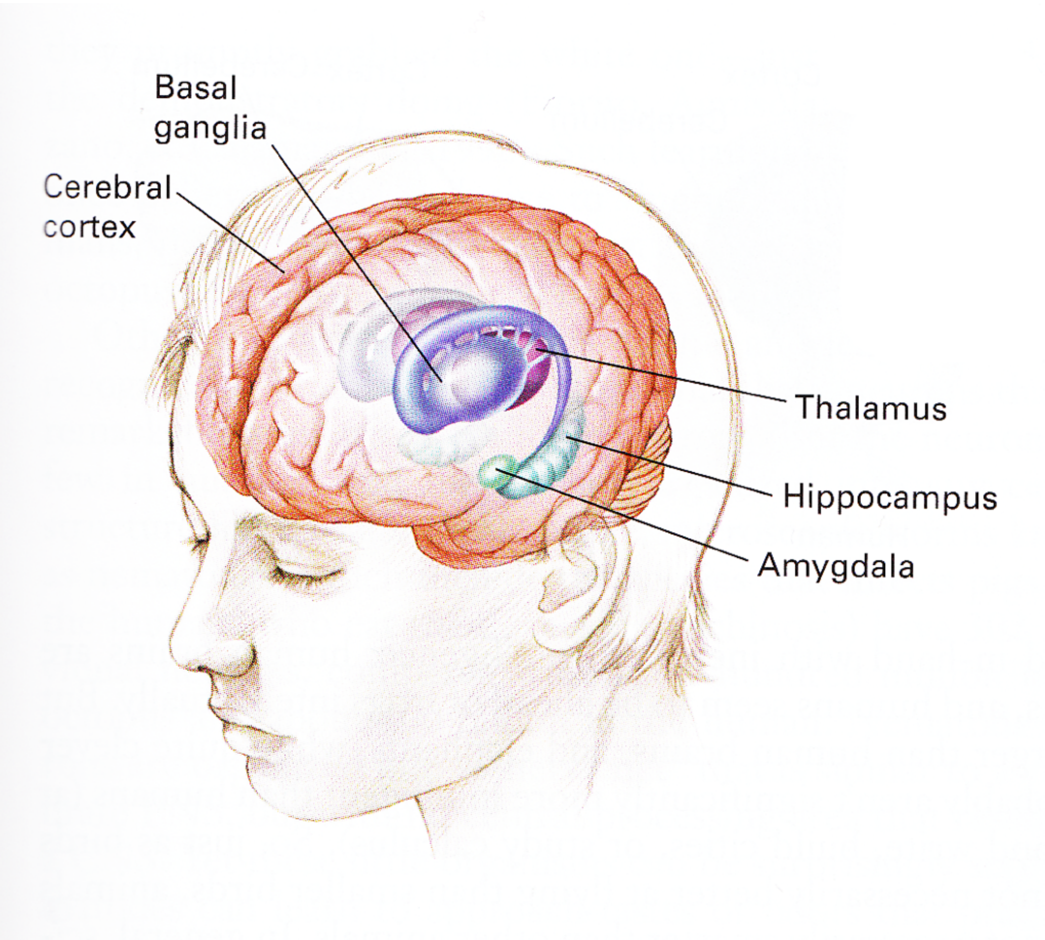


FIGURE 2.13 Levels of the brain and major structures.

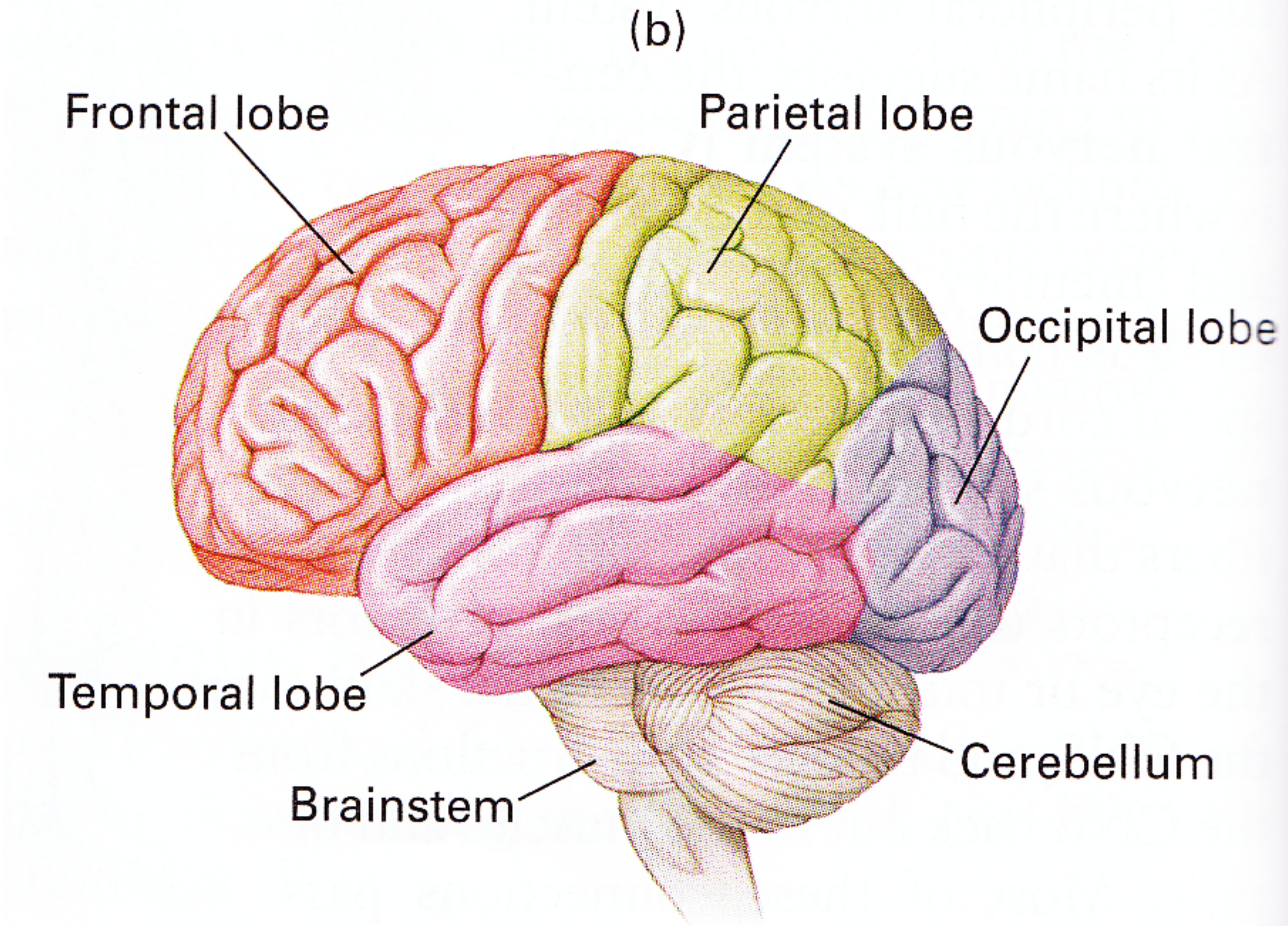
- Two different subdivisions: **thalamus** and **cerebral hemispheres**
- **Thalamus** involved in relay of sensory information to higher cortex, coordinating regions of cortex, etc.. Hypothalamus regulates eating, sleeping, sex
- Hypothalamus connects to pituitary gland which directs hormonal responses

Forebrain



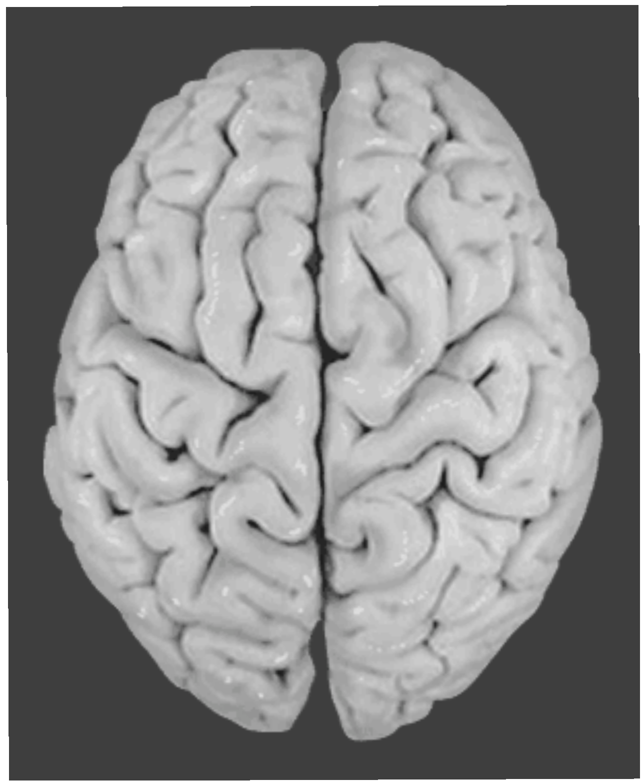
- Sub-cortical areas particular important to learning and memory.
- **Striatum -** controls posture, movement, critically involved in processing learning from feedback
- **Hippocampus -** conscious memory, episodic memory formation, earliest part of cortex to evolve
- **Amygdala** - learns emotional responses to stimuli

Cerebral Cortex - largest part of forebrain/cerebral hemispheres



Organization of cerebral cortex

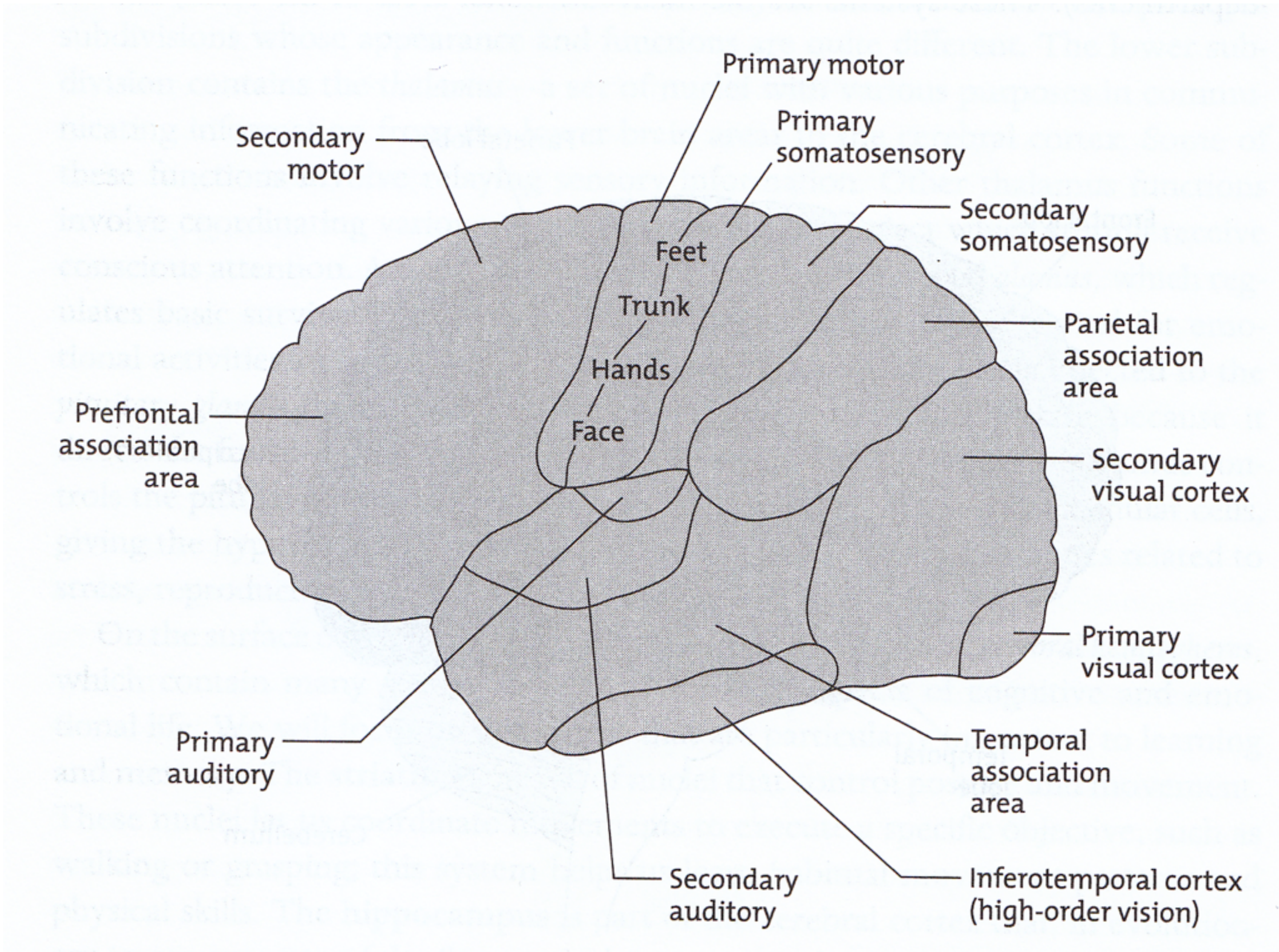
Right



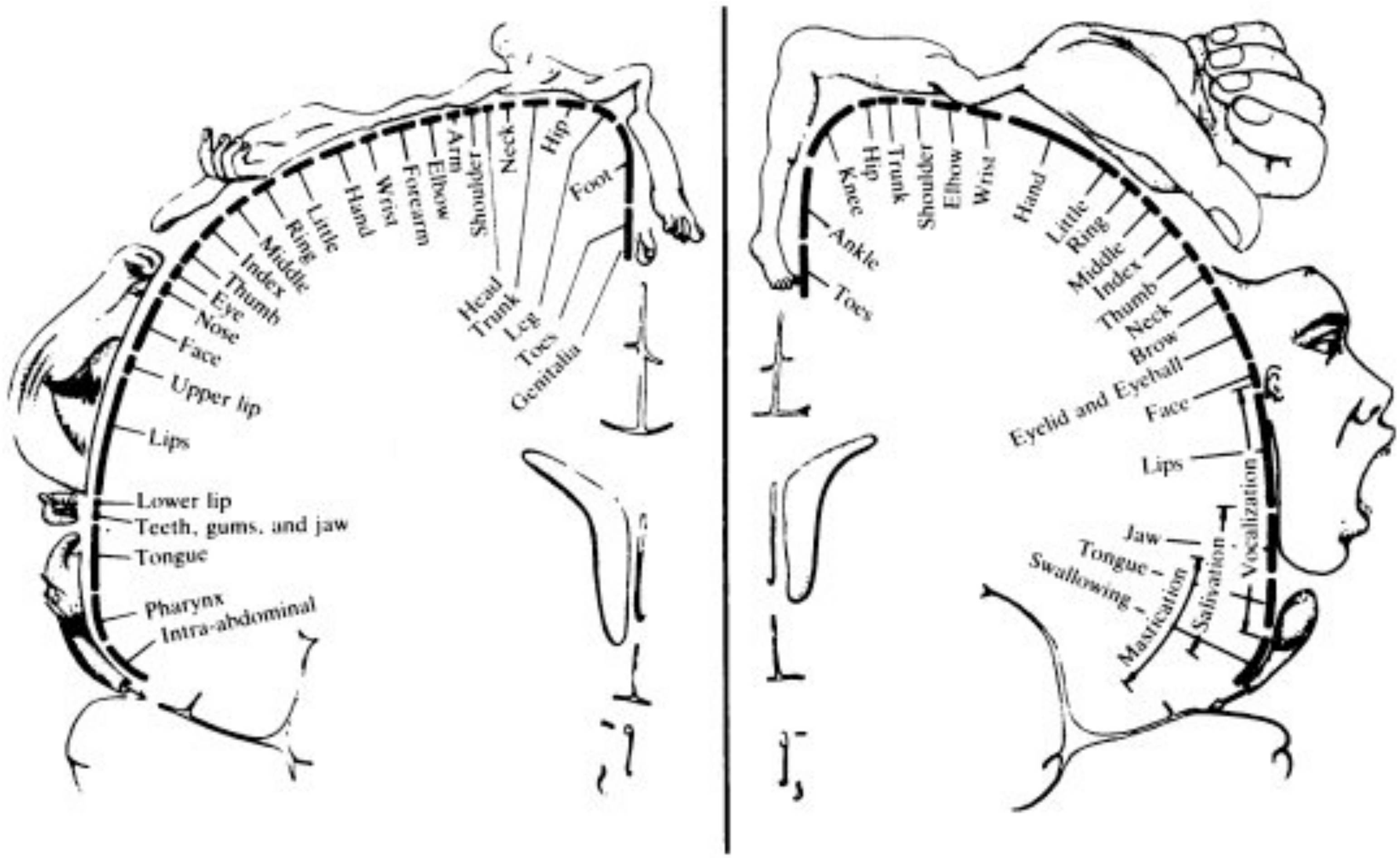
Left

(contralateral organization across hemispheres)

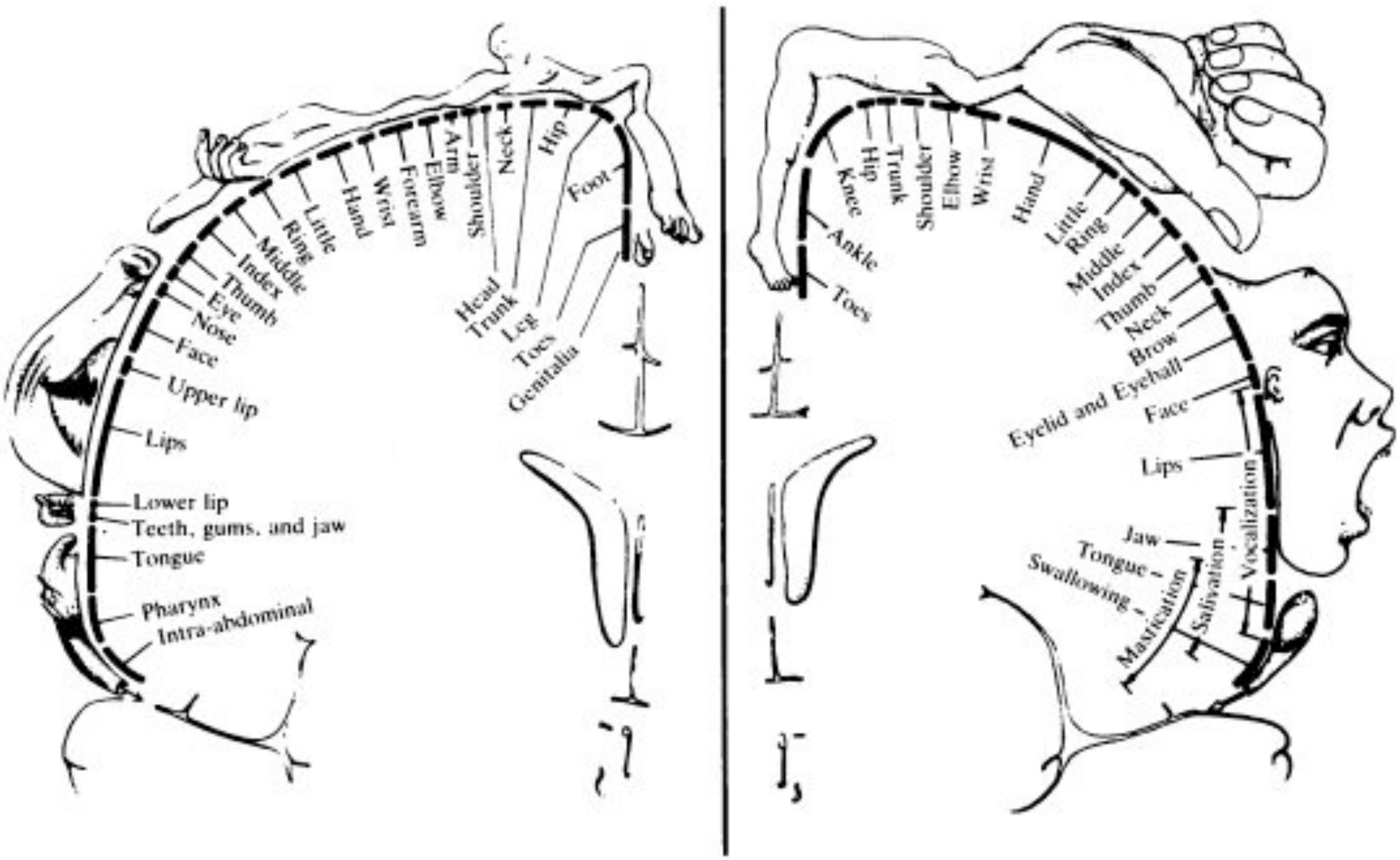
Organization of cerebral cortex



Cortical Maps



Cortical Resource Allocation



More=higher fidelity, better discrimination

Cortical Plasticity

i.e., changes in representational fidelity which “grow” to represent important parts of the environment

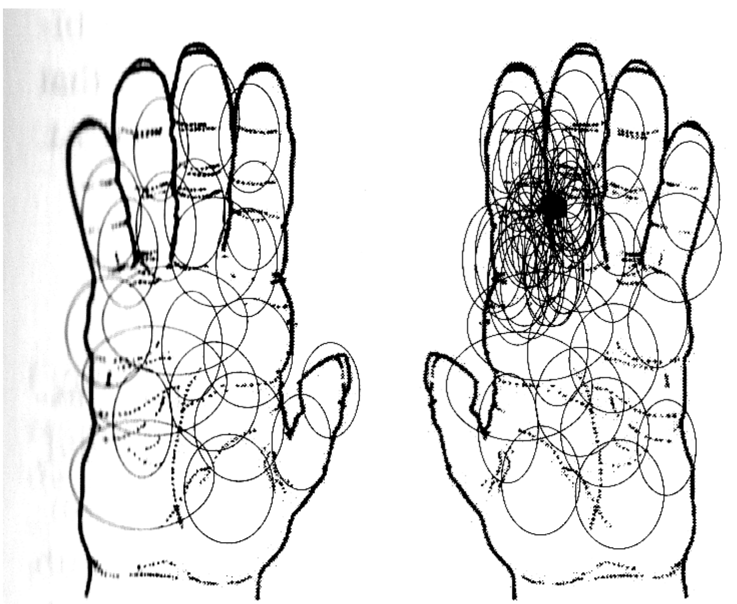


Figure 3.6 — CORTICAL PLASTICITY. The density of receptive fields of somatosensory cortical neurons, mapped onto the monkey palm surface, after prolonged exposure to local stimulation (*right*; the arrow indicates the stimulated spot). The map for the unstimulated hand is shown as a control (*left*). Merely touching the skin repeatedly at the designated location for the period of several days caused that location to become over-represented in the brain.

So, how do we reconcile these views?

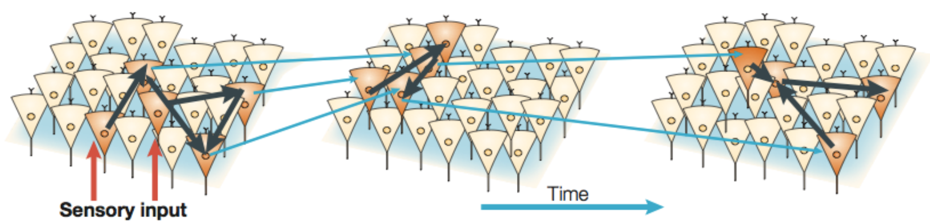
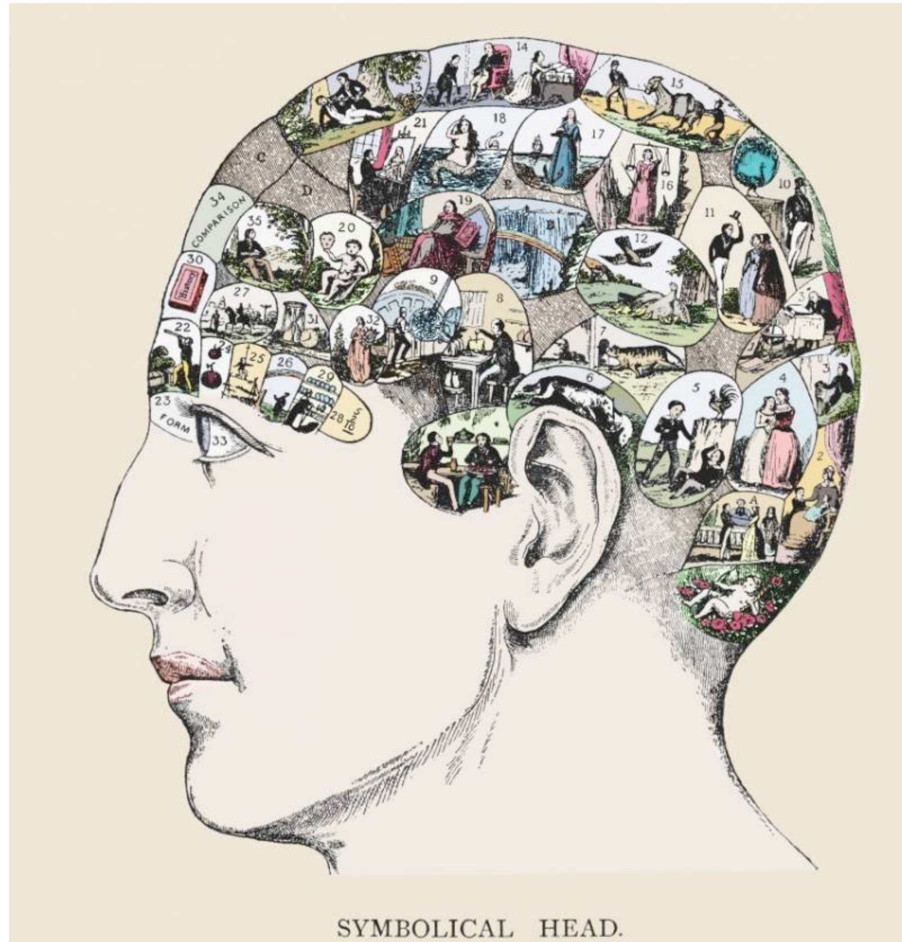


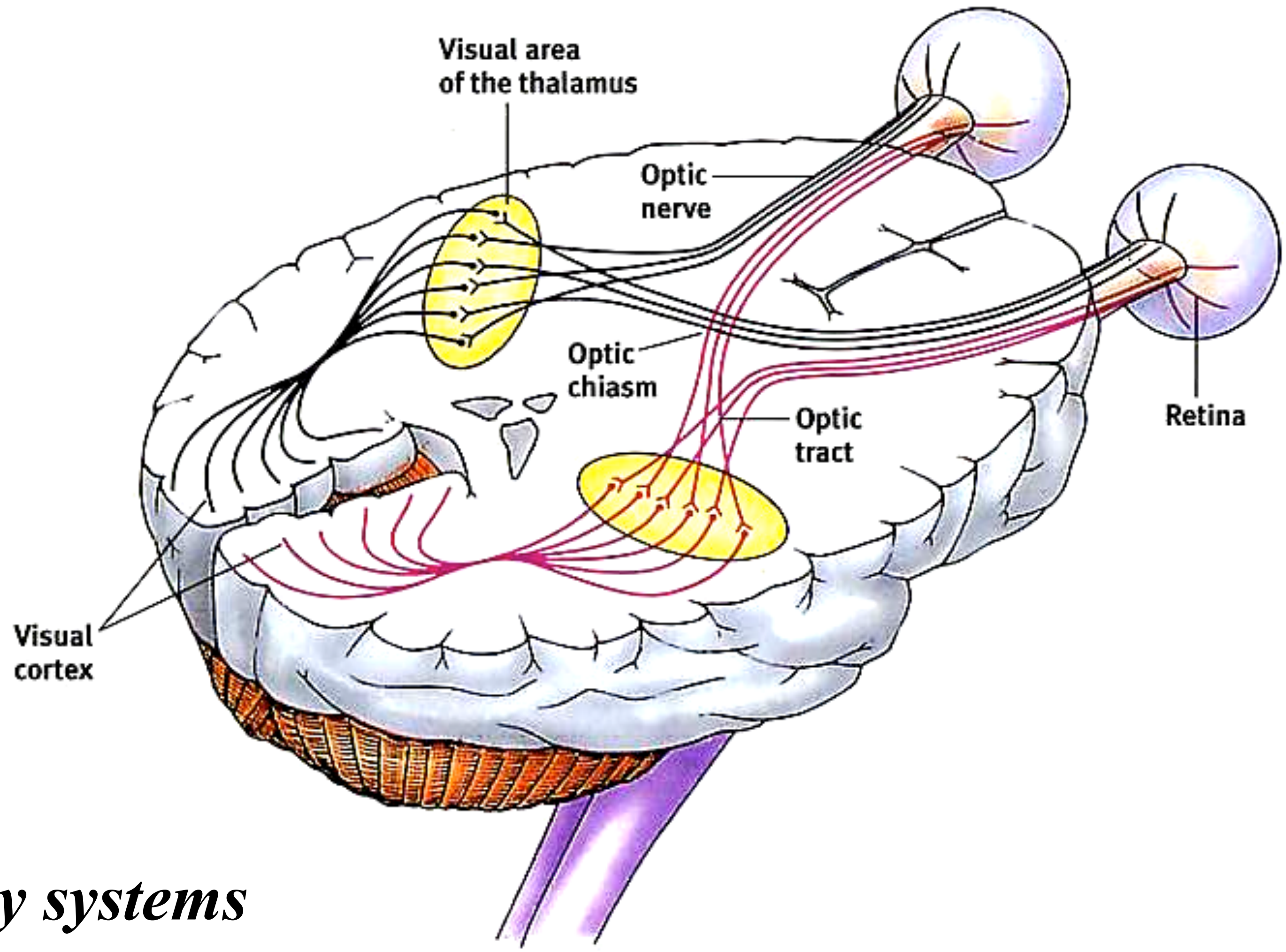
Figure 1 | **The cell assembly hypothesis.** Sensory input (red arrows) drives certain neurons to fire. Thereafter, activity evolves owing to intrinsic cortical dynamics. Strengthened recurrent connections between members of a single assembly (black arrows) transiently stabilize assembly firing through mutual excitation. As the excitability of this assembly fades, inter-assembly connections (blue arrows) lead to subsequent activation of a new assembly. The resulting 'phase sequence' evolves through network dynamics and is not strictly determined by the time series of sensory inputs. The evolution of this phase sequence is the hypothesized substrate of internal cognitive processes (see also BOX 1).

Undifferentiated Mass (Lashley)



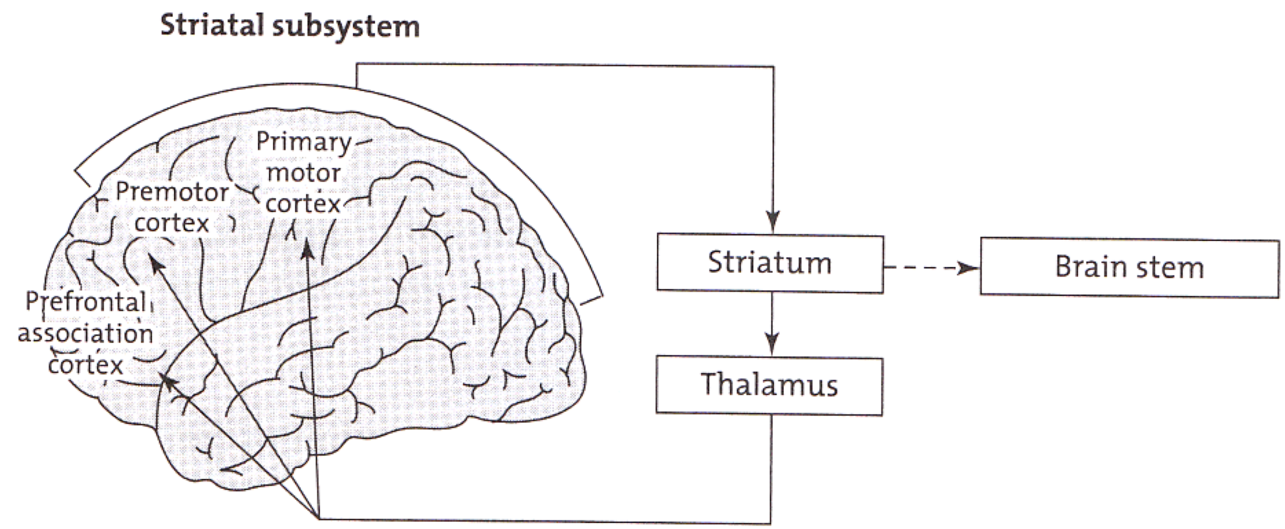
Phrenology: Localized cognitive function in different parts of brain (Gall)

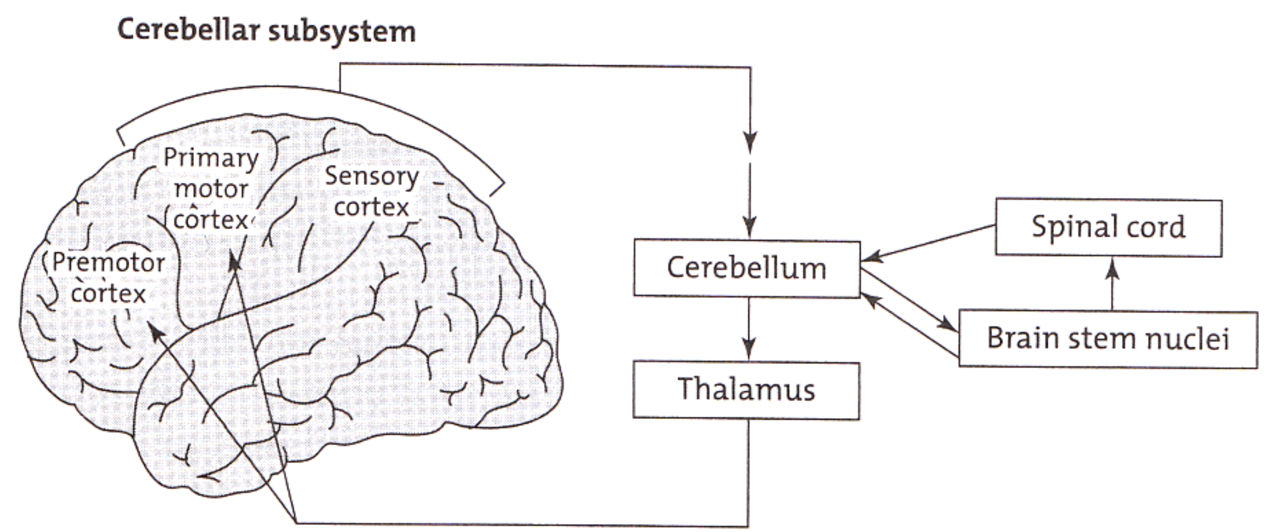
The brain is organized into different, specialized but inter-operative SYSTEMS



Visual/Sensory systems

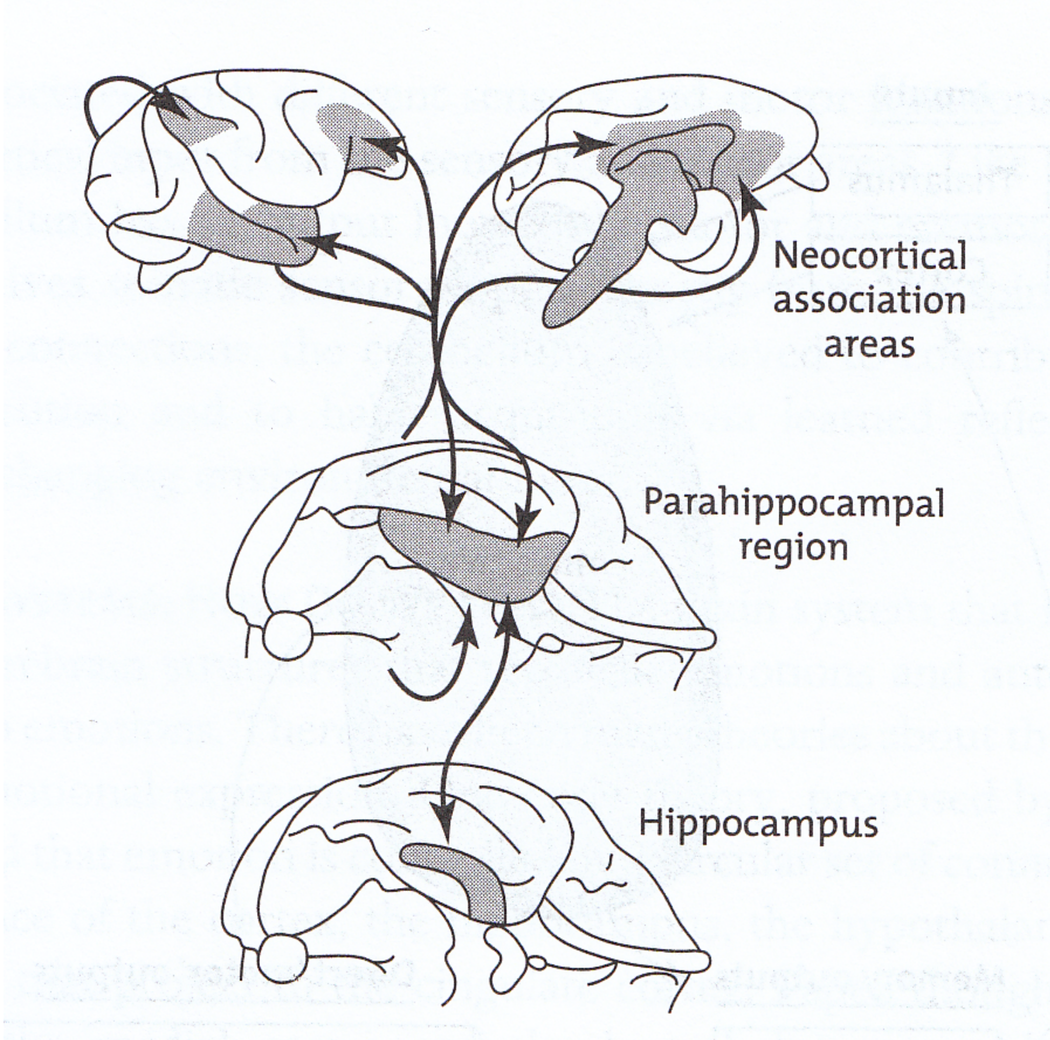
The brain is organized into different, specialized but inter-operative SYSTEMS





Motor systems

The brain is organized into different, specialized but inter-operative SYSTEMS



Cognitive/Declarative Memory systems

Loss of Recent Memory After Bilateral Hippocampal Lesions

William Beecher Scoville
Brenda Milner

Original report on patient H.M. (now famous case study in hippocampal amnesia) who had a bilateral hippocampal bisection as a radical intervention for debilitating epilepsy.

Surgery was Sept. 1, 1953.

Tested on April 26, 1955. “The memory defect was immediately apparent. The patient gave the date as March, 1953, and his age as 27. Just before coming into the examining room he had been talking to Dr. Karl Pribram, yet he had no recollection of this at all and denied that anyone had spoken to him. In conversation he referred constantly to boyhood events and seemed scarcely to realize that he had an operation. ”

Loss of Recent Memory After Bilateral Hippocampal Lesions

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Original report on patient H.M. (now famous case study in hippocampal amnesia) who had a bilateral hippocampal bisection as a radical intervention for debilitating epilepsy.

“**On formal testing the contrast between his good general intelligence and his defective memory was most striking.** On the Wechsler-Bellevue Intelligence Scale he achieved a full scale IQ rating of 112, which compares favorably with the preoperative rating of 104 reported by Dr. Fischer in 1953, the improvement in arithmetic being particularly striking. **An extensive battery failed to find any deficits in perception, abstract thinking, or reasoning ability, and his motivation remained excellent throughout.**”

Loss of Recent Memory After Bilateral Hippocampal Lesions

William Beecher Scoville
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Original report on patient H.M. (now famous case study in hippocampal amnesia) who had a bilateral hippocampal bisection as a radical intervention for debilitating epilepsy.

In summary, this patient appears to have a complete loss of memory for events subsequent to bilateral medial temporal lobe resection 19 months before, together with a partial retrograde amnesia for the three years leading up to his operation; but early memories are seemingly normal and there is no impairment of personality or general intelligence.

Declarative and Nondeclarative Memory: Multiple Brain Systems Supporting Learning and Memory

Larry R. Squire
Veterans Affairs Medical Center
San Diego
and
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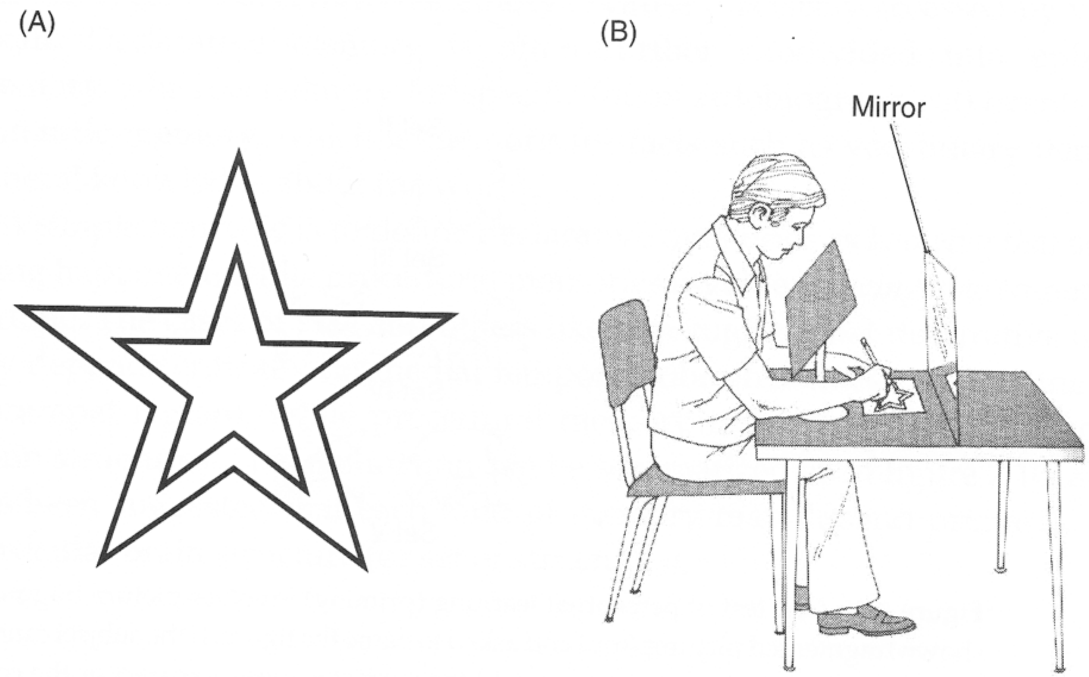
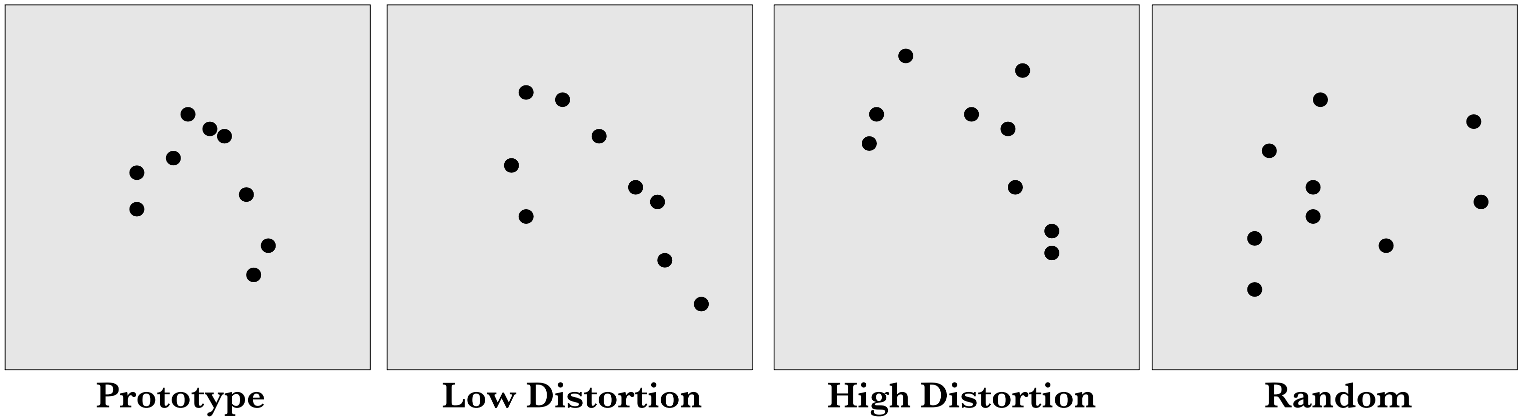
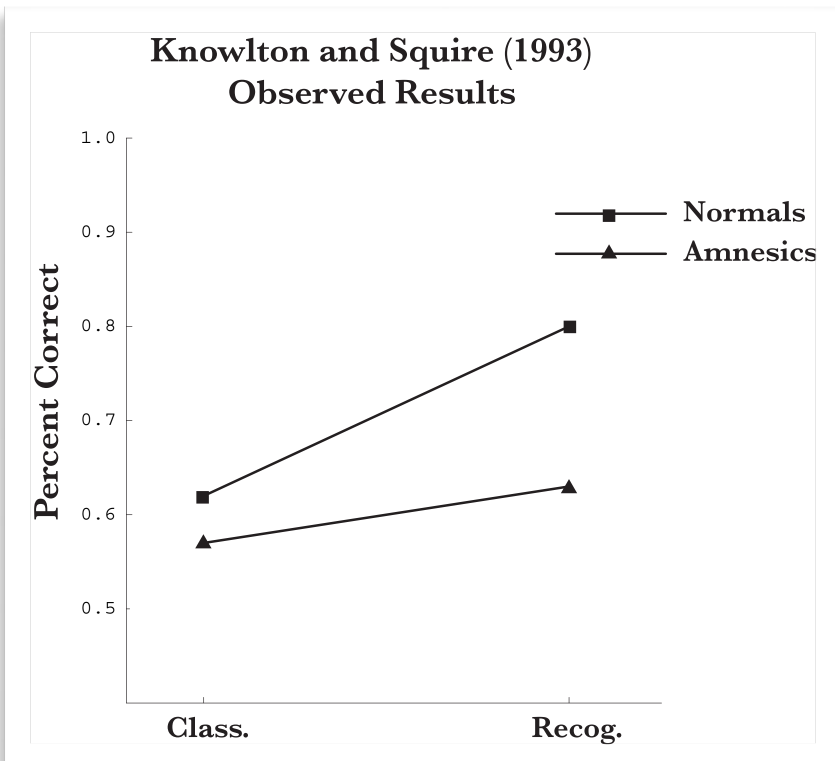
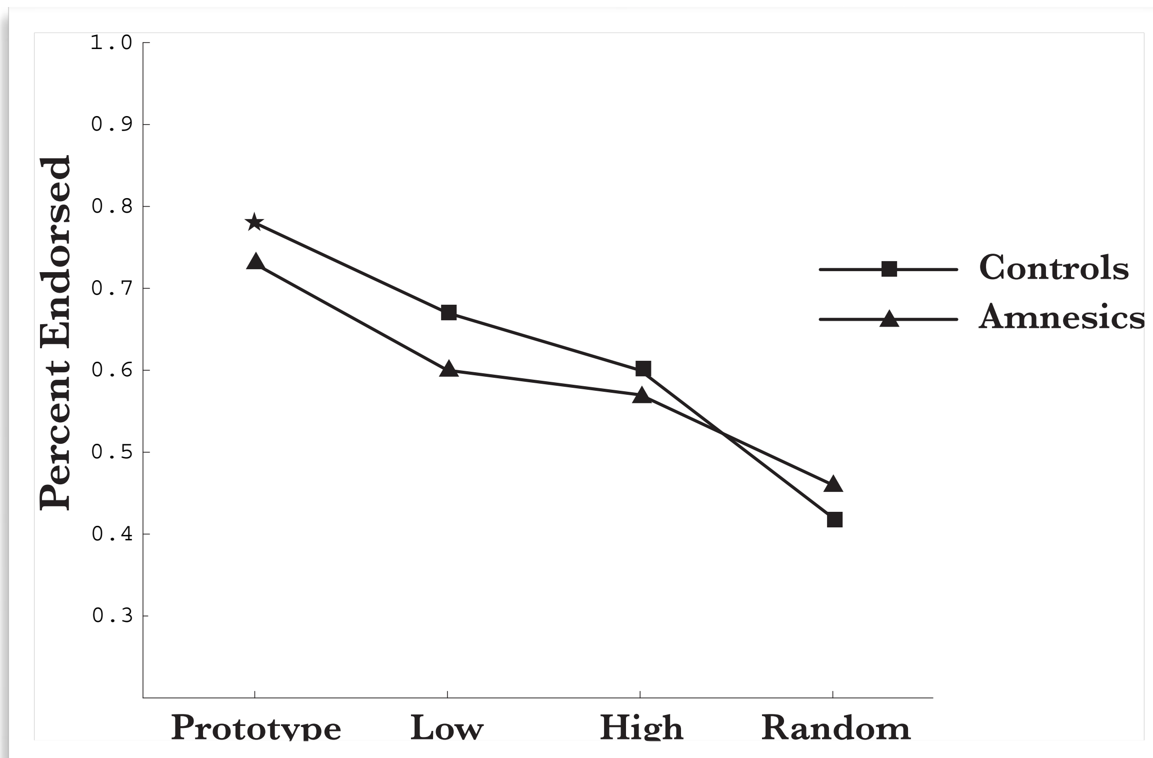


Figure 2.8 The mirror-drawing task. (A) Subjects are given this pattern and asked to trace it, keeping within the borders. (B) A screen is placed above the hand so that the subject can view progress only by watching a mirror, which reverses the apparent motion of the hand. (B is reprinted from Carlson, 1997, Figure 15.5, p. 457.)

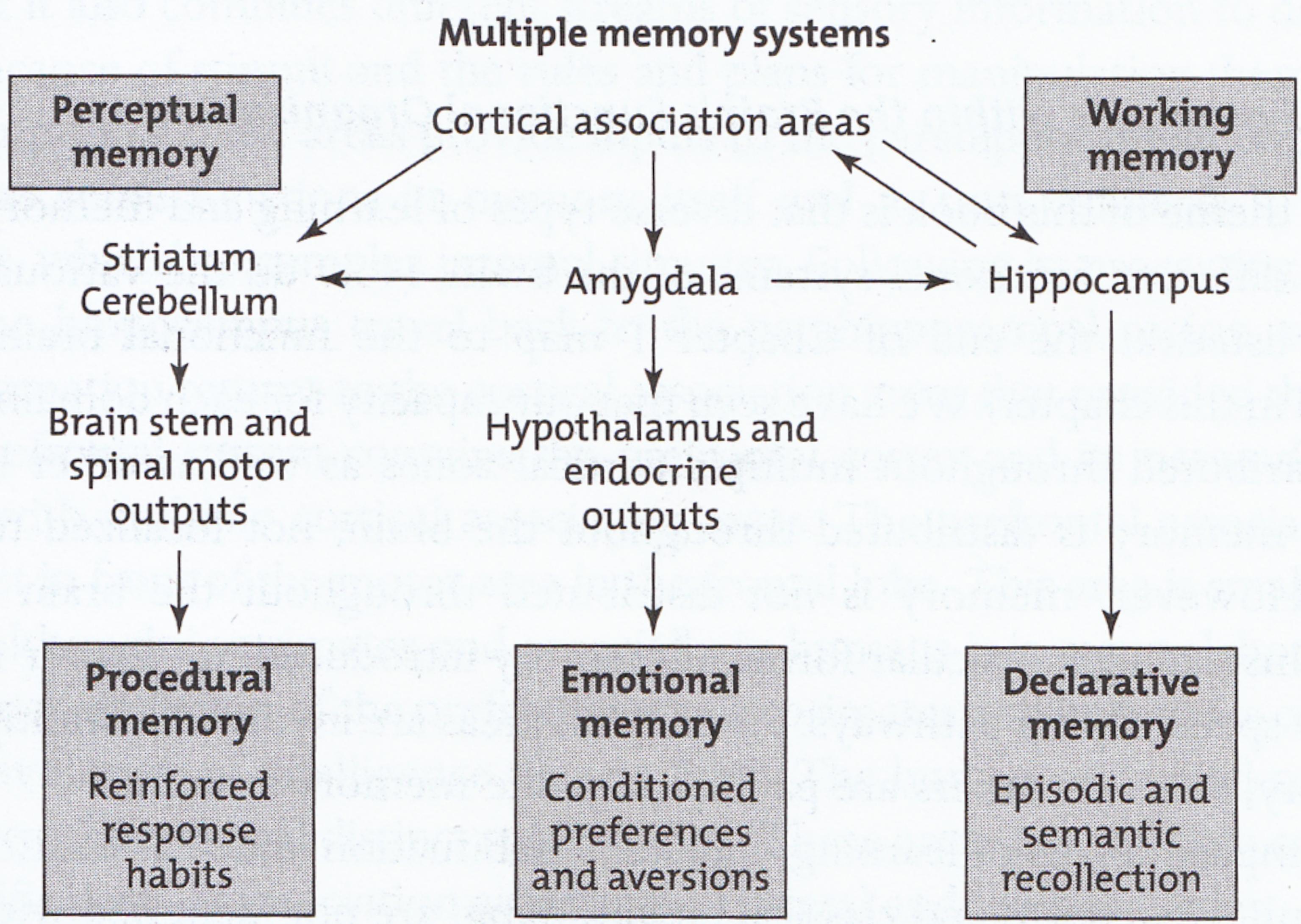

Prototype
Low Distortion
High Distortion
Random


Knowlton and Squire (1993)
Observed Results
Percent Correct
1.0
0.9
0.8
0.7
0.6
0.5
Normals
Amnesics
Class.
Recog.


Percent Endorsed
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
Controls
Amnesics
Prototype
Low
High
Random

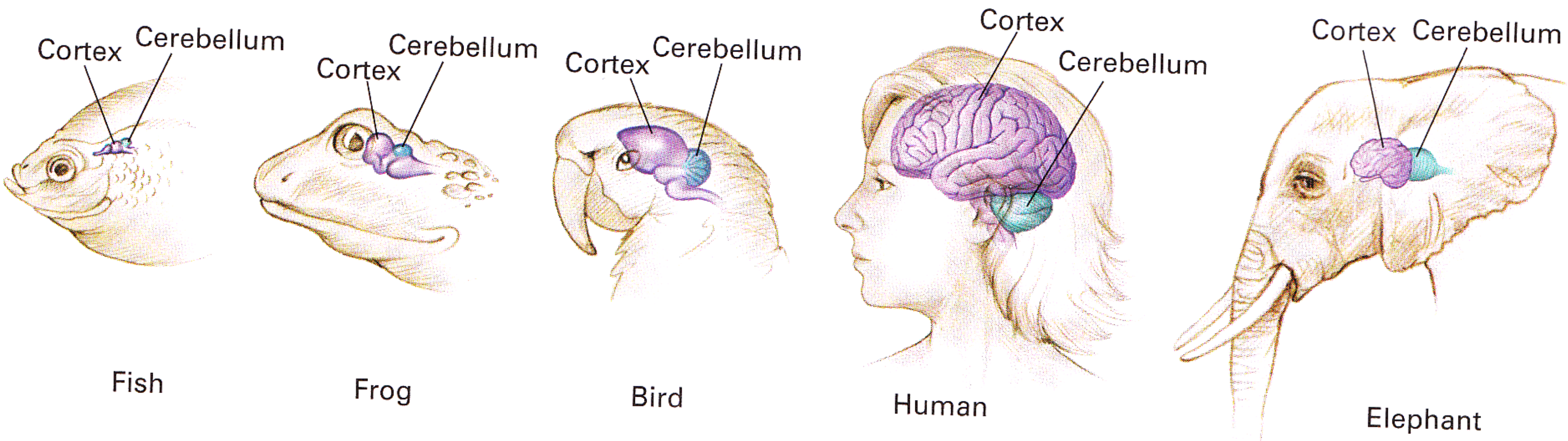
Contribution of Brain Imaging

- We now recognize that no single, localized region of the brain is solely responsible for some aspect of learning or memory
- However, the field does still adopt the view the there is localization of particular functions in different brain regions
- A complex task like “memory” or “learning” involves cooperative action of multiple such systems
- How can we make sense of it all?



Multiple memory systems
Perceptual memory
Cortical association areas
Working memory
Striatum
Cerebellum
Amygdala
Hippocampus
Brain stem and spinal motor outputs
Hypothalamus and endocrine outputs
Procedural memory
Reinforced response habits
Emotional memory
Conditioned preferences and aversions
Declarative memory
Episodic and semantic recollection

Basic organizational principals of brain function conserved across species



Key Summary

- Learning and memory is a central function of the brain
- Learning and memory are basically changes in the connections between neurons
- Different kinds of memories can be reduced to distinct brain pathways supporting each kind of memory
- The is a specialization of function depending on the nature of the information being processes (sensory, motor, reward-related, etc...)
- Three key levels of organization: cells, circuits, and systems

Key Summary

- **Information flows between neurons with action potentials and synaptic transmission (involving neurotransmitters)**
- **The likely mechanism for memory is the changes at the synapses in the form of LTP, dendritic growth, etc..**
- **Circuits represent the collective action of interconnected networks of neurons**
- **Cell assemblies may be the emergent consequence of Hebbian learning in cortex which can support multiple forms of learning (beyond simply stimulus-response)**
- **The brain is organized in interacting hierarchies of control mechanism, and specialized pathways (sensory systems, motor system, cognitive learning systems, emotional learning systems, etc...)**

Key Principles

- Learning and memory are closely related and intertwined states of information processing
- Major insights about learning and memory have come from studies of the brain
- The concept of multiple memory systems unifies the study of learning and memory
- The underlying bases of learning and memory are the same in humans and animals
- Theoretical approaches to studying learning and memory are closely tied to technological/computational advances (e.g., machine learning)