LEARNING AND MEMORY

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Cerebral function

- The mind is a record of events perceived in space-time. Once perceived, are ordered, and then are filed (recede into the past). We think of time as a dimension along which events exist, but this construct is an effect of perception.
- The right cerebral hemisphere functions as a non-linear, parallel processor (as a type of thermostat).
- The left cerebral hemisphere functions as a serial processor in that it corresponds to the linear cause and effect sequencing of time. Pattern recognition takes place in the left inter-parietal sulcus. Association, left dorsal frontal cortex.

Neural networks

- Neural networks (intelligence) are largely inherited.
- Neuronal circuits are internally modulated by feedback loops.
- Neurons either fire or do not fire. Synapses either permit transmission or they do not. The mutual interaction of neuronal fibers (or network) is summed and interpreted as perception.
- When neuronal firing oscillates between 40-80 Hz, it is thought “consciousness” is present.
- There is no statistical distribution of firing that constitutes “traces” of memory. Memory is reformed with each firing.

Neuroanatomy and neurocognition

- Neuronal stem cells exist along the subventricular zone in the CNS as well as in the hippocampus. Found in close anatomic relationship with the microvasculature.
- Lineage-restricted glial progenitor cells are found throughout the subcortical white matter.
- Myelination of frontal lobes continues to the end of the fourth decade. A mature frontal cortex is not seen until that time.

Neuroanatomy and neurocognition

- In the hippocampus, neuronal stem cells generate new dentate gyrus granule cell neurons throughout life. The new cells migrate into the granule cell layer proper, integrate, and at the end of 4 weeks function electrophysiologically as do the older cells.
- Neurogenesis (and plasticity) are stimulated by physical exercise, exposure to an enriched environment, and by hippocampal dependent learning.
- Neural networks may be restructured by remedial (repetetive) action. Repeated electrical stimulation is associated with increased myelin formation.

Synchronization

- The tonic mode of firing means that firing is sustained and the synapse is perpetually depressed as a result. The T Ca^{2+} channels are inactivated.
- If the same cell is sufficiently hyperpolarized (for 100 msec), T Ca^{2+} channels are de-inactivated and primed for action. Now, the very same depolarizing pulse activates the low threshold Ca^{2+} spike; this is the burst mode of firing.

Synchronization

- As tonic firing represents a direct link between an input depolarization, the larger the depolarization, the greater the response (in a linear fashion).
- Burst firing represents an indirect link between the input depolarization and action potential generation, the link being the low threshold Ca^{2+} spike.
- Because a larger depolarization does not evoke a larger low threshold Ca^{2+} spike, this input/output relationship is nonlinear, and approximates a step function.

Synchronization

- The very same input results in a very different message relayed to cortex, depending on the recent voltage history of the relay cell.
- Relatively few but very powerful synapses are needed to get basic information to relay cells, but having many, weak modulatory synapses that can be combined in numerous ways allows for modulation.
- Individual neurons do retain cellular memory; may fire after repeated stimulus ceases though no intermediate external stimulus (information conveyed in retrograde fashion by axon to cell body)

Cerebral organization

- Functional systems are hierarchically arranged
- Map topographically
- Processing occurs in series of relays.
- Sensory information processed in parallel through primary sensory cortex and unimodal association cortex and multimodal association cortex
- Sensory information representing different modalities converge and are integrated into a polysensory event

Cerebral organization

- Posterior association areas project onto frontal association areas (process leads to plan)
- The thalamus compensates for neural speeds as well as path lengths. Feeds-forward to cortex.
- Afferent parenchyma modified by use
- Dorsal post ganglion is sensory receptor
- Enhanced post-synaptic potentiation facilitates associative learning.

Cerebral cortex

- The cerebral cortex is organized vertically.
- II, III and IV are **INPUT LAYERS**
- V and VI are **OUTPUT LAYERS**
- I, II and III are **INTERCONNECTING LAYERS**
- 75% of cortical neurons are excitatory; 25%, inhibitory.
- Most excitatory neurons are **pyramidal** and these neurons are the output of the cerebral cortex.
- **Stellate** neurons are local circuit neurons
- **Interneurons** are inhibitory.

Thalamus

- The anterior thalamus receives projections from the hippocampus and projects to the cingulate and frontal cortex. The dorso-lateral nucleus has reciprocal connections with the posterior part of the cingulate cortex (memory).
- The medial thalamus receives projections from the basal ganglia, amygdala, and spinpothalamic tracts, and projects to frontal cortex. The dorso-medial nucleus receives inputs from the olfactory and limbic systems and is reciprocally connected with the prefrontal cortex (cognition, judgment, mood).

Thalamus

- The ventral thalamus receives projections from basal ganglia and cerebellum (ventro-anterior, ventro-lateral); ventro-posterior receives somatosensory input and projects to cortex.
- The posterior lateral nucleus and pulvinar are a single complex that receives afferents from the superior colliculus and project to the visual and parietal association cortices [medial (auditory); lateral geniculate (vision); pulvinar (association regions)].

Thalamus

- Intralaminar nuclei project to the hippocampus and amygdala
- The reticular nucleus modulates thalamic activity
- Loss of thalamic integrative function characterizes vegetative state.

Synchronization

- First order relays represent the first relay to cortex of a particular type of sub-cortical information.
- Higher order relays instead relay information already in cortex via driver input from layer V of one cortical area to middle layers of another cortical area.
- All thalamic relays receive a feedback from layer VI of cortex (as well as local and brainstem inputs), but the higher order relays receive an additional (driver) input from layer V of cortex, and this is in a feed-forward configuration.

Synchronization

- For the somatosensory system, the ventral posterior nucleus is first order, and the posterior nucleus is higher order (the posterior nucleus receives some spinothalamic input that may be driver).
- Information is processed in parallel between direct corticocortical and indirect cortico-thalamo-cortical pathways.
- Corticocortical pathways are modulators.

Anatomic locations

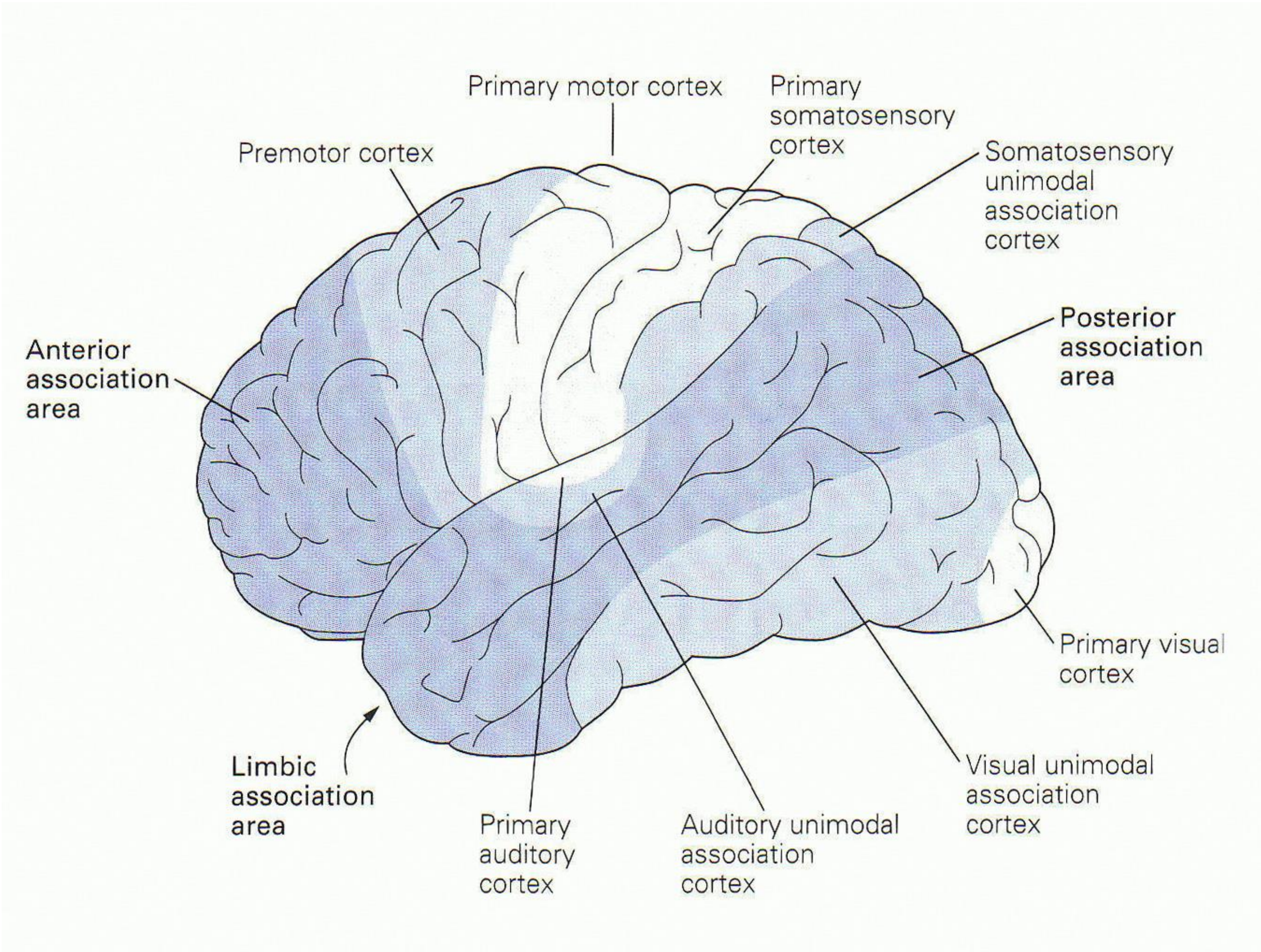
- The primary somatosensory cortex is found in the postcentral gyrus of the parietal lobe. The unimodal association cortex is found in the posterior parietal lobe.
- The visual cortex is found on the banks of the calcarine fissure in the occipital lobe. The unimodal association cortex is found on the inferolateral surface of the occipito-temporal lobe. The ability to grasp a scene at a glance resides in the lateral occipital cortex.
- The auditory cortex is found in Herschl's gyrus in the temproal lobe. The unimodal association cortex is found in the superior temporal gyrus.

Anatomic locations

- Multimodal sensory association areas (visuospatial localization, language, attention) are found at junction between parietal and temporal lobes
- Motor planning, language, judgment in prefrontal cortex, rostral to premotor areas are found on the dorsal and lateral surfaces
- The motor association area (premotor preparation and programs) are rostral to primary motor cortex and in the frontal lobe; the primary motor cortex (movement of a joint along a vector) is found in precentral gyrus (frontal lobe)

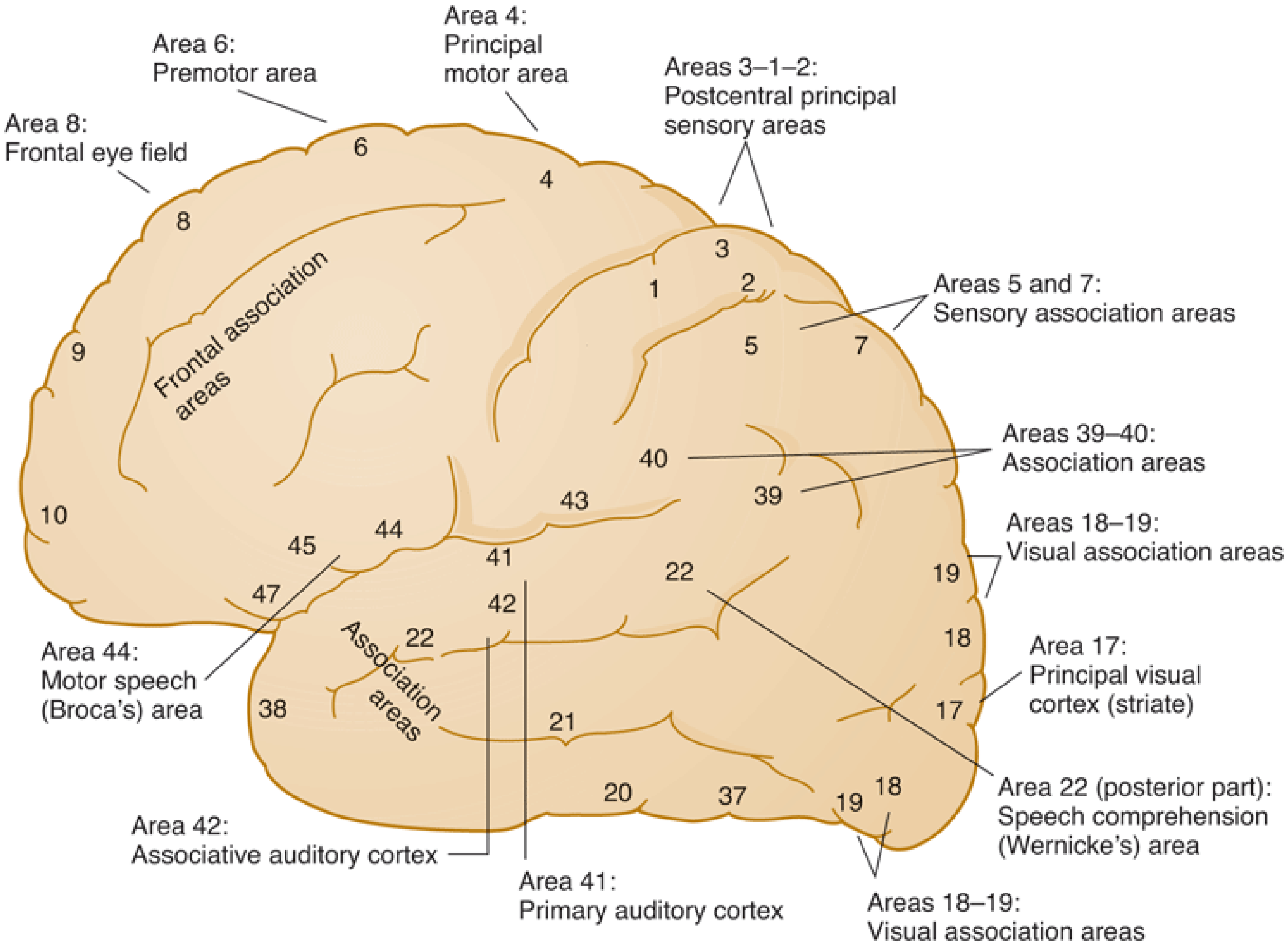
Anatomic locations

- The limbic system is also multimodal (emotion, memory) and involves the cingulate gyrus, hippocampal formation, parahippocampal gyrus, and amygdala.
- Touch and position sense are coordinated in the posterior parietal cortex.



Source: Kandel ER, Schwartz JH, Jessell,TM, *Principles of Neural Science 4th edition*
Fig. 19-1 Accessed 04/04/2011

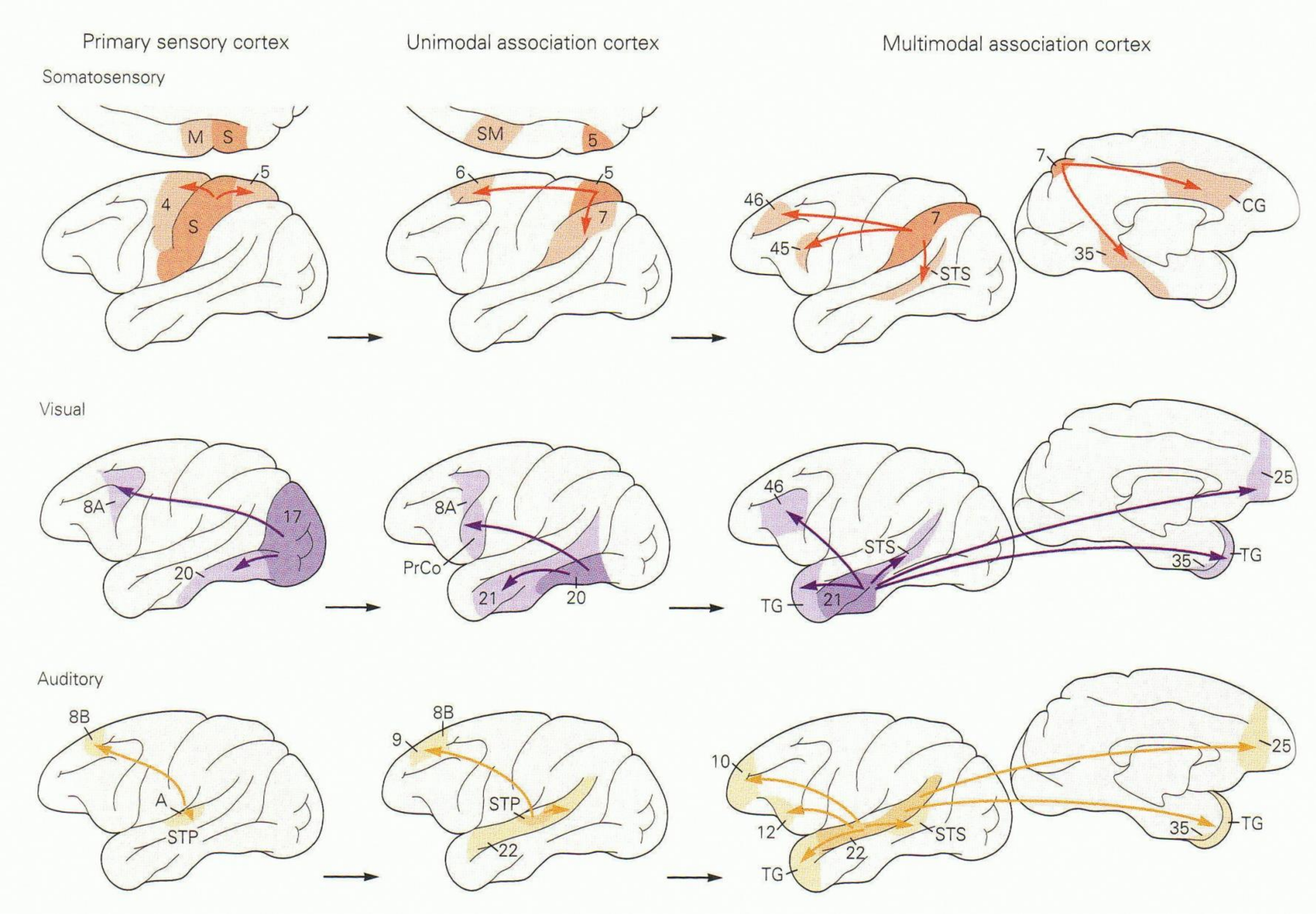
Brodmann areas



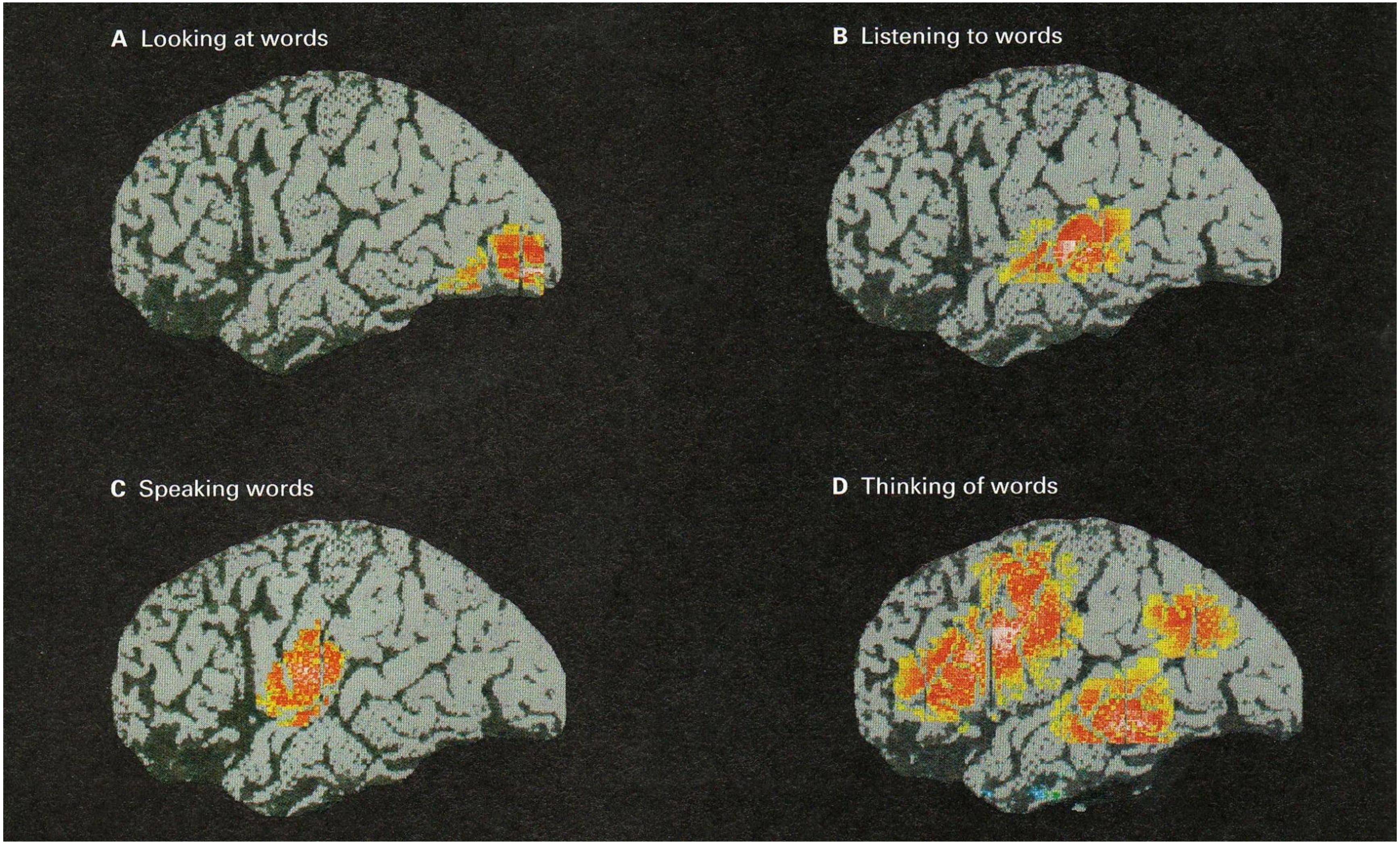
Source: Waxman SG: *Clinical Neuroanatomy, 26th Edition*: http://www.accessmedicine.com

Fig. 10-11   Accessed 02/01/2010

Sensory flow



Source: Kandel ER, Schwartz JH, Jessell, TM, *Principles of Neural Science." 4th edition.*
Fig. 19-3 Accessed 04/04/2011



Source: Kandel ER, Schwartz JH, Jessell, TM, *Principles of Neural Science." 4th edition.*
Fig. 1-6   Accessed 04/04/2011

The three “R’s”

- The left hemisphere is dominant in virtually all right-handed persons as well as in 70% of right-handed persons.
- Language processing also involves ventromedial pre-frontal cortex and the left anterior temporal lobe in addition to Broca’s and Wernicke’s area.
- Visual processing area active in language processing in those born blind.

Anatomic locations

- Wernicke’s area processes the auditory input for language and is important to the understanding of speech. It lies near the primary auditory cortex and the angular gyrus. The angular gyrus combines auditory input with information from other senses.
- Broca’s area controls the production of intelligible speech. It is located near the region of the motor area that controls the movements of the mouth and tongue.
- Wenicke’s area communicates with Broca’s area by a bidirectional pathway, part of which is made up of the arcuate fasciculus.

The three “R’s”

- Wernicke's area in the dominant hemisphere processes principal word meanings.
- The area corresponding to the Wernicke’s area in the non-dominant cerebral hemisphere processes and resolves subordinate meanings of ambiguous words.
- Aspects of gestures such as goal or intention are translated (into words) within Broca's area.
- Pronoun reversal (switch from “me” to “you”) involves coordination between the right anterior insula and the precuneus.

The three “R’s”

- Broca's area also plays a significant role in language comprehension as well as speech. It is essential for syntax and grammar.
- Area 20 is active as well in processing complex sentences. The more complex or ambiguous the sentence, the greater the information retrieval required.
- Wernicke’s area as well as the prefrontal and cingulate cortices are active when attention is required.

The three "R's"

- Tones or words activate area 9 and the auditory cortex as well as Wernicke's area. Limbic association areas are also activated by words.
- The upper pathway between Broca and Wernicke areas is associated with syntax.
- The lower pathway between Broca and Wernicke areas is associated with lexicon and semantics.

The three “R’s”

- Retinal projections terminate in area 17 (V1) of the occipital lobe.
- From the primary visual area, there is a dorsal stream to the mid temporal (V5) and mid-superior temporal cortex where motion, position, and stereovision are determined.
- From the primary visual area, there is a ventral stream (in a feed-forward direction) to association areas 18-19 (V2-V3) to the inferior temporal cortex where color, orientation, shape, texture, and direction are determined.
- The pre-frontal cortex is involved in the moment-to-moment control of the visual system.

The three “R’s”

- Tactile sensations are processed in the orbito-frontal cortex.
- The primary auditory and association cortex is also activated.
- Area 20 is activated.
- Language association areas (Broca, Wernike) are activated.
- Information is relayed both to the amygdala and the orbito-frontal cortex.
- The motor cortex is activated if speech is uttered or words are written.

Reading sequence

- In all cognitive activities requiring attention, Area 32 of the left anterior cingulate gyrus is active.
- In reading, the left lateral prefrontal cortex (Area 46) is activated.
- **Visual processing**
- Areas 17-19 bilaterally; processed information in right. Areas 18-19 transferred to left side through Forceps Major (traverse splenium of corpus callosum)
- Arabic letter recognition is a right brain function alone.
- **Orthographic processing**
- Medial Area 19

Reading sequence

- **Phonological assembly**
- Area 39 (lingual gyrus) and Area 21 (middle temporal gyrus) are involved in converting graphemes to phonemes.
- **Semantic retrieval**
- Area 45 with Area 37 (posterior temporal lobe) and Area 40 (supramarginal gyrus in inferior parietal lobule)
- **Phonological execution (inner speech)**
- Area 44-5, premotor and motor cortex, medial Area 6 (supplementary motor cortex), contralateral cerebral hemisphere

Dyslexia

- Males three times more affected than are females.
- Sensory and motor processing more affected in females than in males. Language processing centers more affected in males.
- Magnocells (M cells) of the ganglionic layer of the Retina and the lateral geniculate nucleus are smaller than normal; axons conduct more slowly.
- Scanning movements controlled by M cell inputs to superior colliculus are inefficient.

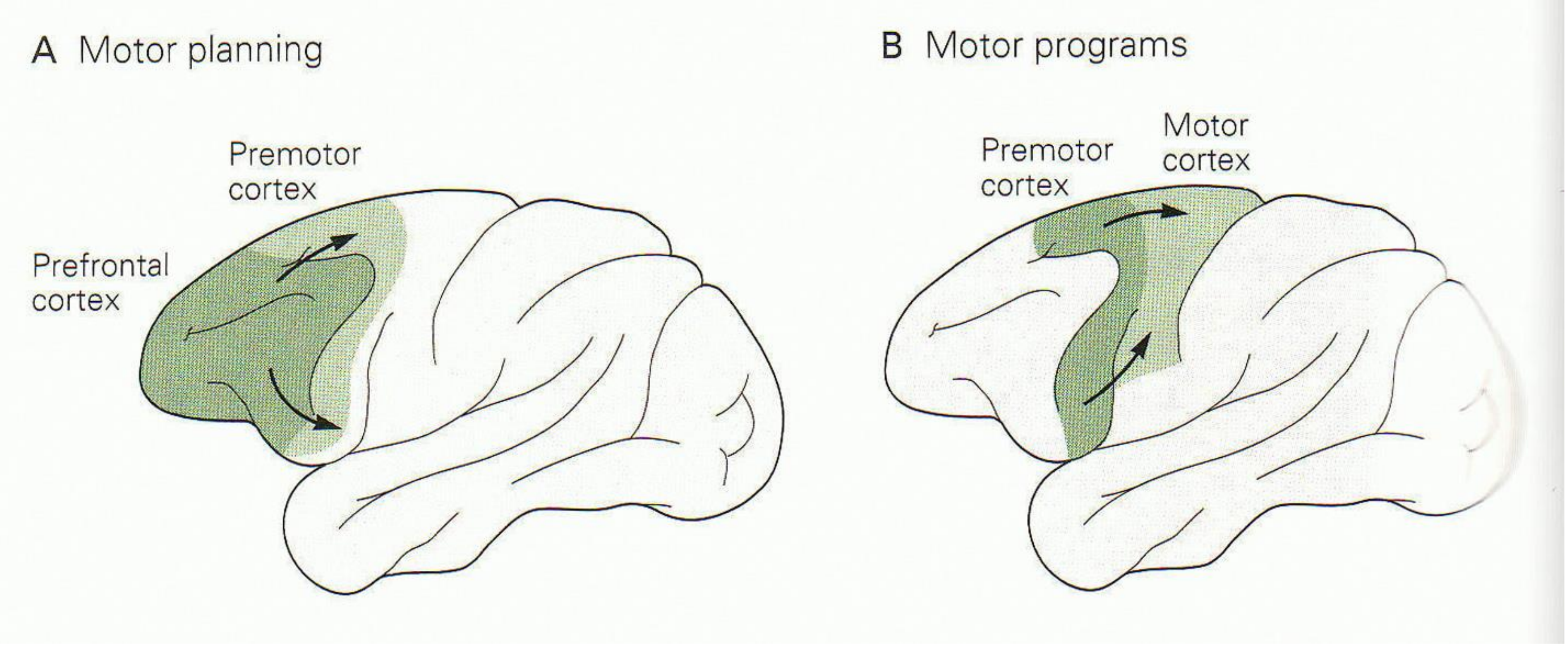
Dyslexia

- M cells of the medial geniculate nucleus which project to the primary auditory cortex are also smaller than normal, leading to reduced detection of the frequency and amplitude of sounds (perception of phonemes).
- Insula inactive (links supramarginal and angular gyri to Broca’s area); defective “inner speech”.

Dyslexia

- Right cerebral hemisphere important for stress, timing, intonation (prosody)
- Developmental dyslexia relates to poorly developed phonological awareness.
- Magnocellular pathway of the visual system may be impaired (rapidity of processing).
- Planum temporale (cortical area posterior to the auditory cortex or Herschel’s gyrus in the Sylvian fissure that forms the triangular center of Wernicke’s area) smaller in male dyslectics (may represent defect in hemispheric specialization).

Motor activity



The flow of information in the frontal lobe motor control system is the reverse of that in the sensory systems.

Source: Kandel ER, Schwartz JH, Jessell, TM, *Principles of Neural Science.” 4th edition.*
Fig. 19-5 Accessed 04/04/2011

Motor cortex

- **The primary motor cortex** requires the lowest level of stimulation to produce movements and all other areas converge on the primary cortex.
- Control is focused on distal muscle of an extremity to execute delicate and precise movements.
- It codes for direction, force, velocity.

Motor cortex

- Direct stimulation of the **pre-motor area** does not produce movement
- There is an increase in activity in anticipation (mental rehearsal), but a decrease in activity during execution of the movement.
- The lateral pre-motor area selects action as well as is involved in sensorimotor transformation (voluntary movements have a behavioral component).

Motor cortex

- Stimulation of the **supplemental motor area** produces movements involving entire limbs or the entire hand.
- The pre-motor area and supplemental motor area are responsible for translating strategy into actions.
- The **posterior parietal area** is active during motor acts.
- Direct stimulation does not cause movement.
- Related to motivation or intent.

Motor activity

- Voluntary movements are goal directed and improve with practice as a result of feedback and feed-forward mechanisms.
- A purposeful movement is represented in the brain in an abstract form rather than a series of actions. The least path is always taken.
- The brain represents the outcome of motor actions independently of the specific effector used or the specific way the action is achieved. There is a balance between the speed of a movement and its accuracy. The time taken to respond to a stimulus is related to the amount of information that needs to be processed to accomplish the task.

Basal ganglia

- The **direct loop** facilitates thalamo-cortical activity.
- The **indirect loop** inhibits thalamo-cortical activity.
- When phasic excitatory input transiently activates the direct pathway from the striatum to the globus pallidus, the tonically active neurons in the globus palidus are suppressed, permitting the thalamus (and cortex) to be activated. Positive feedback.
- Phasic activation of the indirect pathway transiently increases inhibition of the thalamus. Negative feedback.
- The ventral striatum is more active in adolescence.

Basal ganglia

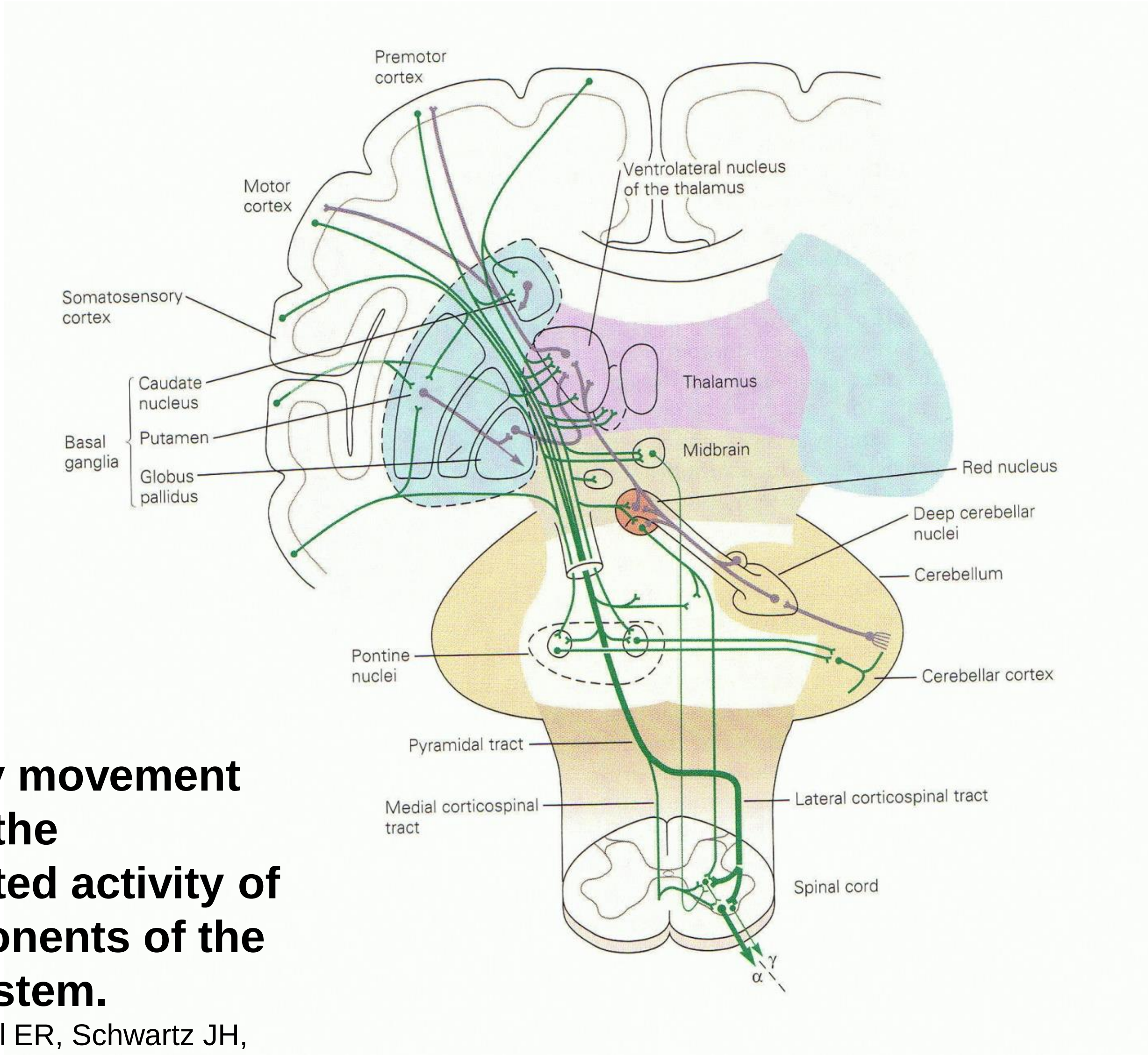
- **Cognitive loop**, concerned with motor intentions.
- The head of the caudate is involved in planning ahead (ventral anterior nucleus of the thalamus as relay). When the novel motor task has been practiced to the level of automation, the motor loop becomes active.
- **Motor loop**, concerned with learned movements.
- The substantia nigra is tonically active, favoring activity in the direct pathway. The putamen and globus pallidus are somatotopic.
- Foxp2 gene necessary for speech function.

Basal ganglia

- **Limbic loop**, concerned with giving motor expression to emotions.
- This loop passes from the inferior prefrontal cortex through the nucleus accumbens and ventral pallidum, with return to the inferior prefrontal cortex via the medial dorsal nucleus of the thalamus.

Basal ganglia

- **Oculomotor loop**, begins in the frontal eye field and posterior parietal cortex. It passes through the caudate nucleus and the reticular portion of the substantia nigra and returns via the ventral anterior nucleus of the thalamus.
- When the eyes are fixated, the substantia nigra is tonically active.
- When a saccade is to be made, the loop is activated and the superior colliculus is disinhibited, reinforcing activity of the direct pathway. Following movement, vigilance is resumed.



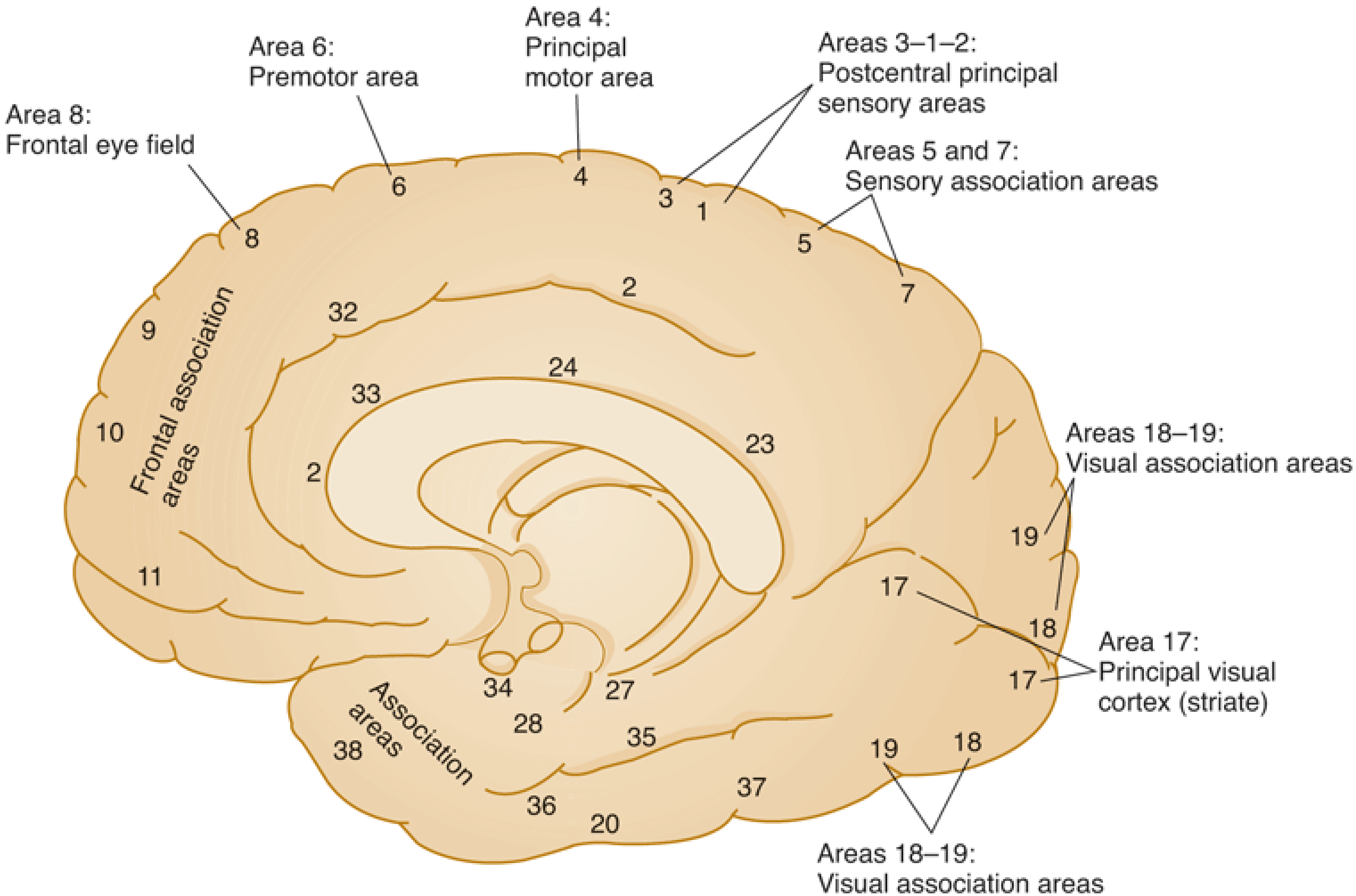
Voluntary movement requires the coordinated activity of all components of the motor system.

Source: Kandel ER, Schwartz JH, Jessell, TM, *Principles of Neural Science." 4th edition.*
Fig. 18-9 Accessed 04/04/2011

Somato-sensory input

- The cerebellum is required for precise control and coordinated movements.
- Functions to modify acts initiated by the motor cortex and basal nuclei.
- Vestibulo-cerebellar and Spino-cerebellar output affect the descending motor system at the brainstem level (red nucleus, CN motor nuclei and vestibular nuclei); they affect the motor act while it is in progress.
- Cerebro-cerebellar inputs information about a command about to be executed so it can modulate motor command information before execution of the command.

Brodmann areas



Source: Waxman SG: *Clinical Neuroanatomy, 26th Edition*: http://www.accessmedicine.com

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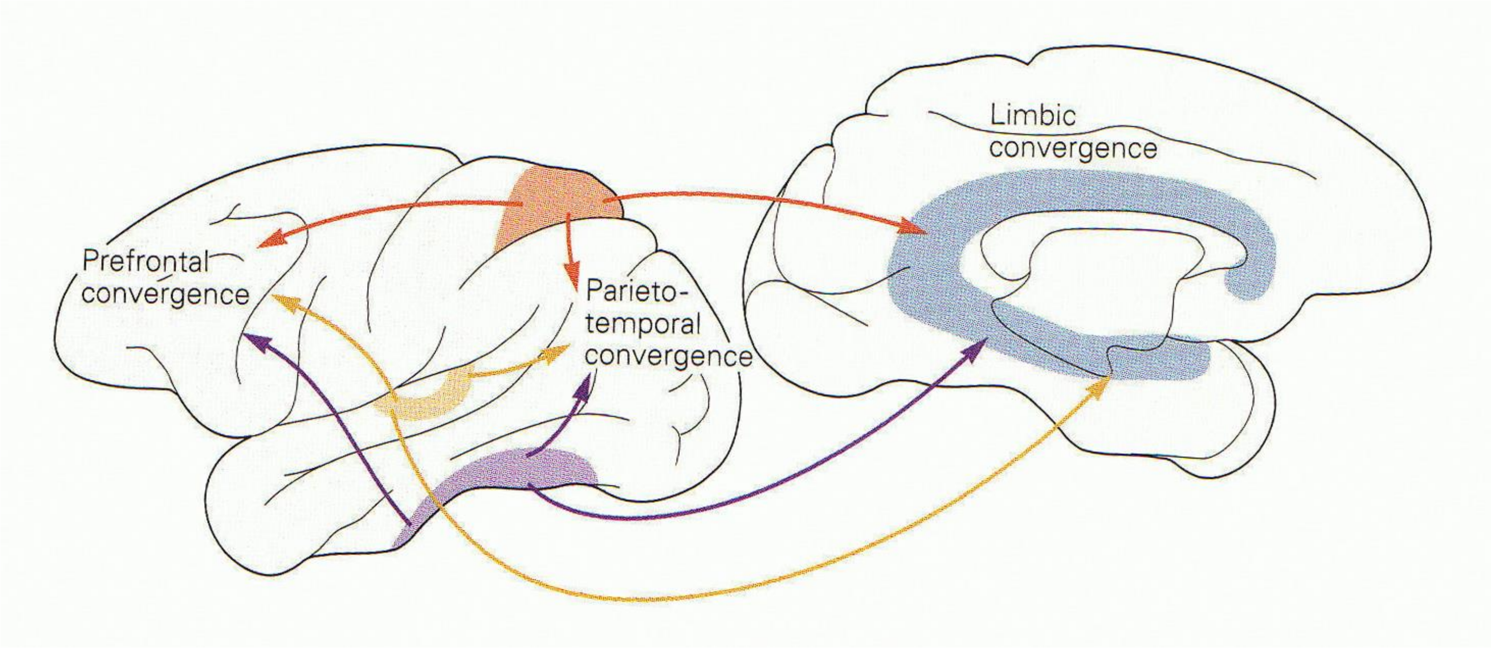
Convergence



Source: Kandel ER, Schwartz JH, Jessell, TM, *Principles of Neural Science.” 4th edition.*
Fig. 19-4 Accessed 04/04/2011

Anterior cingulate cortex

- Executive area. Areas 24, 32. Connected with the dorsolateral prefrontal cortex (generating appropriate motor plan selection) and the supplementary motor area.
- Pain perception area. An emotional area lies adjacent to the pain perception area. Afferents from the medial dorsal nucleus of the thalamus.
- Micturition area.
- Vocalization area. (left) Active with executive area for sentence construction.
- Autonomic area. Below rostrum of corpus callosum. Visceral responses.

Hippocampus

- Hippocampus has three major patways:
- (1) The perforant pathway projects from the entorhinal cortex to the granule cells of the dentate gyrus.
- (2) The mossy fiber pathway contains axons of granule cells and runs to pyramidal cells in the CA3 region of the hippocampus.
- Involved in non-associative learning.
- Ca^{2+} influx into presynaptic cell is limiting step.
- Noradrenergic modulation.

Hippocampus

- (3) The Schaffer collateral pathway consists of the excitatory collaterals of the pyramidal cells in the CA3 region and ends on the pyramidal cells in the CA1 region. 5000 CA3 cells converge on one CA1 cell; same CA3 cells also pass collaterals to other CA1 cells (en passant, Schaffer collaterals).
- The Schaffer collateral pathway is involved with associative learning.
- Repeated stimulation (late phase) leads to new synapse formation. Place fields form.
- Stimulus to any of the three paths increases the EPSP in the target hippocampal neurons.

Emotion

- Feelings are cognitive translations of ambiguous peripheral signals. Hypothalamus coordinates the peripheral expression of emotional states; amygdala coordinates.
- Posterior pituitary and circumventricular organs (area postrema, subfornical organ, laminar terminalis, subcommissural organ, median eminence, neurohypophysis) lack blood-brain barrier. Hormonal regulation.

Connections of septal area in amygdala

- Nucleus accumbens (dopamine). Reward center.
- Stria medullaris (gluatamate). Synapse with Habenular nucleus (acetylcholine). To pineal and reticular formation. With cerulean nucleus, Sleep-wake cycle.
- Septo-hippocampal path via fornix (glutamate). Pacemaker. (Cholinergic neurons determine amplitude.) Episodic memory.
- Septal nucleus and Basal nucleus of Meynert in basal forebrain have somas of cholinergic neurons. Tonically active. Muscarinic. Diminsh K^+ conductance.

Differences between men and women

- The anterior commissure and the corpus callosum are smaller in the male. There is less cross-talk as these connect the two temporal lobes as well as contain decussating fibers from the olfactory tracts, and is a part of the neospinothalamic tract for pain. The anterior commissure also serves to connect the two amygdala.
- The stria terminalis is more prominent in males (major output of the amygdala);
- as are the anterior nuclei (2,3, preoptic) of the hypothalamus (regulation of blood pressure and heart rate, thermoregulation).

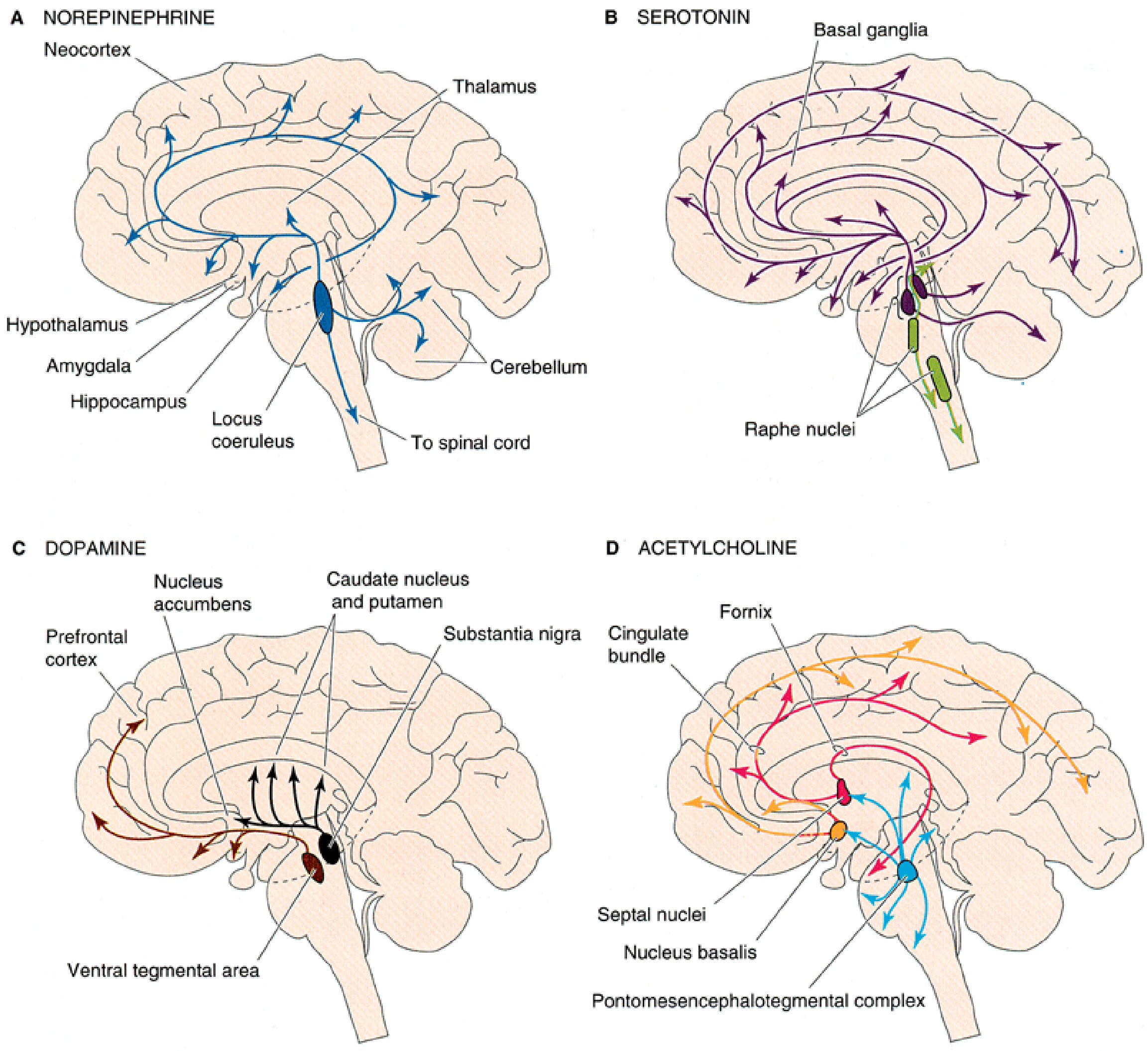
Differences between men and women

- Men tend to objectify women. When presented with a variety of female figures, a waist to hip ratio of 0.7 in the woman is associated with a maximal response in the man.
- More verbal activity is present in the woman when presented with a male figure.

Behavior

- Dopamine regulates movement, reward, cognition.
- Norepinephrine regulates mood, arousal, cognition.
- Serotonin regulates mood, anxiety, sleep, pain, and cognition.
- Acetylcholine regulates memory, arousal, cognition.

Neurotransmitters and pathways



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

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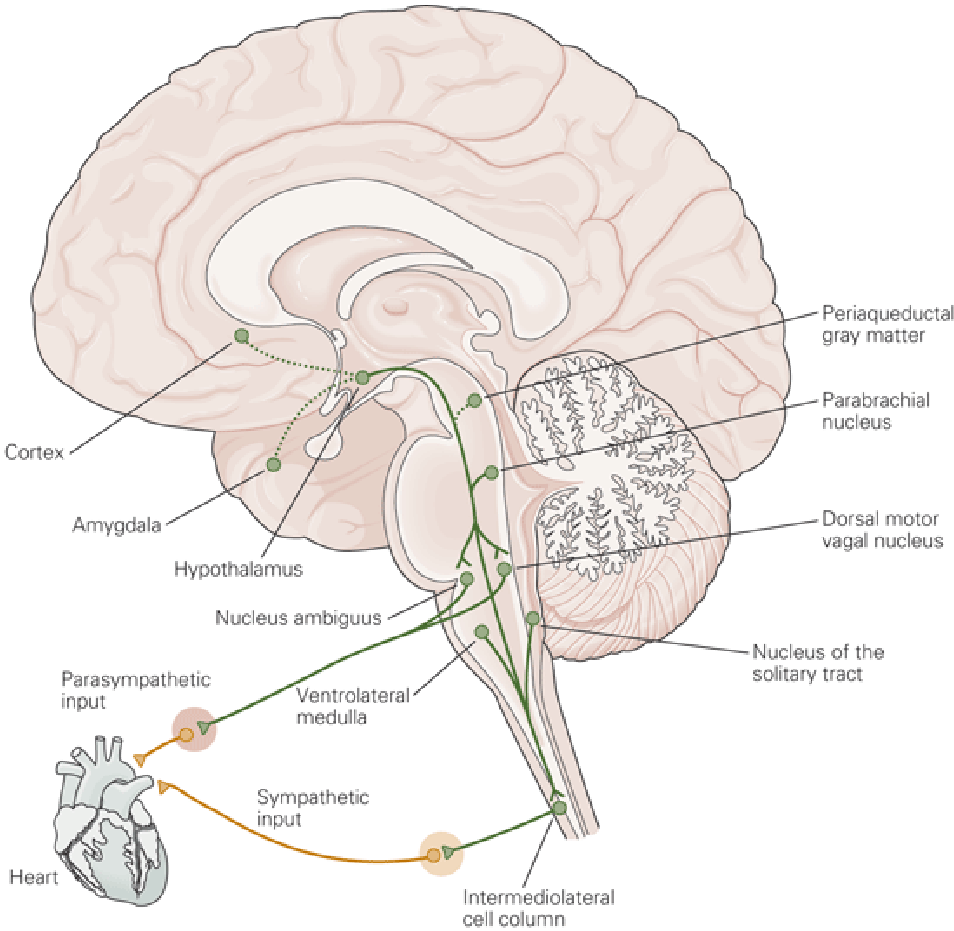
Fig. 7-2 Accessed 02/01/2010

Descending autonomic pathways

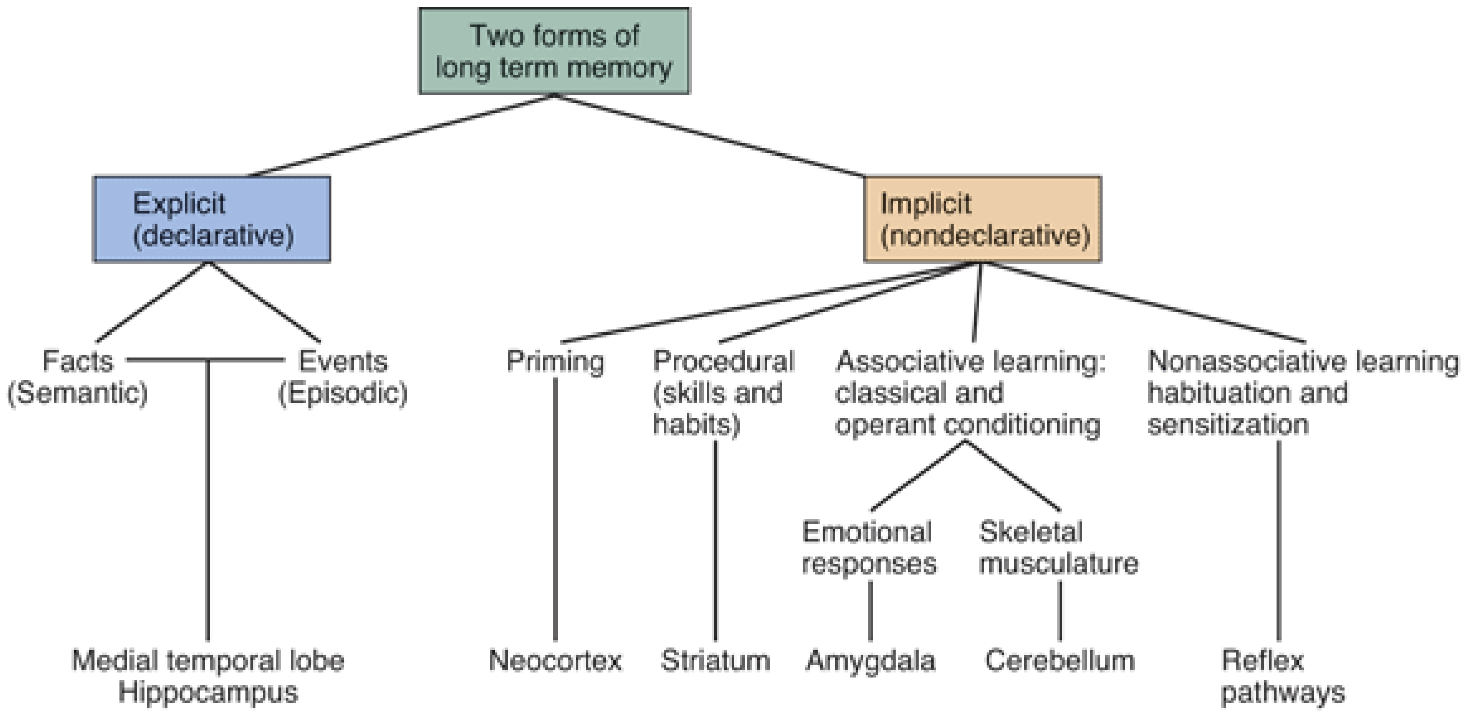


Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

Direct projections (solid lines) to autonomic preganglionic neurons include the hypothalamic paraventricular nucleus, parabrachial nucleus, nucleus of the solitary tract, ventrolateral medulla, and medullary raphé.
Indirect projections (dashed lines) include the cerebral cortex, amygdala, and periaqueductal grey matter.

(From Kandel ER, Schwartz JH, Jessell TM (editors): *Principles of Neural Science,* 4th ed. McGraw-Hill, 2000.) Fig. 17-6 Accessed 02/01/2010

Long-term memory



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

(Modified from Kandel ER, Schwartz JH, Jessell TM (editors): *Principles of Neural Science,* 4th ed. McGraw-Hill, 2000.)
Fig. 19-2 Accessed 02/01/2010

Memory

- The right hippocampus is involved in processing external environment; the left hippocampus, verbal memory.
- The right posterior hippocampus and right inferior parietal lobe are engaged in familiar spatial tasks.
- The left anterior hippocampus (CA1 and the peri-rhinal cortex) and dorso-lateral prefrontal cortex are engaged in encoding and embedding novel material including language function. (Blanes cells are inhibitory, act in a feed-forward fashion in the olfactory cortex. Essential for learning aromas.)

Memory

- The dentate gyrus is organized as a metric (cognitive map). Pyramidal cells in the hippocampus and granular cells in the dentate gyrus are associated with sense of place.
- The dentate gyrus is connected with the CA3 and CA1 levels of the hippocampus; from there, to the subiculum; and, finally, to the entorhinal cortex.
- Associative learning integrated in the hippocampus and dentate gyrus.

Memory

- Cholinergic activity essential for learning.
- Amyloid precursor protein, found at synapses, is also essential for learning.
- The production of the c-AMP response binding protein (CREB) is essential for retention of memory. The protein has histone acetyl-transferase activity and acts as a scaffold to stabilize the transcription complex.
- Sensory cues fine-tune neural activity.

Explicit memory

- Explicit memory is first acquired through processing in one or more of the three polymodal association cortices (prefrontal, limbic, parieto-occipital-temporal).
- From there information is conveyed in series to the parahippocampal and perirhinal cortices, the entorhinal cortex, the dentate gyrus, the hippocampus, the subiculum, and finally back to the entorhinal cortex.
- From there the information returns to the association areas via the parahippocampal and perirhinal cortices.
- Involves long term potentiation in the hippocampus.

Working memory

- Working memory is short-term memory required for both the encoding and recall of explicit knowledge.
- Stores items as long as the information is being stored in the consciousness.
- Functions if the information is being (sub)- vocalized or integrated in existing memory.
- Limited by attention; easily distracted.

Working memory

- The working memory is comprised of a central executive (prefrontal cortex) that keeps track of and gathers information; a system that holds visual-spatial representations of objects as well as a system that holds verbal information (articulatory loop); and an episodic buffer that is capable of binding together information into a coherent trace. The executive regulates information flow into these rehearsal systems. Limited capacity.
- Neurons in the posterior parietal and dorsolateral frontal lobes (particularly in area 46) provide the functional basis for working memory.

Episodic memory

- Allows the recollection of experiences with associated details such as sight and sound.
- May persist for hours and enter permanent memory or be discarded.
- Individual elements are stored in the same areas of neocortex involved in the initial processing (and analysis) of the information that becomes the memory.
- The hippocampus binds the different regional contributions into a coherent memory trace.

Episodic memory

- When a particular cue activates cells in the cortical regions, the medial thalamic network that is associated with that cue is reactivated and the entire neocortical representation is strengthened.
- With repeated reactivation, the connections between the relevant neocortical regions are slowly strengthened until the memory trace is entirely represented in the cortex and no longer is dependent upon thalamic connections.

Semantic memory

- Involves generic information
- Accessed without accompanying details of the time when the words or facts were remembered.
- Vocabulary and associations between verbal concepts make up the bulk of semantic memory.
- The anterior temporal lobes are concerned with organization of object knowledge in categories. The attributes of an object are stored close to the regions of the cortex that mediate perception of those attributes.
- Autobiographical knowledge about time and place involves the prefrontal cortex.

Procedural memory

- Involves motor, perceptual, and cognitive processes.
- As the formation of skills and habits requires extensive practice, the acquisition of the memory is slow.
- Long-lasting.
- Declarative memory and the cortico-striatal procedural memory systems operate independently from each other. They compete for cognitive resources.

Procedural memory

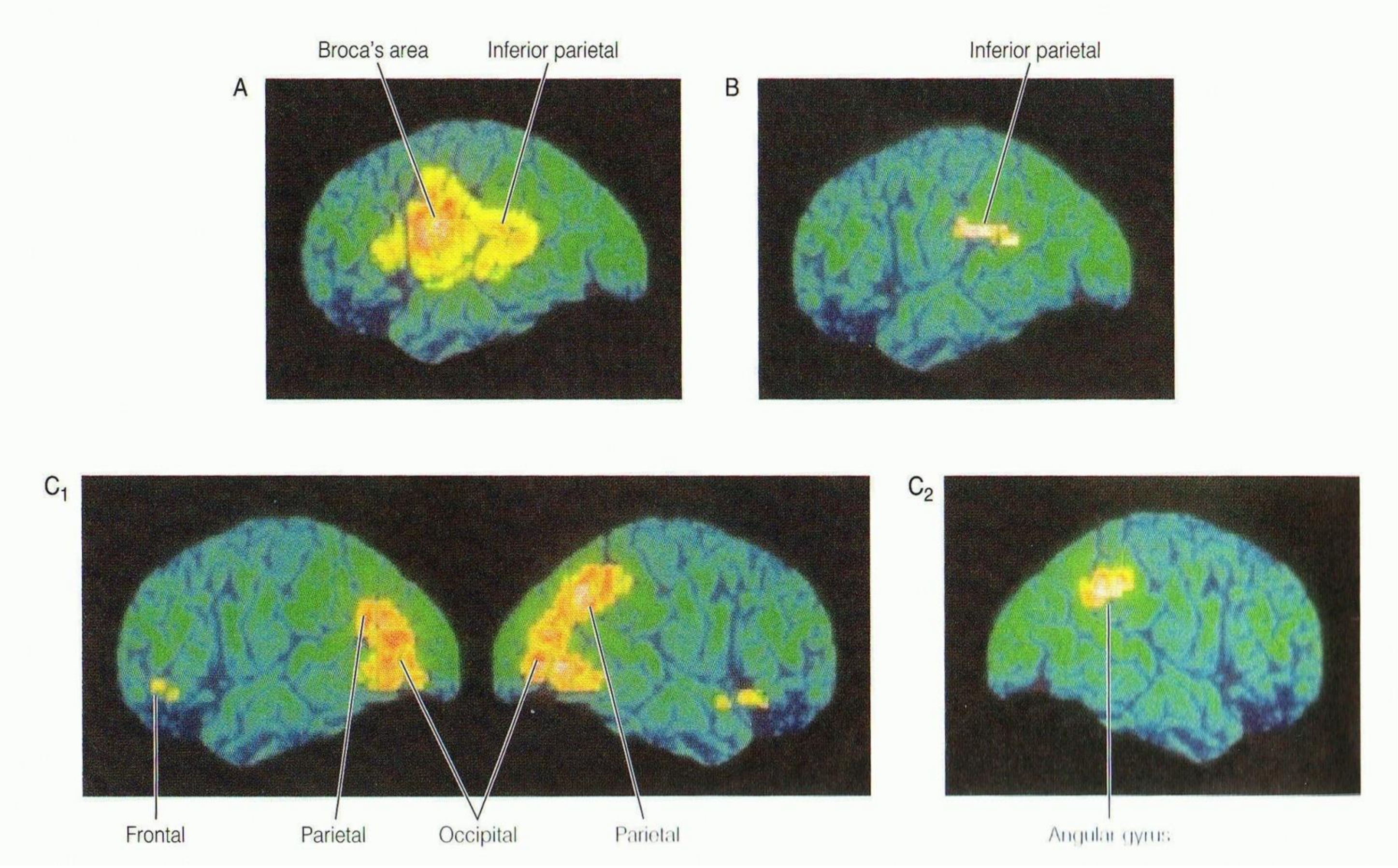
- The forms of perceptual and motor learning that can occur without conscious recollections are mediated in part by contractions and expansions of representations in the sensory and motor cortex.
- The basal ganglia are essential in motor skill learning.
- The cerebellum is involved in the association of a visual cue with a motor action.

Procedural memory

- Procedural memory is retained even if the hippocampus is damaged (the cerebellum is the primary store for procedural memory, linked to the motor teaching function of the inferior olivary nucleus).

Implicit memory

- Implicit or non-declarative memory involves unconscious recall. Implicit memory tightly connected to the original stimulus conditions under which the learning occurred.
- Nonassociative learning (habituation, sensitization, imitation learning, conditioning).



- **A. Short term verbal memory task for letters. B. Rhyming task with no memory demands (phonological loop). C1. Remembered line drawings. C2 Line drawings examined. (visuospatial buffer).**

Source: Kandel ER, Schwartz JH, Jessell, TM, *Principles of Neural Science."* *4th edition.* (Courtesy of E Paulesu). FIg. 19-9 Accessed 04/04/2011

Non-associative learning

- Habituation involves an activity dependent presynaptic depression of synaptic transmission.
- There is reduced mobilization of glutamate transmitter vesicles.
- The memory of diminished strength of the connection is stored at more than one site in the circuit.

Non-associative learning

- Sensitization involves presynaptic facilitation of synaptic transmission.
- Serotonin binds to G-protein leading to cAMP activation which activates Phosphokinase A which together with Phosphokinase C enhance neurotransmitter release.

Non-associative learning

- PKC phosphorylates K^+ channels, prolonging action potential and increasing influx of Ca^{2+}.
- Vesicles are mobilized to the releasable transmitter pool and the efficiency of exocytic release is increased.
- L-type Ca^{2+} channels are opened which lead to Phospholipase C activation that leads to diacyl glycerol (DAG) activation of PKC, reinforcing vesicle mobilization and L-channel activation.

Non associative learning

- Conditioning involves presynaptic facilitation of synaptic transmission that is dependent upon activity in both the presynaptic and postsynaptic cell. Conditioned stimulus must precede unconditioned stimulus by a very short interval. Facilitating neuron is serotonergic. Postsynaptic event is a retrograde signal to the sensory neuron.
- Long term storage of implicit memory for conditioning and sensitization involves the cAMP/PKA/MAPK/CREB pathway. (CREB1 facilitates; CREB2 inhibits)

Memory

- Poor left dorso-lateral prefrontal cortex function is associated with “incomplete” (or false) memory.
- Poor left hippocampal function is noted with post traumatic stress disorder.
- Loss of the left anterior hippocampus is followed by anterograde amnesia; a loss of declarative memory. (Short-term memory loss may be seen with interruption in this area).

Memory

- (Anterograde memory loss may be seen with interruption of Papez circuit as well as with Korsakoff syndrome, a result of thiamine deficiency.)
- Development of retrograde amnesia requires posterior left hippocampal damage. Is episodic.
- Long-term memory damage involves damage as well to the neocortex.