Behavioral Sciences

MD3

Behavioral Sciences

Brain Function and Neurocognitive Disorders

Brain Function and Neurocognitive Disorders

Learning Objectives

- Demonstrate understanding of left and right brain dominance
- Be able to correlate specific function with corresponding part of the Brain
- Demonstrate understanding of how healthy parts of the brain differ from injured parts
- Answer questions about how dominant parietal lobe dysfunction differs from non-dominant dysfunction
- Demonstrate understanding of the different neurotransmitters and how they affect the brain
- Demonstrate understanding about how the neurocognitive disorders differ

Brain Function and Neurocognitive Disorders

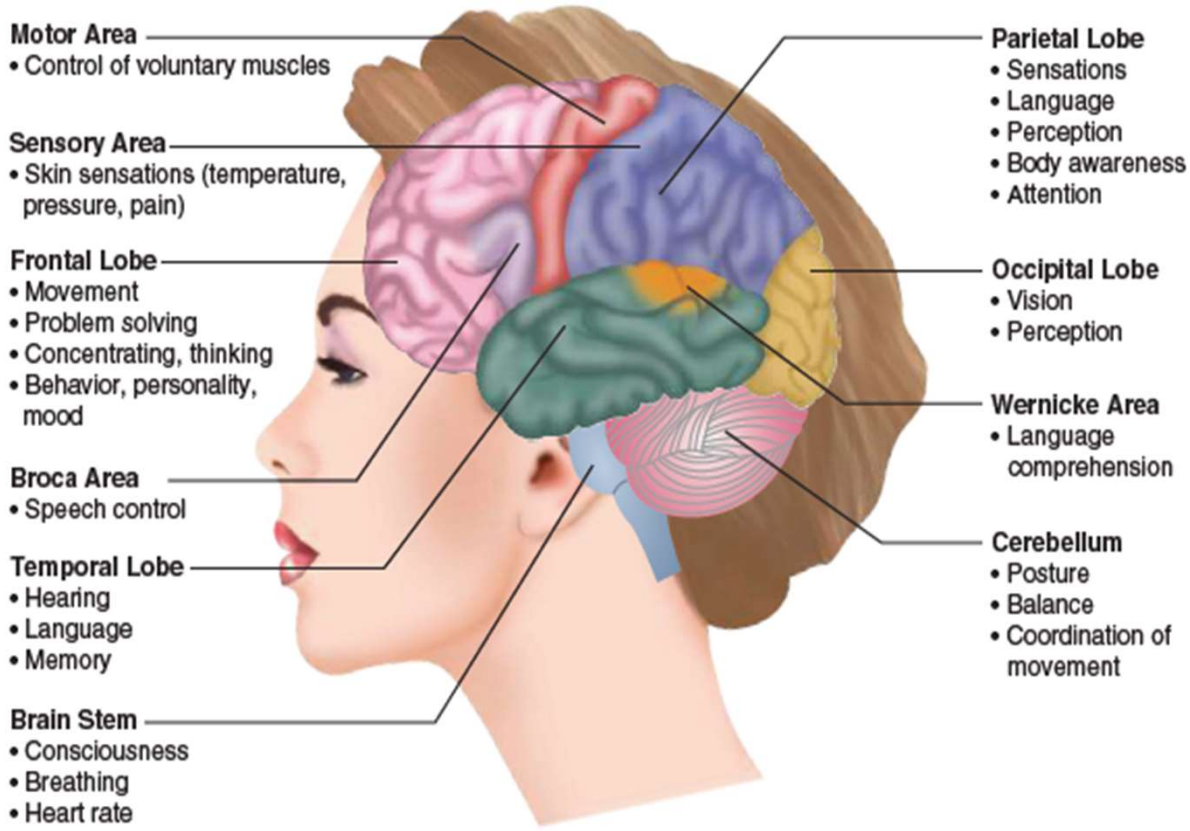
LEFT AND RIGHT BRAIN DOMINANCE

The left hemisphere is dominant in language and calculation-type problem solving. It is dominant in 97% of the population (60–70% in left-handed persons).

- Stroke damage to the left hemisphere is more likely to lead to depression. The right hemisphere is dominant in perception, artistic, and visual–spatial tasks. It is activated for intuition-type problem solving.
- Stroke damage to the right hemisphere is more likely to lead to apathy and indifference.

Brain Function and Neurocognitive Disorders

Functional areas of the brain



Brain Function and Neurocognitive Disorders

Functional Areas of the Brain

Brain Areas	Healthy Brain	Injured Brain
Frontal Lobe	• Personality, emotion • Intelligence • Attention/concentration • Judgement • Body Movement • Problem-solving • Speech, Speaking and laughing	• Loss of movement (paralysis) • Repetition of a single thought • Unable to focus on a task • Mood swings, irritability, impulsiveness • Changes in social behaviour and personality • Difficulty problem solving • Difficulty with language; cannot get the words out (aphasia)
Parietal lobe	• Sense of touch, pain, and temperature • Distinguishing size, shape, and colour • Spatial perception • Visual perception	• Difficulty distinguishing left from right • Lack of awareness or neglect of certain body parts • Difficulty with eye-hand coordination • Problems reading, writing, naming • Difficulty with mathematics

Brain Function and Neurocognitive Disorders

Functional Areas of the Brain

Brain Areas	Healthy brain	Injured Brain
Occipital Lobe	• Vision	• Defects in vision or blind spots • Blurred vision • Visual illusions/hallucinations • Problems reading and writing
Temporal Lobe	• Speech (understanding language) • Memory • Hearing • Sequencing • Organization	• Difficulty understanding language and speaking (aphasia) • Difficulty recognizing faces • Difficulty identifying/naming objects • Problems with short- and long-term memory • Changes in sexual behavior • Increased aggressive behavior

Brain Function and Neurocognitive Disorders

Functional Areas of the Brain

Brain Areas	Healthy Brain	Injured Brain
Cerebellum	• Balance • Coordination	• Difficulty coordinating fine movements • Difficulty walking • Tremors • Dizziness (vertigo) • Slurred speech
Brain Stem	• Breathing • Heart rate • Alertness/consciousness	• Changes in breathing • Difficulty swallowing food and water • Problems with balance and movement

Brain Function and Neurocognitive Disorders

APHASIA

Aphasia is an impairment of language affecting one's ability to speak/understand speech, read, or write.

Dominant (left) parietal lobe dysfunction (in most right-handed and some left-handed patients):

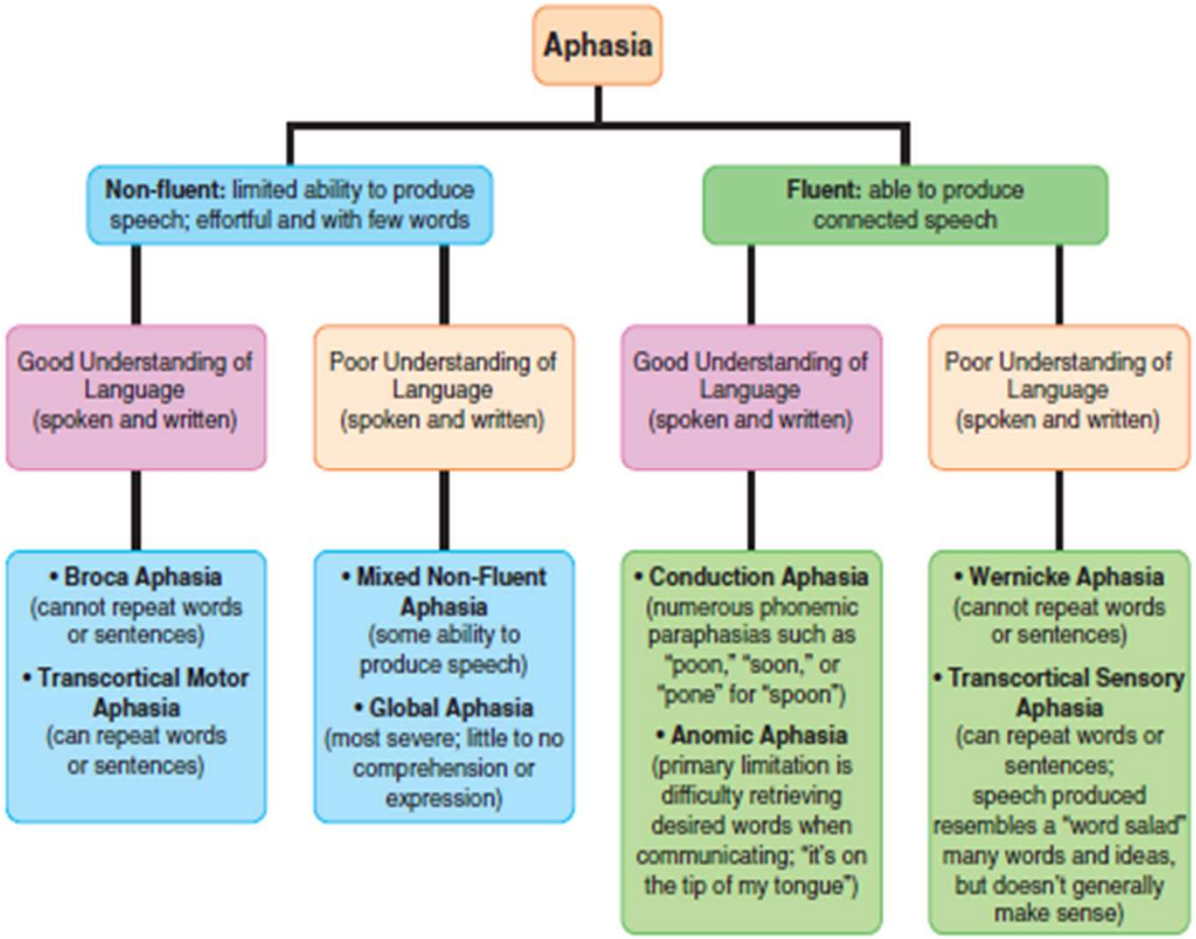
- Language disorders (aphasia, alexia)
- Gerstmann syndrome (dyscalculia, dysgraphia, finger agnosia, right-left confusion)
- Apraxia

Non-dominant (right) parietal lobe dysfunction:

- Hemi spatial neglect
- Sensory and visual inattention
- Constructional and dressing apraxia (more severe for right-sided lesions)

Brain Function and Neurocognitive Disorders

Aphasia



Brain Function and Neurocognitive Disorders

Acetylcholine (ACh)

ACh is a neurotransmitter at nerve-muscle connections for all voluntary muscles of the body and many of the involuntary (autonomic) nervous system synapses. The exact role of ACh in the brain is unclear.

- Cholinergic neurons concentrated in the RAS and basal forebrain
- Significant role in Alzheimer disease
- Neurocognitive disorder in general associated with decreased Ach Concentrations in amygdala, hippocampus, and temporal neocortex
- Associated with erections in men
- Muscarinic and Nicotinic receptors
- In the corpus striatum, ACh circuits are in equilibrium with dopamine neurons

Brain Function and Neurocognitive Disorders

Norepinephrine

Norepinephrine (NE) is one of the catecholamine neurotransmitters. It is a transmitter of the sympathetic nerves of the autonomic nervous system, which mediate emergency response.

- Acceleration of the heart
- Dilatation of the bronchi
- Elevation of blood pressure

NE is implicated in altering attention, perception, and mood. The key pathway is locus ceruleus in upper pons. It is implicated in monoamine hypothesis of affective disorders.

- Depletion of NE leads to depression
- Excess of NE (and serotonin) leads to mania
- Based on 2 observations: Reserpine depletes NE and causes depression; antidepressant drugs block NE reuptake, thus increasing the amount of NE available postsynaptic ally Receptors:
- Alpha-1: sympathetic (vasoconstriction)
- Alpha-2: on cell bodies of presynaptic neurons, inhibit NE release
- Beta-1: excitatory for heart, lungs, brain
- Beta-2: excitatory for vasodilatation and bronchodilation

Brain Function and Neurocognitive Disorders

Dopamine

Dopamine is the other catecholamine neurotransmitter, synthesized from the amino acid tyrosine.

- D2 receptors most important
- D1 and D5 stimulate G-protein and increase cAMP and excitation
- D2, D3, and D4 inhibit G-protein and decrease cAMP and excitation

Three pathways of known psychiatric importance:

- Nigrostriatal pathway: blockade leads to tremors, muscle rigidity, bradykinesia
- Mesolimbic-cortico pathway: blockade leads to reduction of psychotic symptoms
- Tuberoinfundibular system: blockade leads to increases in prolactin (DA = PIF)

Brain Function and Neurocognitive Disorders

Serotonin (5-Hydroxytryptamine, 5-HT)

Serotonin is the transmitter of a discrete group of neurons that all have cell bodies located in the Raphe nuclei of the brain stem. Changes in the activity of serotonin neurons are related to the actions of psychedelic drugs. It is involved in the therapeutic mechanism of action of antidepressant treatments (most are 5-HT reuptake inhibitors; a few new ones are 5-HT agonists).

Has inhibitory influence; linked to impulse control

Low 5-HT = low impulse control

- Has role in regulation of mood, sleep, sexual activity, aggression, anxiety, motor activity, cognitive function, appetite, circadian rhythms, neuroendocrine function, and body temperature

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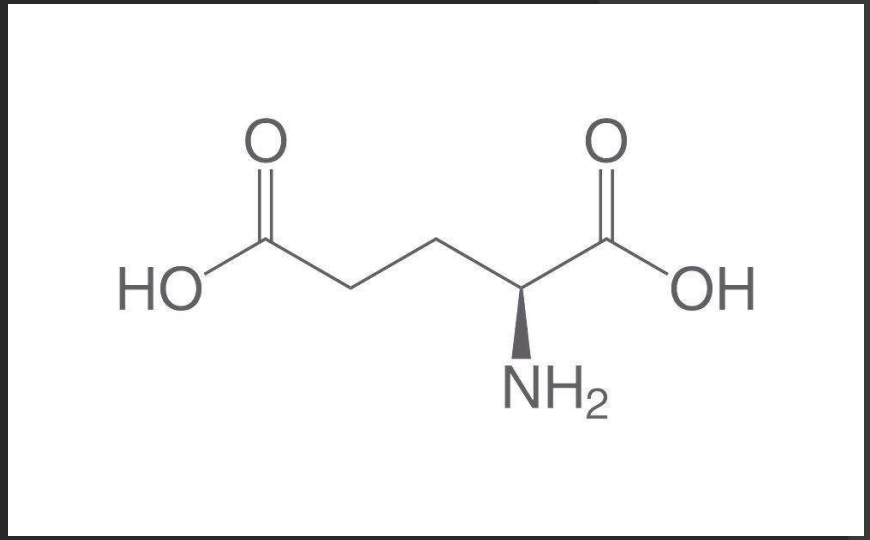
Glutamic Acid

Glutamic acid is one of the major amino acids in general metabolism and Protein synthesis; it is also a neurotransmitter.

• Stimulates neurons to fire Is the principal excitatory neurotransmitter in the brain and the neurotransmitter of neuronal pathways connecting the cerebral cortex and corpus striatum

Is the transmitter of the granule cells, the most numerous neurons in the cerebellum

There is evidence that glutamic acid is the principal neurotransmitter of the Visual pathway. It may have a role in producing schizophrenic symptoms; is the reason for PCP symptoms (antagonist of NMDA glutamate receptors). Glutamate agonists produce seizures in animal studies.



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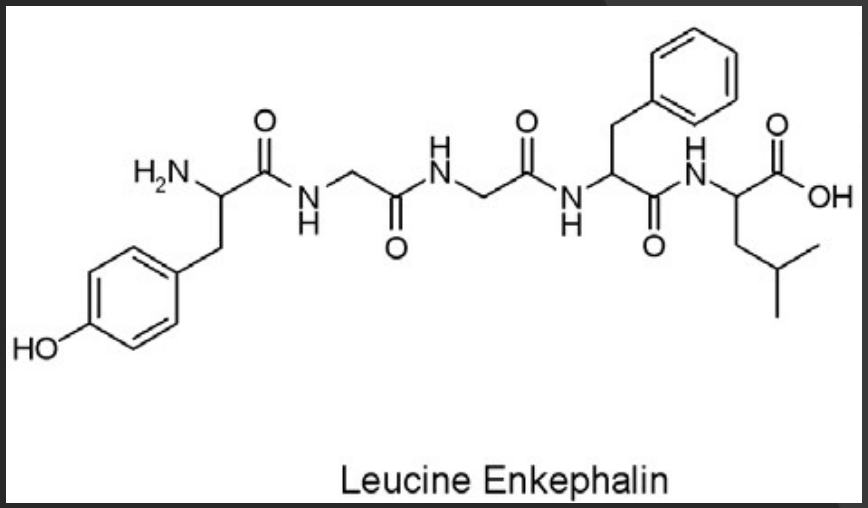
Enkephalins

Enkephalins are composed of 2 peptides, each containing 5 amino acids. They are normally occurring substances that act on opiate receptors, mimicking the effects of opiates. Neurons are localized to areas of the brain that regulate functions influenced by opiate drugs.



Leucine Enkephalin

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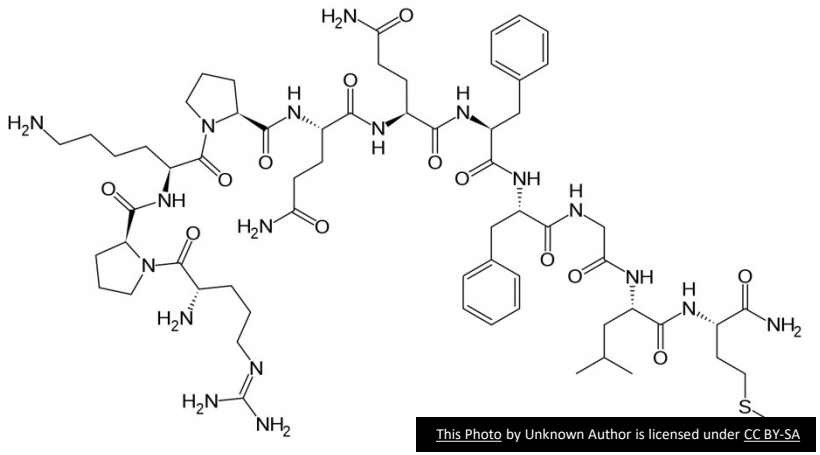
Substance P

Substance P is a peptide containing 11 amino acids and is a major transmitter of sensory neurons that convey pain sensation from the periphery, especially the skin, into the spinal cord; also found in numerous brain regions. Opiates relieve pain in part by blocking the release of substance P.



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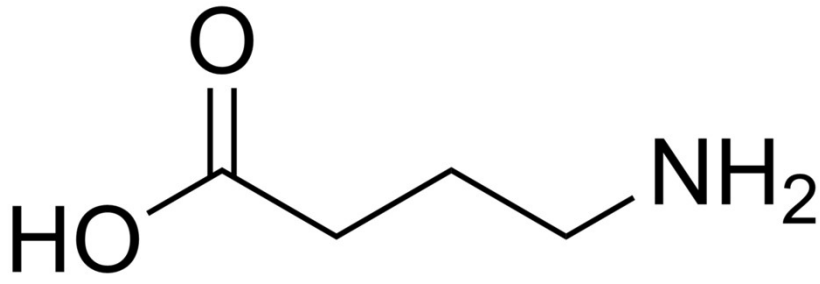
Brain Function and Neurocognitive Disorders

Gamma Aminobutyric Acid

Gamma aminobutyric acid (GABA) is one of the amino acid transmitters in the brain. It occurs almost exclusively in the brain, reduces the firing of neurons, and is the brain's principle inhibitory neurotransmitter (present at 25–40% of all synapses in the brain). GABA is associated with anxiety, cannabis, and benzodiazepines.



Brain Function and Neurocognitive Disorders

NEUROCOGNITIVE DISORDERS

Delirium is an acute onset of impaired cognitive functioning that is fluctuating, brief, and reversible. Neurocognitive disorder is a loss of cognitive abilities, impairment of social functioning, loss of memory, and/or change in personality that may be progressive or static. It is reversible only 15% of the time.

Mild neurocognitive disorder is moderate cognitive decline that has minimal interaction with functioning. Major neurocognitive disorder is significant cognitive decline that interferes with functioning and independence

Brain Function and Neurocognitive Disorders

Neurocognitive Disorder Due to Alzheimer Disease

Neurocognitive disorder due to Alzheimer disease is seen in >50% of nursing home patients and 50–60% of those with neurocognitive disorder.

- Risk factors: Female, family history, head trauma, Down syndrome
- Neuroanatomic findings: cortical atrophy, flattened sulci, enlarged ventricles
- Histopathology: Senile plaques (amyloid deposits), Neurofibrillary tangles, Neuronal loss, synaptic loss, Granulovacuolar degeneration of neurons
- Associated with chromosome 21 (gene for the amyloid precursor protein)
- Decreased ACh and NE
- Deterioration is gradual: Average duration from onset to death ~8 years
- Focal neurologic symptoms rare

Treatment is long-acting cholinesterase inhibitors such as Donepezil, Rivastigmine, Galantamine, and Memantine. Antipsychotic medications may be helpful when psychotic symptoms are present but contraindicated to control behavior

Brain Function and Neurocognitive Disorders

Vascular Neurocognitive Disorder (Multi-Infarct Neurocognitive Disorder)

Vascular neurocognitive disorder is seen in 15–30% of those with neurocognitive disorder.

- Risk factors: male, advanced age, hypertension or other cardiovascular disorders
- Affects small and medium-sized vessels
- Examination may reveal carotid bruits, fundoscopic abnormalities, and enlarged cardiac chambers
- MRI may reveal hyperintensities and focal atrophy suggestive of old infarctions
- Deterioration may be stepwise or gradual, depending on underlying pathology
- Focal neurologic symptoms (pseudobulbar palsy, dysarthria, and dysphagia are most common)
- Abnormal reflexes and gait disturbance often present

Treatment is directed toward the underlying condition and lessening cell damage.

Control of risk factors such as hypertension, smoking, diabetes, hypercholesterolemia, and hyperlipidemia is useful.

Brain Function and Neurocognitive Disorders

Alzheimer Disease vs. Vascular Disorder

Alzheimer	Vascular
Women	Men
Older age	Younger age
Chromosome 21	Hypertension
Linear or progressive deterioration	Stepwise or patchy deterioration
No focal deficits	Focal deficits
Treatment is supportive	Treat underlying condition

Brain Function and Neurocognitive Disorders

Frontotemporal Neurocognitive Disorder (Pick Disease)

- Neuroanatomic findings: atrophy in frontal and temporal lobes
- Histopathology: Pick bodies (intraneuronal argentophilic inclusions) and Pick cells (swollen neurons) in affected areas of brain
- Etiology unknown
- Most common in men with family history of Pick disease
- Difficult to distinguish from Alzheimer disease. May see features of Klüver-Bucy syndrome (hypersexuality, hyperphagia, passivity)

Brain Function and Neurocognitive Disorders

Neurocognitive Disorder Due to Prion Disease

- Rare spongiform encephalopathy caused by a slow virus (prion)
- Presents with neurocognitive disorder, myoclonus, and EEG abnormalities (e.g., sharp, triphasic, synchronous discharges and, later, periodic discharges)
- Symptoms progress over months from vague malaise and personality changes to neurocognitive disorder and death
- Findings include visual and gait disturbances, choreoathetosis or other abnormal movements, and myoclonus
- Other prions causing neurocognitive disorder (e.g., Kuru) may exist

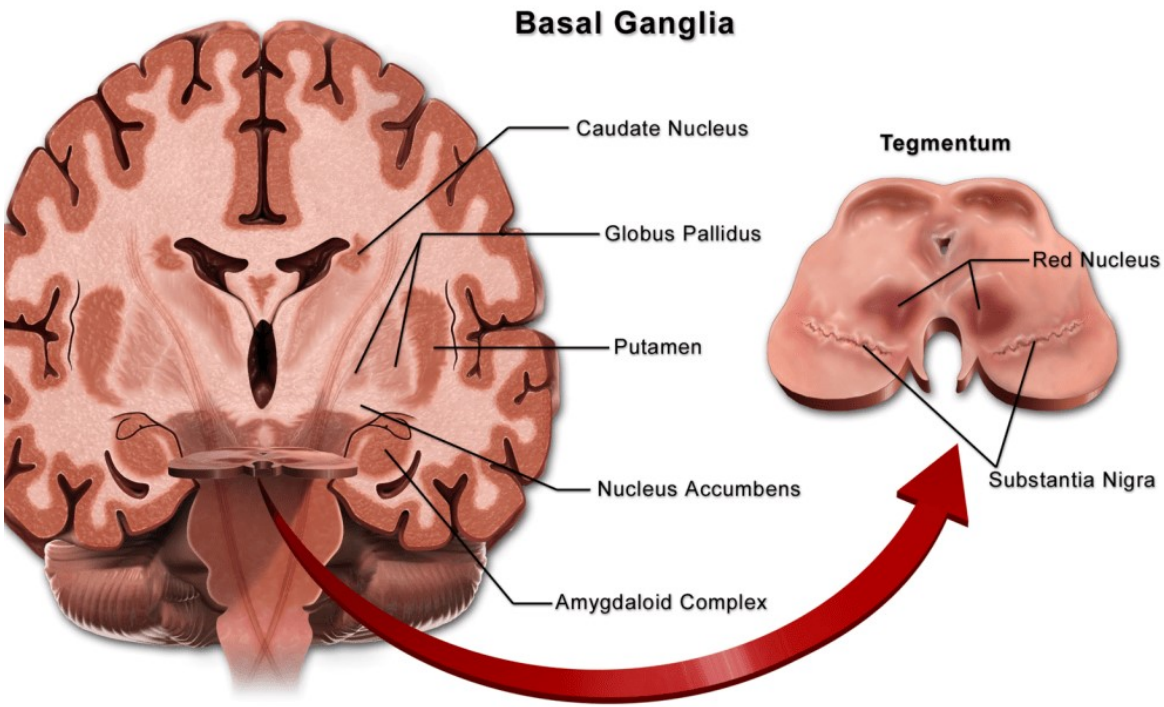
Brain Function and Neurocognitive Disorders

Neurocognitive Disorder Due to Huntington Disease

- Rare, progressive neurodegenerative disease that involves loss of GABAergic neurons of the basal ganglia; manifested by choreoathetosis, neurocognitive disorder, and psychosis
- Caused by a defect in an autosomal dominant gene located on chromosome 4
- Atrophy of the caudate nucleus, with resultant ventricular enlargement, is common
- Clinical onset ~age 40
- Suicidal behavior common

Brain Function and Neurocognitive Disorders

Basal Ganglia



Brain Function and Neurocognitive Disorders

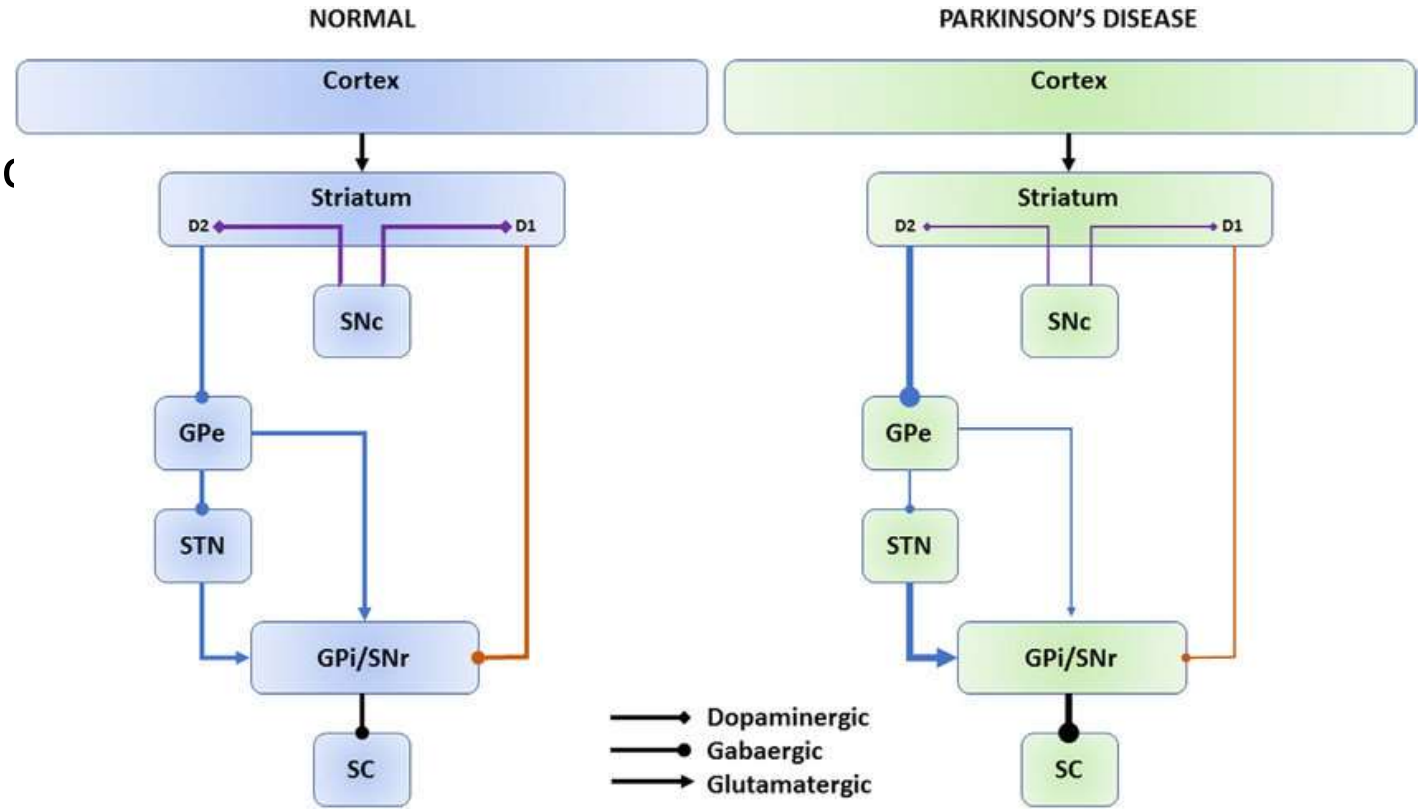
Neurocognitive Disorder due to Parkinson Disease

- Common, progressive, neurodegenerative disease that involves loss of dopaminergic neurons in the Substantia Nigra
- Clinical onset ~age 50–65
- Motor symptoms include resting tremor, rigidity, bradykinesia, and gait disturbances
- Neurocognitive disorder occurs in 40% of cases; depressive symptoms common
- Destruction of dopaminergic neurons in the substantia nigra is a key pathogenic component; may be caused by multiple factors including environmental toxins, infection, genetic predisposition, and aging

Treatment of Parkinson disease involves use of dopamine precursors (e.g., levodopa, carbidopa), dopamine agonists (e.g., bromocriptine), anticholinergic medications (e.g., benztropine, trihexyphenidyl), amantadine, and selegiline. Antiparkinsonian medications can produce personality changes, cognitive changes, and psychotic symptoms.

Brain Function and Neurocognitive Disorders

Parkinsc



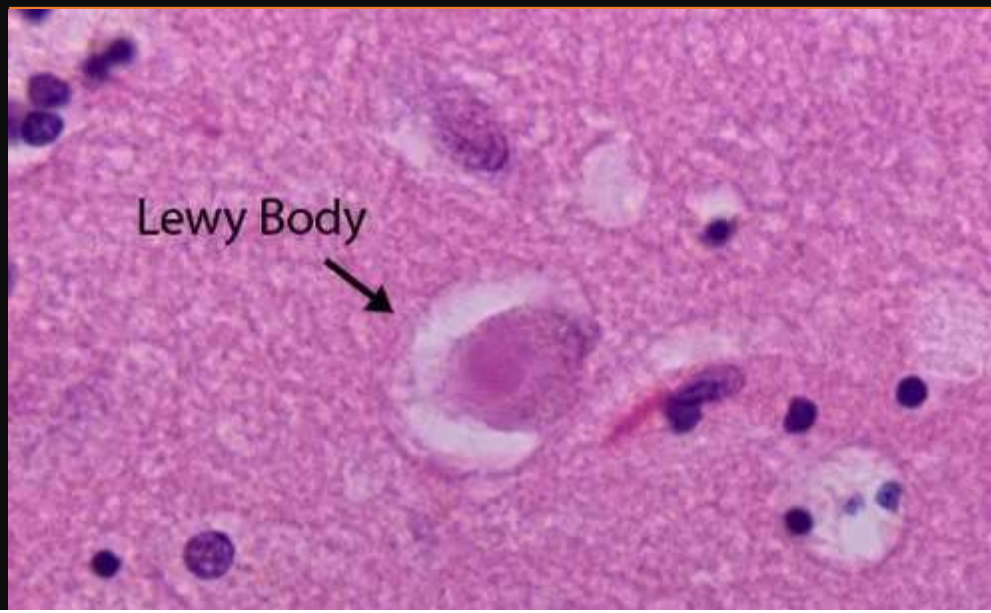
Brain Function and Neurocognitive Disorders

Neurocognitive Disorder with Lewy Bodies

- Hallucinations, parkinsonian features, and extrapyramidal signs
- Antipsychotic medications may worsen behavior
- Patients typically have fluctuating cognition, as well as REM sleep behavior disorder

Brain Function and Neurocognitive Disorders

Lewy Body



Brain Function and Neurocognitive Disorders

Neurocognitive Disorder Due to HIV Infection

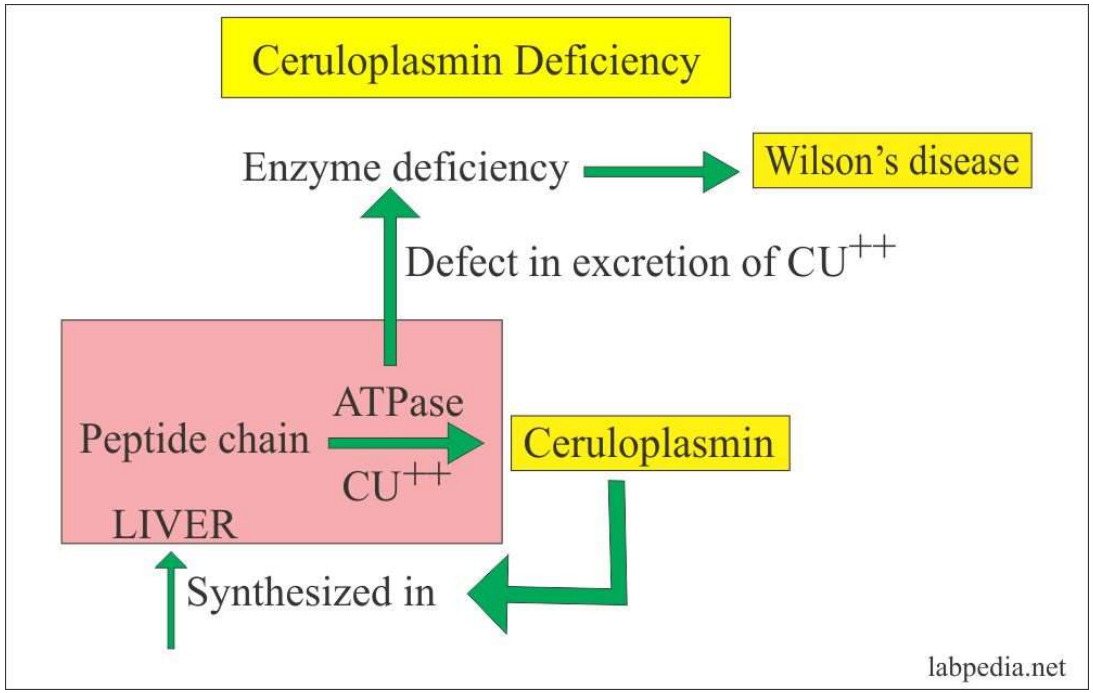
- HIV directly and progressively destroys brain parenchyma.
- Becomes clinically apparent in at least 30% of those with AIDS, starting with subtle personality changes.
- Diffuse and rapid multifocal destruction of brain structures occurs; delirium is often present.
- Motor findings include gait disturbance, hypertonia and hyperreflexia, pathologic reflexes (e.g., frontal release signs), and oculomotor deficits.
- Mood disturbances in those with HIV infection are apathy, emotional liability, or behavioral disinhibition

Brain Function and Neurocognitive Disorders

Wilson Disease

- Ceruloplasmin deficiency
- Hepatolenticular degeneration
- Kayser-Fleischer rings in the eye
- Asterixis

Wilson Disease



Brain Function and Neurocognitive Disorders

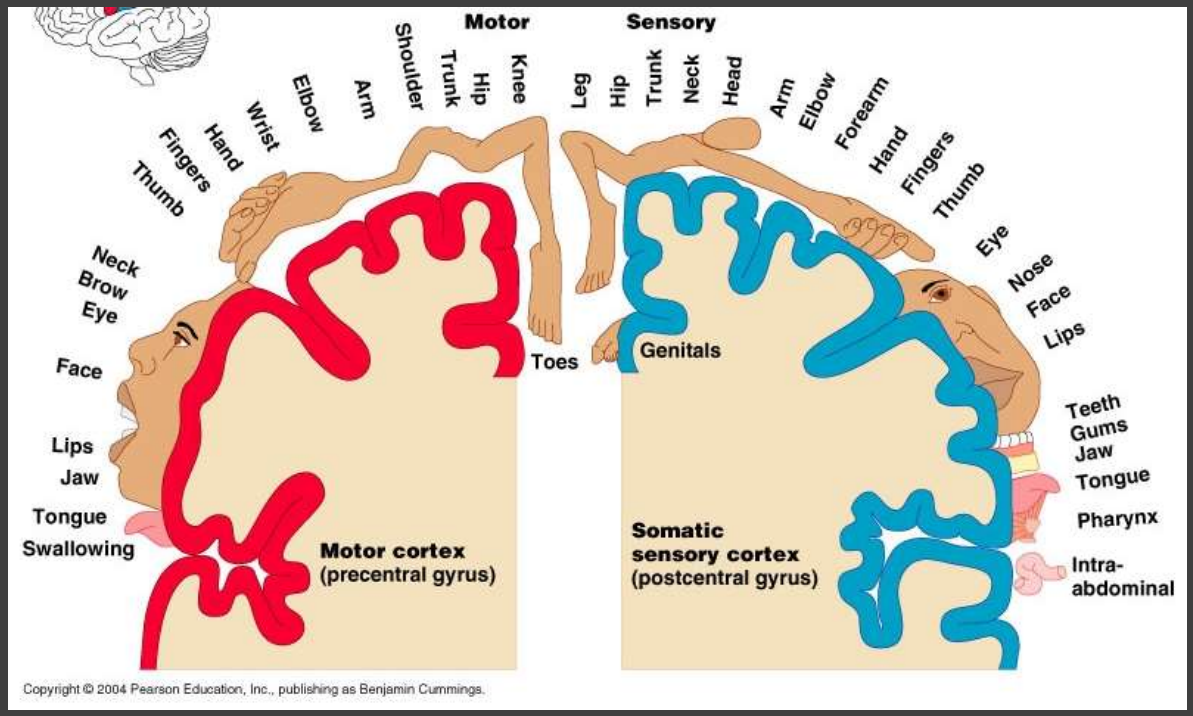
KF ring

Brain Function and Neurocognitive Disorders

Normal Pressure Hydrocephalus

- Enlarged ventricles
- Normal pressure
- Neurocognitive disorder, urinary incontinence, and gait apraxia

Treatment is shunt placement.



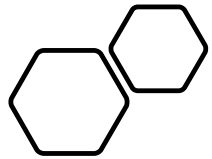
Brain Function and Neurocognitive Disorders

Motor Cortex

Typical Age of Onset	Older Adults	Older Adults	Older Adults
Symptoms	Gait dysfunction Balance dysfunction Incontinence Cognitive impairments (subcortical)	Initially cognitive impairments (cortical) including difficulty with problem solving In later stages, difficulty with gait, balance, activities of daily living	Resting tremor Rigidity Bradykinesia Postural instability
Diagnosis	CT MRI Spinal tap a/o lumbar puncture	Medical history review Mental status tests Brain imaging Neurological tests	Medical history and neurological examination
Medical Management	Ventroperitoneal shunt Medications May benefit from a wellness program	Medications to slow the progression of the disease Wellness programs	Medications Deep brain stimulation Wellness programs

Brain Function and Neurocognitive Disorders

Normal Pressure Vs Alzheimer's Vs Parkinsoism



Brain Function and Neurocognitive Disorders

Pseudodementia

- Typically seen in elderly patients with a depressive disorder who appear to have symptoms of neurocognitive disorder
- Improvement should be seen after treatment with antidepressants
- Onset of symptoms can usually be dated

Delirium	Neurodegenerative disorder
Acute onset	Insidious Onset
Fluctuating course	Chronic Course
Recent memory problems	Recent then remote memory problems
Disrupted sleep wake cycle	Normal sleep-wake cycle
Disorientation	Less disorientation as first
Hallucinations common	Hallucinations, Sundowning
Treat underlying condition	Supportive treatment

Brain Function and Neurocognitive Disorders

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