


Lectures
General medicine
Stomatology
Special pathophysiology
1995 -2025

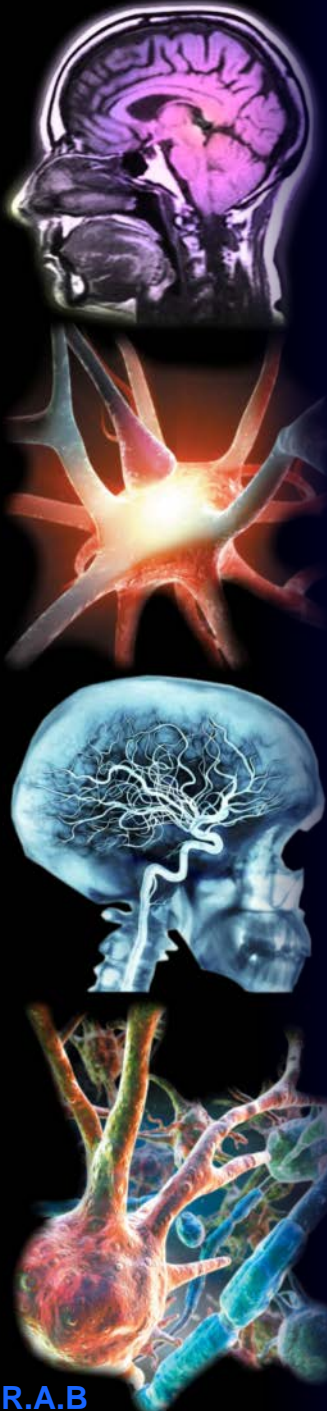


8 NEUROPATHO- PHYSIOLOGY

Higher nervous 2

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Hemispheric lateralisation in cognitive functions



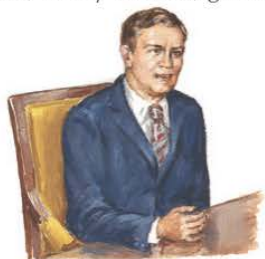
	Left hemisphere	Right hemisphere
Cognitive processes	Speech (full), verbal analytic, deductive sequential processing conscious, planned	Symbols, iconic holistic, synthetic simultaneous processing subliminal, automatic
Visual functions	Right visual field Sceneries	Left visual field Faces
Motor functions	Right side of the body	Left side of the body
Emocional functions	Poditive emotions Laesions mostly lead to depressive mood Recognition of emotions	Negative emotions – laesions lead to euphoria Expression of emotions
Constructive functions	Abstraction, rational, reasoning	Factual, intuitive,
Meaning	Me in the word	The word inside of me

Disorders of higher nervous functions

- 1. Dysphasias** (disordered usage of symbols)
Aphasia (speech)
Agrafia (handwriting, printed text)
Alexia (reading) Acalculia (calculations)
- 2. Agnosias** (disordered perception of the body and the world outside)
- 3. Dyspraxia** (disordered execution of motor programs)

A. Appearance and interpersonal behavior

Pleasant, neatly dressed, good spirits



Depressed, sloppily dressed, careless



Belligerent



B. Language

Doctor: "Write me a brief paragraph about your work."

Good

I have been an executive secretary to the vice president of the Zilch corporation for many years. My working conditions are satisfactory and I look forward to each day's business activity. I tend to many details for and supervise other

Defective

I dont mush much do it yestideay way lousy day five alock when no to go to a job when

C. Memory

Doctor: "Here are 3 objects: a pipe, a pen, and a picture of Abraham Lincoln. I want you to remember them and in 5 minutes, I will ask you what they were."



5 minutes later: Patient: "I'm sorry, I can't remember. Did you show me something?"

D. Constructional praxis and visual-spatial function

Doctor: "Draw me a simple picture of a house."



Good

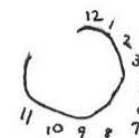


Abnormal

"Draw a clock face for me."



Good



Abnormal

E. Reverse counting

Doctor: "Count backward from 5 to 1 for me."
Patient: "5...3...4..., sorry, I can't do it."

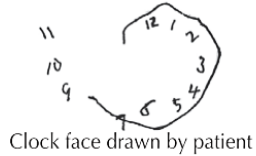


Doctor: "Spell the word *worlds* backward for me."
Patient: "W..L..R..D..S."

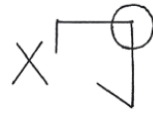
F. Netter M.D.

Figure 2-7 Testing for Defects of Higher Cortical Function.

A. Constructional dyspraxia and spatial disorientation



Clock face drawn by patient



Patient asked to copy



Draws this



House drawn by patient

B. Neglect of left-sided stimuli



Patient shown picture



Sees this

THE LORD is my shepherd; I shall not want.
 2 He maketh me to lie down in green pastures: he leadeth me beside the still waters.
 3 He restoreth my soul: he leadeth me in the paths of righteousness for his name's sake.
 4 Yea, though I walk through the valley of the shadow of death, I will fear no evil: for thou art with me; thy rod and thy staff they comfort me.

Patient shown printed page

my shepherd; I shall not want.
 me to lie down in green pastures: he leadeth me beside the still waters.
 my soul: he leadeth me in the paths of righteousness for his name's sake.
 I walk through the valley of the shadow of death, I will fear no evil: for thou art with me; thy rod and thy staff they comfort me.

Sees this

C. Anosognosia (unawareness of deficit)

Patient with obvious left hemiplegia. Asked, "What is wrong with you?" Answers, "Nothing is wrong, I am perfectly all right."



Not recognizing deficit, patient insists on trying to walk and falls, but still fails to recognize deficit.



D. Motor impersistence



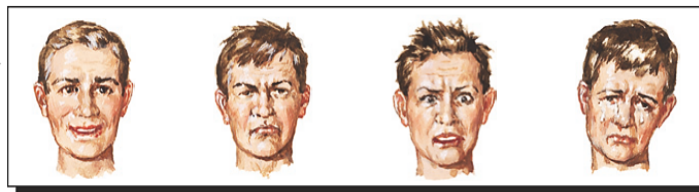
Patient asked to raise arms over head and to keep them up



Raises arms but then drops them quickly

E. Abnormal recognition of nonlanguage cues (facial expression, voice tone, mood)

Patient shown picture. Asked, "Which is the happy face?"



Patient answers, "I don't know, they are all the same."

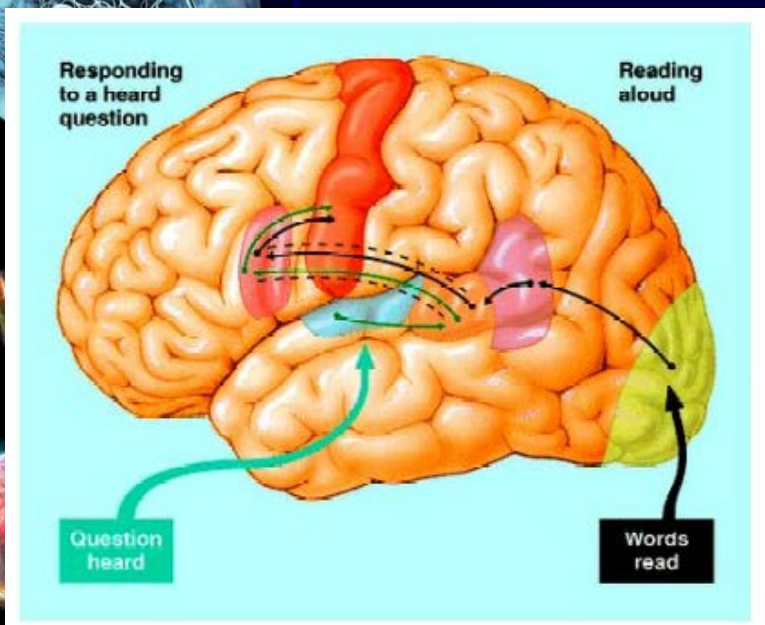
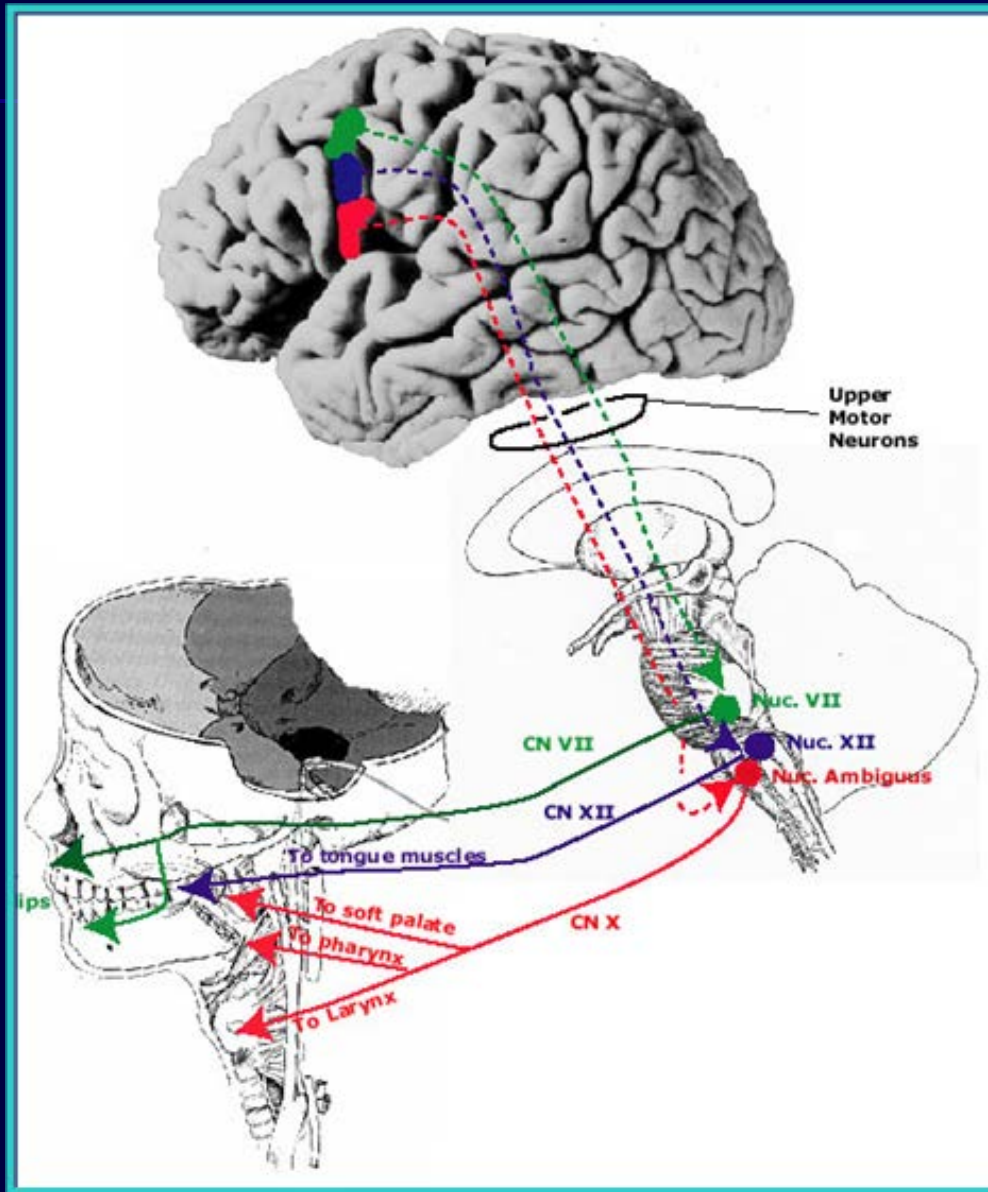
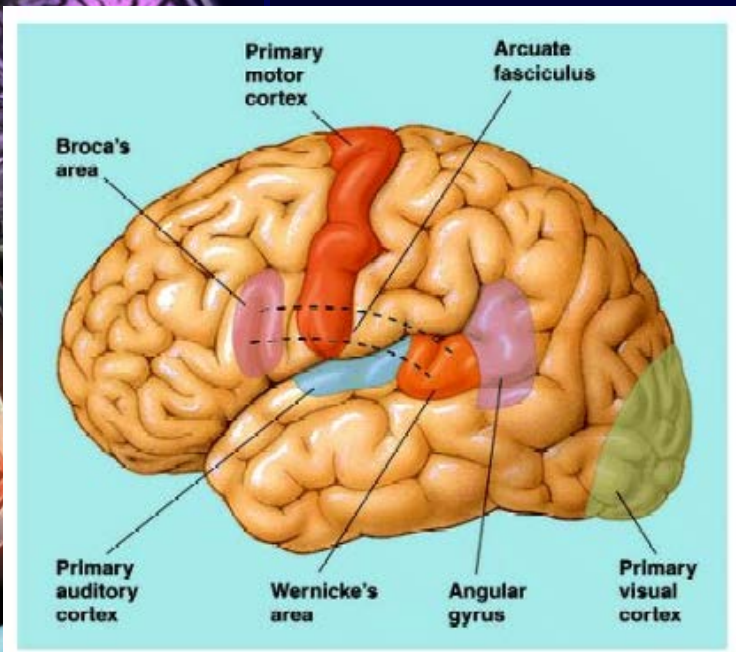
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Figure 2-8 Nondominant Hemisphere Higher Cortical Function.

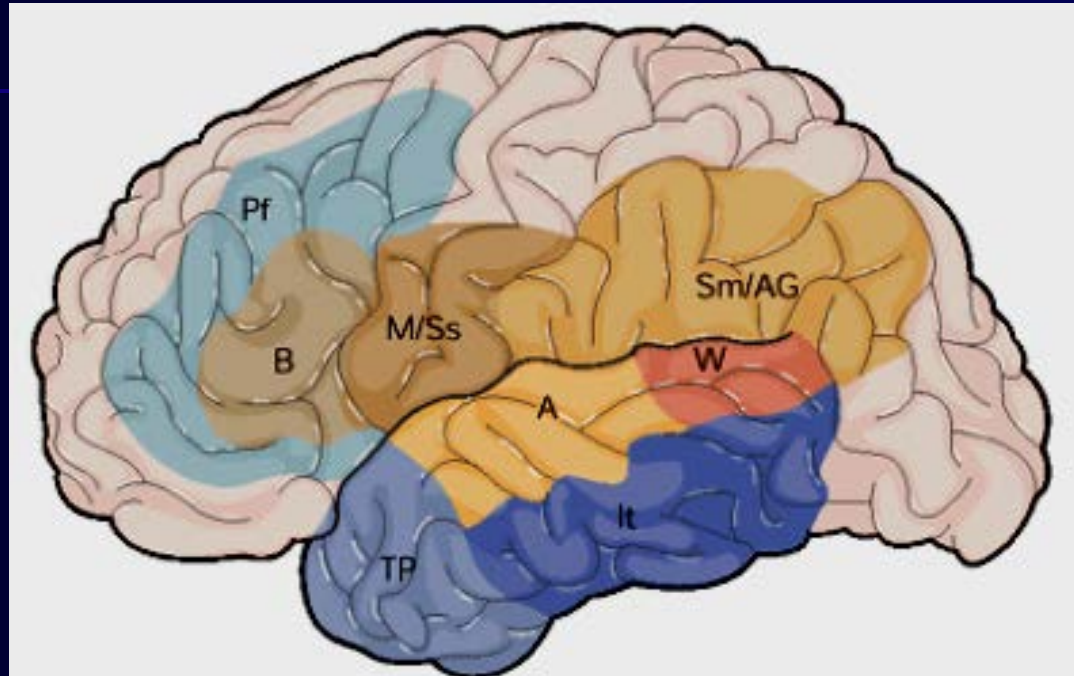


Dysphasias

Speech processing



Critical areas for speech



1. Implementation system

Broca's area (B), Wernicke's area (W), motor cortex (M), somesthetic cortex (Ss), auditory cortex (A), g. angularis (AG) g. supramarginalis (Sm)

2. Mediative system

left prefrontal cortex (Pf), left infratemporal cortex (It), left temporopolar cortex (TP)

3. Conceptual system

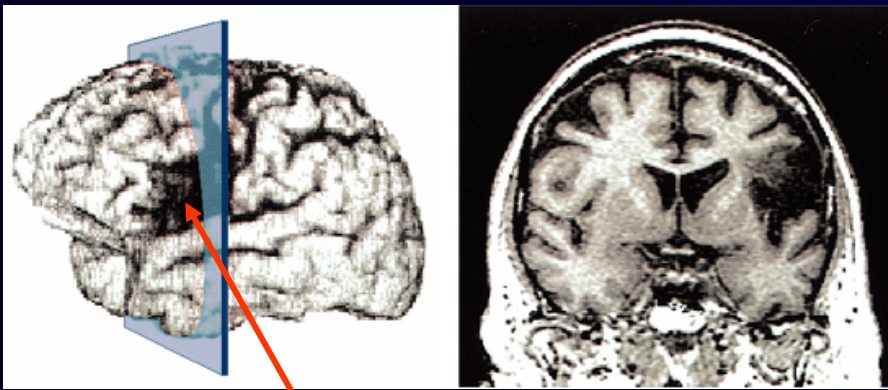
Disorders of speech

- **Aphasia (dysphasia)** - spontaneous production, understanding and reproduction of read or heard words
- **Disorders of speech content and fluency**
 - Paraphasia (verbal, literary)** - erroneous speech (syllables, words)
 - Paralexia (verbal, literary)** - erroneous reading (syllables, words)
 - Neologisms** - new nonsense words instead of proper naming
 - Circumlocutio** - description instead of proper name
 - Telegraphic speech** - fragmentation and reduction of speech
 - Echolalia** - automatic repetition, usually without comprehension, of all or part of what someone has just said (children when learning speech)
 - Glossolalia** - rapid, fluent burst of speech, usually unintelligible
 - Stuttering or stammering** -
 - Cluttering** - uncontrolled speed of speech

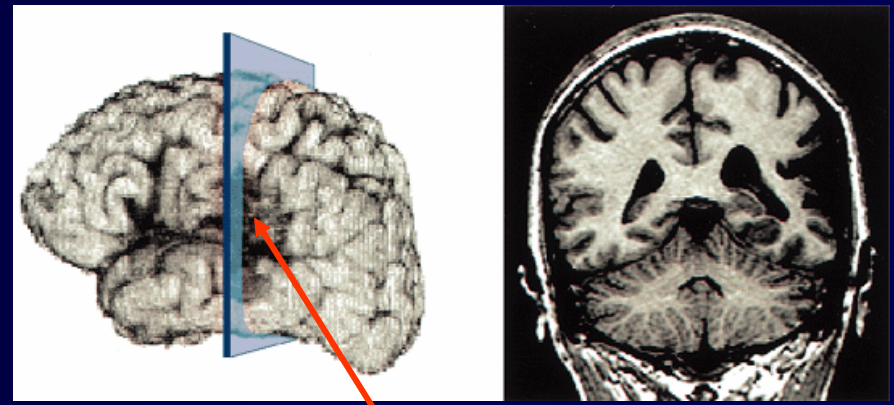
Aphasia (dysphasia) - I

Main types

1. **Expressive, motor, Broca's** - posterior-inferior frontal lobe
speech fragmented; seeking for common words, names, terms;
understand to listened speech; reading & writing skills little impaired
2. **Receptive, sensory, Wernicke's** - posterior-superior temporal lobe
speech fluent but full of agrammatisms & neologisms;
misunderstanding of listened speech; reading & writing impaired +
anozognosia (do not realize the defect)
3. **Global sensoric-motor** - frontal & temporal lobes (occlusion a. cerebri media sin., a. carotis interna. sin.)
speech fragmented, telegraphic, reč neplynulá, strohá (pár slov, fráz opakovaných dookola), porozumenie počutému neprítomné (ani jednoduché slová); čítanie, písanie narušené

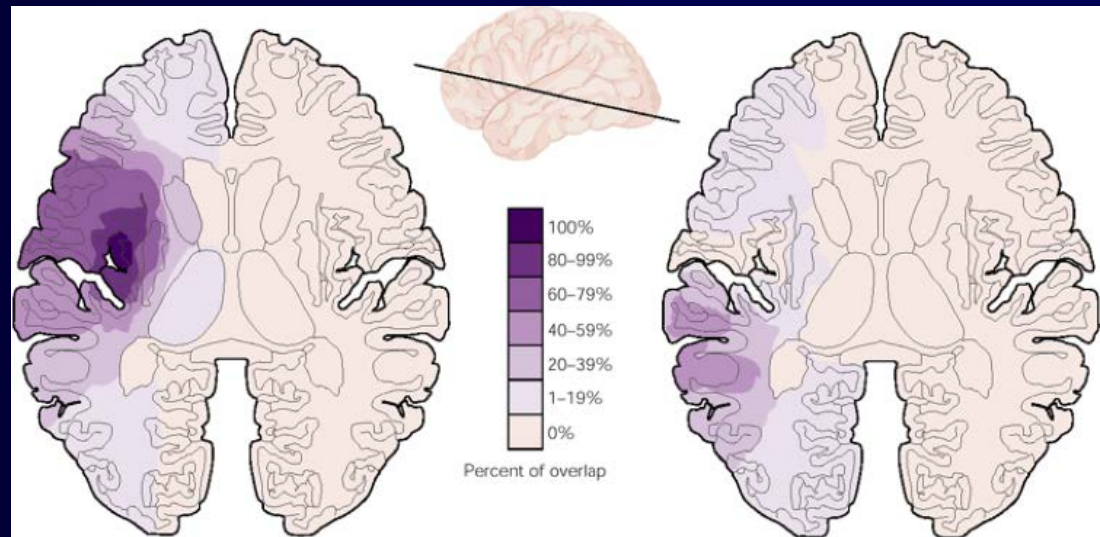


Broca aphasia



Wernicke aphasia

Role of insula in pronunciation

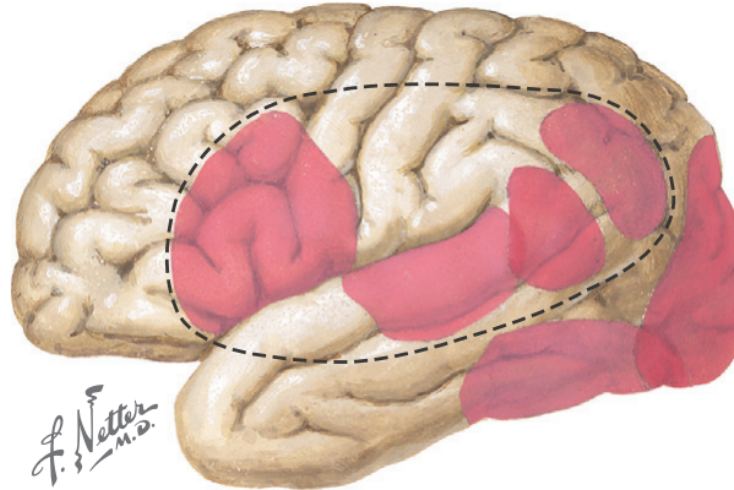


Disorders of articulation motorics

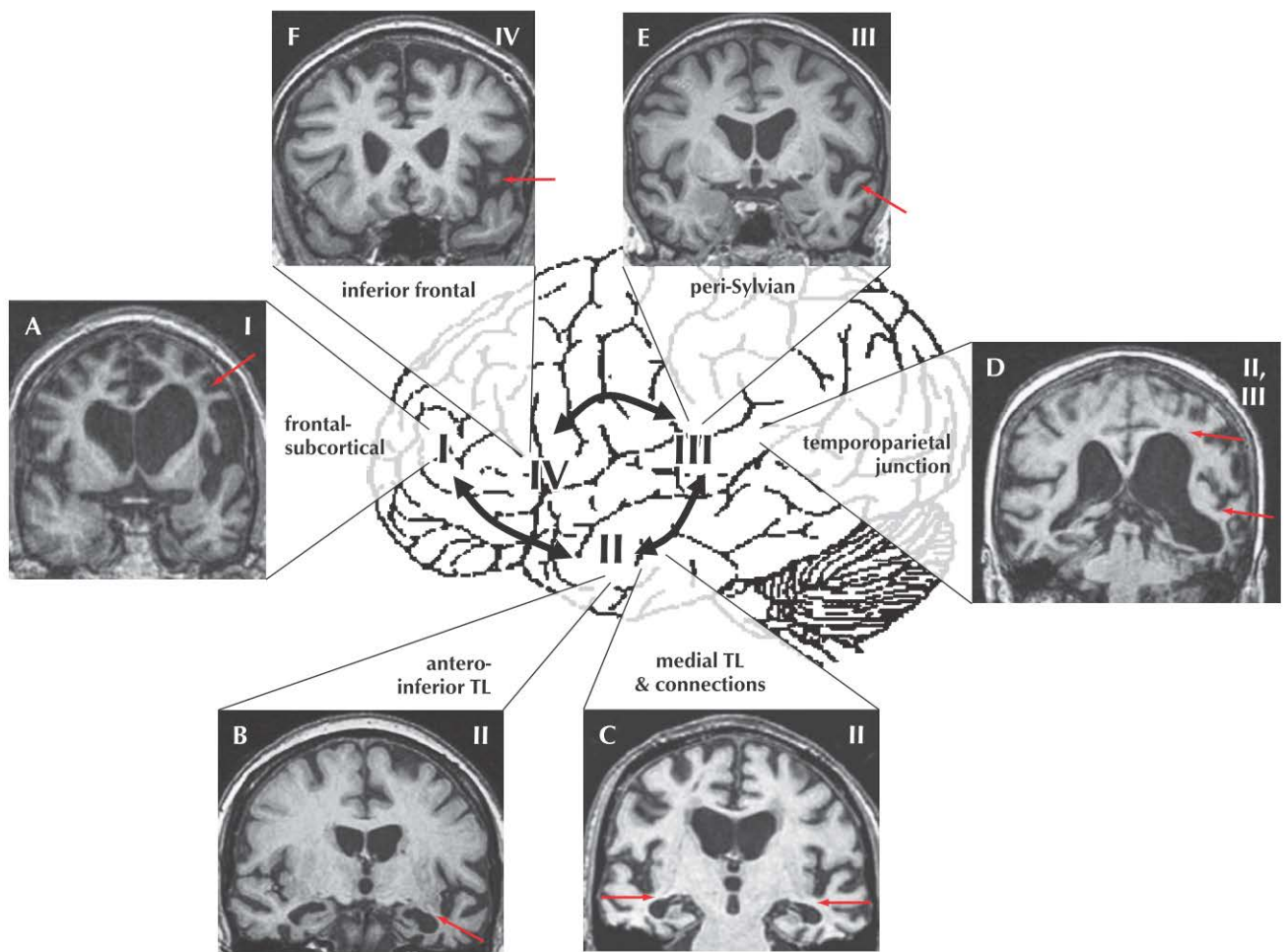
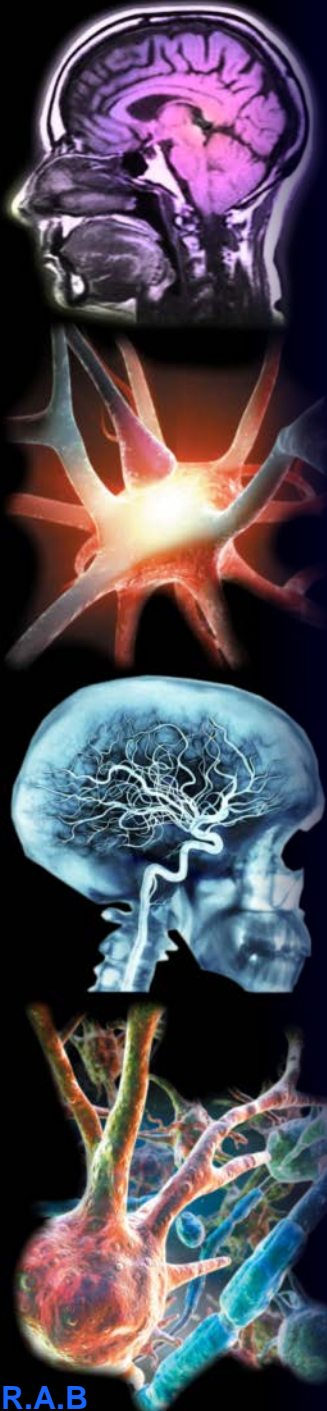
Without disorders of articulation

Dominant hemisphere language dysfunction

Clinical syndromes related to site of region



	Broca aphasia	Wernicke aphasia	Angular gyrus	Global aphasia
Pronunciation, speech rhythm	Dysarthria, stuttering, effortful	Normal, fluent, loquacious	Normal	Very abnormal
Speech content	Missed syllables, agrammatical, telegraphic	Use of wrong or nonexistent words	Often normal	Very abnormal
Repetition of speech	Abnormal but better than spontaneous	Abnormal	Normal	Very abnormal
Comprehension of spoken language	Normal	Very abnormal	Normal	Very abnormal
Comprehension of written language	Not as good as for spoken language	Abnormal but better than for spoken	Very abnormal	Very abnormal
Writing	Clumsy, agrammatical, misspelling	Penmanship OK but misspelling and inaccuracies	Very abnormal, spelling errors	Very abnormal
Naming	Better than spontaneous speech	Wrong names	Often abnormal	Very abnormal
Other	Hemiplegia, apraxia	Sometimes hemianopsia and apraxia	Slight hemiparesis, trouble calculating, finger agnosia, hemianopsia	Hemiplegia



Roman numerals I through IV indicate proposed operational stages in the pathway for language output. Key anatomical areas are indicated along with superimposed MRI images as follows: (A) asymmetric (left greater than right) frontal lobe atrophy, dynamic aphasia; (B) focal left anterior/inferior temporal lobe atrophy, semantic dementia; (C) bilateral mesial temporal atrophy, Alzheimer's disease (anomia); (D) left posterior superior temporal/inferior parietal atrophy, progressive 'mixed', logopenic or jargon aphasia; (E) focal left superior temporal lobe/insular atrophy, progressive nonfluent aphasia; (F) focal left inferior frontal gyrus/frontal opercular atrophy, progressive apraxia of speech. Bidirectional arrows suggest reciprocal communications between key anatomical regions.

From Rohrer JD, Warren JD, Omar R, et al. *Brain* 2008. January; 131(Pt 1):8-38. By permission of Oxford University Press.

Figure 2-13 Structural Anatomy of Word-Finding Difficulty in Degenerative Disorders.

Aphasia - II

Other types

- 1. Auditory sensoric** - temporal lobe; paths between primary and secondary auditory cortex
speech is fluent, understanding to talk is impaired
- 2. Conductive** - g. supramarginalis, insula, fasc. uncinatus (path between temporal lobe and pre-motoric cortex)
speech is fluent, understanding to speech normal, impaired reproduction of heard speech
- 3. Anomia** - g. angularis, gg. temporales sup. (transient hypoxia etc.)
speech is fluent, problems with isolated usage of names, terms etc.
- 4. Mixed motoric and sensory**

Other phatic disorders

Graphic symbols of speech

Agraphia - acquired inability to write the letters, words (literary, verbal)

Dysgraphia - developmental inability to write

Alexia - acquired inability to read and comprehend the text; as a part of aphasia (e.g. expressive, global, sensory, mixed) or isolated (literary, verbal, spatial),

agnosic alexia (word blindness) - unable to identify the letters and words,

aphasic alexia (visual asymbolia) - can neither read nor write **alexia+agraphia**

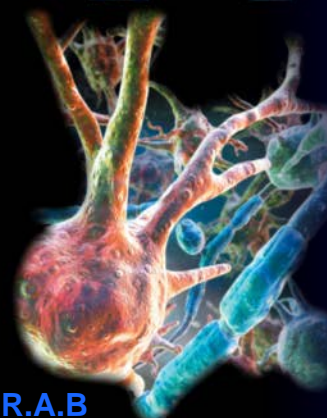
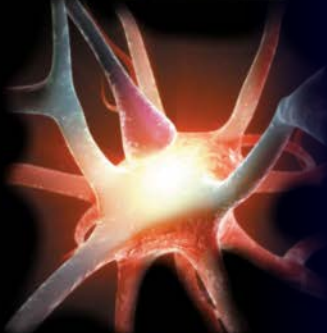
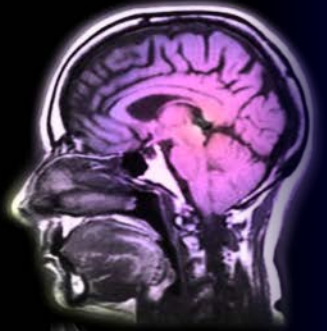
Dyslexia - developmental (social) inability to read (boys > girls)

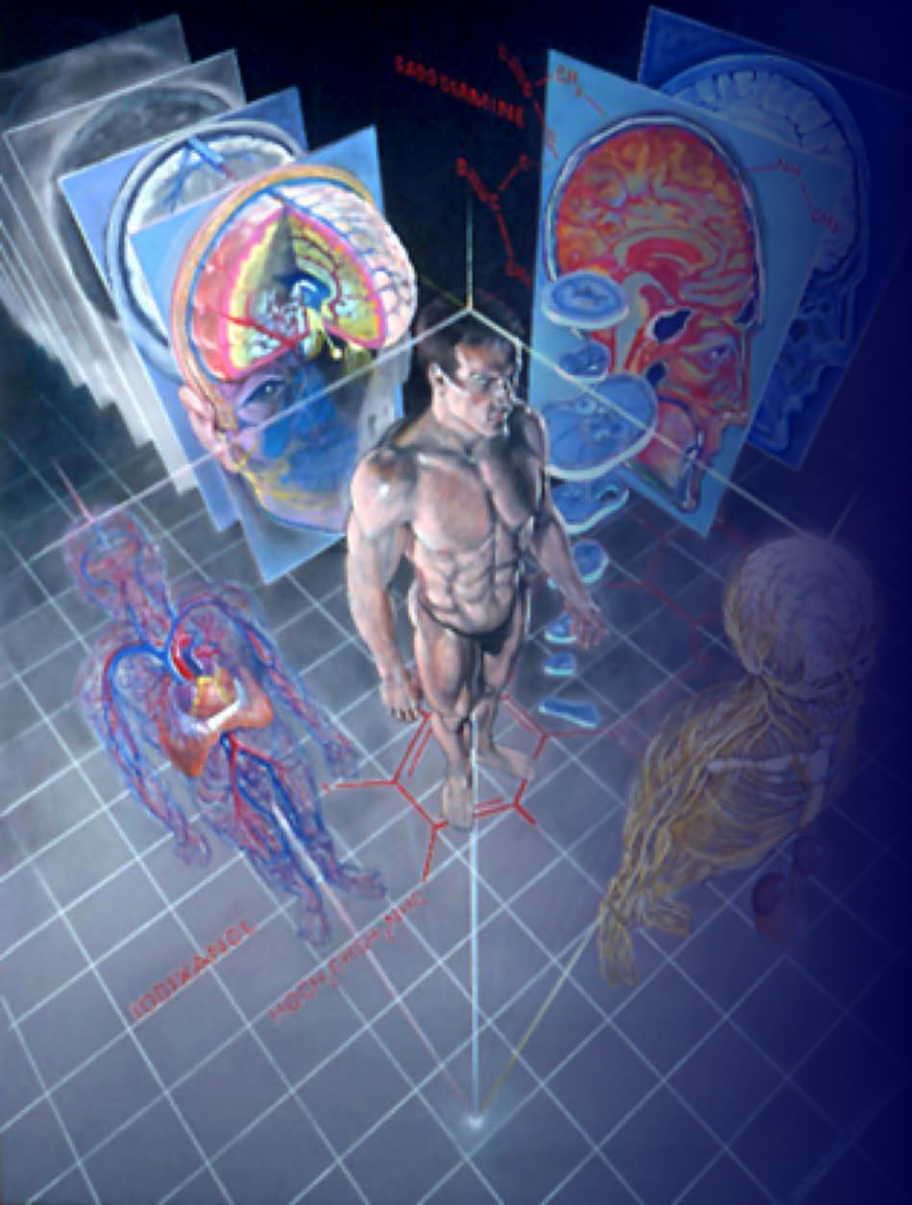
Paralexia

Other symbolic disorders

- **Acalculia (+alexia)** - inability to manipulate with abstract numbers

- **Asymbolia (e.g. pain)** – various somatic experiences (agnosia)





Agnosias

Agnosia - I

1. **Tactile (astereognosia)** – false identification of things by touch

Amorphognosia - shape, surface

Ahylognosia – matter substance (wood, metal, liquid etc.)

Parietal association cortex

2. **Visual** – misidentifications of objects by vision (not blindness !)

Global – identification by touch, hearing and smelling

preserved **Temporal-occipital-parietal lobe borderline zone**

Colors – loss of colour concept (different from color blindness)

Corpus callosum, occipital lobe

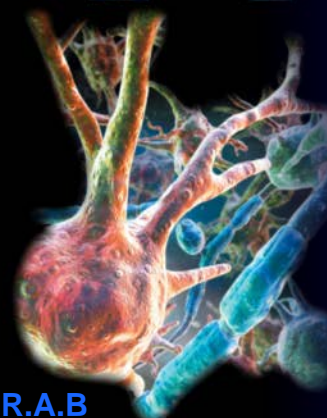
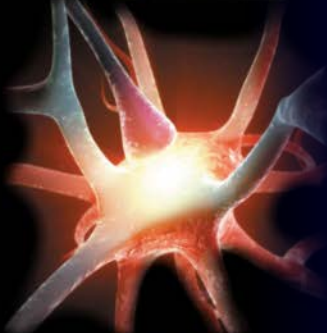
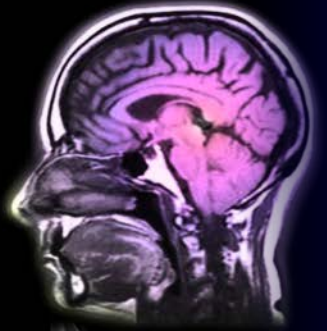
3. **Auditory** - misidentification of meaningful sounds (not

deafness !)

Verbal – inability to recognize sounds of speech from other sounds

Amusia – inability to recognize melodies, music from other sounds

Temporal-parietal borderline zone



Agnosia - II

4. **Asomatognozia** Parietal lobes (mostly parietal)

Autotopagnosia – wrong determination of different parts of the body

Acoenesthesia - misidentification of the own body

Prosopagnosia – wrong identification of human faces

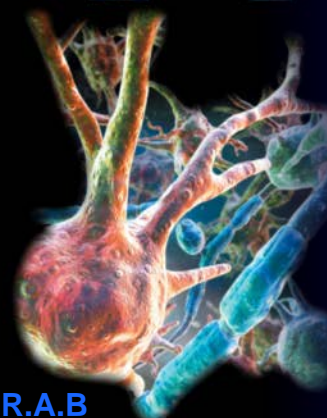
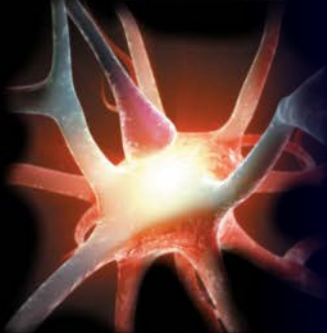
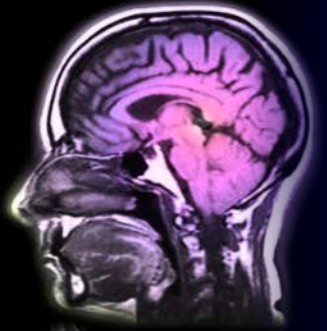
Anozognosia - unawareness of own illness or the deficits resulting from illness (transiently in 50% of stroke victims)

5. **Sy. of sensory extinction**

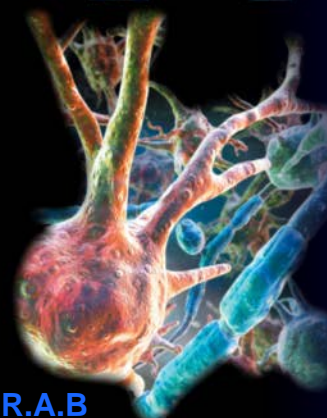
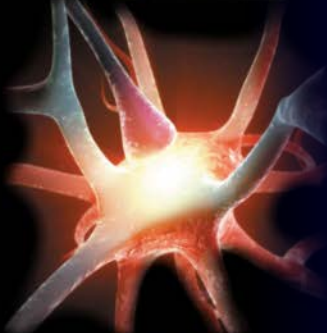
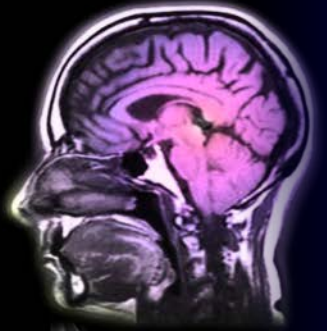
moderate form of combined tactile and visual agnosia (ignoring of perceptions from impaired part of the body)

6. **Neglect sy.** (sensory extinction, autotopagnosia, visual agnosia)

7. **Gerstman sy.** (agraphia, acalculia, alexia, agnosia of fingers, „right-left“ confusion) G. angularis of dominant hemisphere



TYPE OF AGNOSIA	DEFINITION	LOCATION OF INJURY
Spatial agnosia	Inability to recognize objects by touch	Parietal lobe
Gerstmann syndrome	Incapacity to find one's way around familiar places; disturbance of perception of space (disorders of [1] topographic [extrapersonal] orientation or [2] topographic and geographic memory [construction])	Parietal lobe
Finger agnosia (digital agnosia)	Loss of spatial orientation of fingers, body, sides, and numbers	Left angular gyrus (parietal lobe)
Right-left confusion	Inability to identify the names of one's fingers	
Agraphia	Inability to distinguish right from left	
Acalculia	Inability to write	
Visual agnosia	Inability to perform mathematic calculations	
Object agnosia		
Prosopagnosia	Inability to recognize objects and pictures	Temporo-occipital area
Color agnosia	Inability to recognize faces	Temporo-occipital ventromesial region
Body image agnosias (may be spatial)	Inability to understand colors as qualities of objects; faulty color concepts and inability to evoke color images in the absence of color blindness; specific types: (1) "hue" problem, (2) color anomia (cannot name color)	Inferior occipital cortex in left hemisphere
Anosognosia		
Autotopagnosia	Ignorance or denial of existence of the disease	Right parietal lobe
Word blindness (alexia/dyslexia)	Loss of ability to identify the body, in whole or in part, or to recognize relationships among various parts	Right parietal lobe
	Inability to recognize written symbols	Left parietotemporal region
Auditory agnosia (pure word deafness)	Inability to recognize speech sounds	Superior temporal area
Amusia (music deafness)	Loss of capacity to recognize tones and melodies	

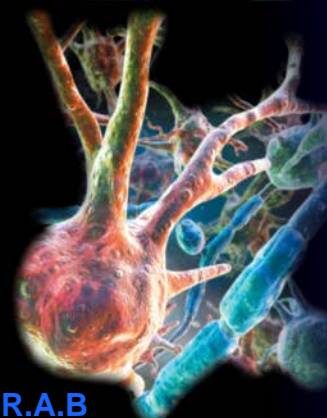
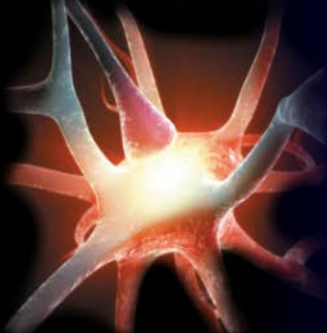
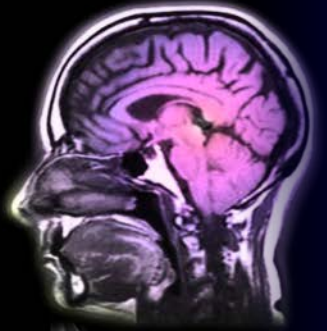


Dyspraxias

Apraxia

Def: inability to produce a movement that is not due to paresis (paralysis) - specific loss of skill (Liepmann 1900)

- various forms depending on site of damage (not complete agreement on designations and criteria)
 - **ideational apraxia** = misuse of objects due to disturbance of identification (agnosia)
 - **ideomotor apraxia** = simple movements can be executed, but complex movements cannot
 - **limb kinetic apraxia (motor)** = inability to make movements or use objects or the purpose intended by the will
- clinical / experimental testing necessary to **distinguish damage to a motor system from damage to areas that control it**
 - **tests with no bilateral impairment** = finger-tapping speed , movement steadiness, repetitive screw rotation,
 - **tests with bilateral impairment** = finger tapping on 2 keys , finger tapping with rhythm



Apraxias (dyspraxias)

A. General dyspraxias

1. **Ideative apraxia** Diffuse cortical damage
purpose of movement is unrecognized; plan and execution of movement are correct
2. **Ideomotoric apraxia** Gg. pariet. inf + tempor. sup.+ frontalis
purpose of movement is recognized ; plan of movement is missing (which separate activities are involved and what is their order)
3. **Constructive apraxia** Premotor area - frontal lobe
intention, purpose and plan of movement are correct; execution of movement is impaired (butter-fingers, clumsiness)

B. Specific dyspraxias

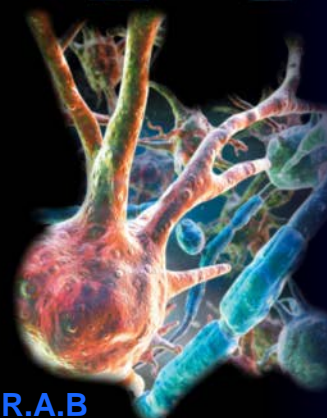
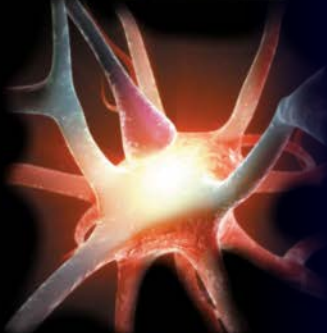
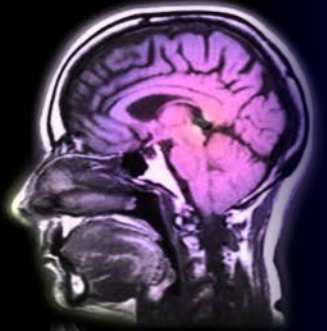
1. **Constructive dyspraxia** (perspective, shapes, geometry)
2. **Speech dyspraxia** (motor program of voice muscles)
3. **Mimic dyspraxia** (disorder of articulation and facial mimic)
3. **Gait apraxia** (frontal ataxia)
4. **Dyspraxia of corpus callosum** (cross – coordination of limbs)

Apraxia

- Premotor cortex (area 6 - lateral)
 - inability to produce indirect trajectories
 - ablation of premotor cortex impairs conditional motor behaviour
- Supplementary motor area (area 6 - medial) Brinkman sy
 - bimanual coordination deficit
 - absence of speech
- Prefrontal
 - deficits in delayed response tasks
 - dorsolateral - spatial
 - ventral - object
- Posterior parietal cortex (areas 5, 7)
 - Gerstmann's syndrome
 - Following left parietal (in normal right hand dominant)
 - left-right confusion
 - finger agnosia
 - dysgraphia , dyscalculia, apraxia
 - Balint's syndrome
 - Following bilateral damage
 - unable to make voluntary eye movements into affected hemifield
 - optic ataxia - deficit in visually guided reaching, deficit in visual attention
 - Neglect
 - Following right (nondominant) hemisphere damage
 - Constructional apraxia



Thinking (**thought**) disorders



1. Disorders of thinking dynamics

Bradypsychism – besides thinking memory, intellect, emotion are involved

Mutism - blackouts of speech (expressive & receptive), elective mutism

Thought jets - acceleration thinking (vs. logorhoea)

Tachypsychia - periods of great physical stress or in violent confrontation

2. Disorders of the structure of thoughts

Perseverations - „repeating the same again and again“, Distractible

thinking - „frequent jumps from the main topic“, Symbolic thinking-

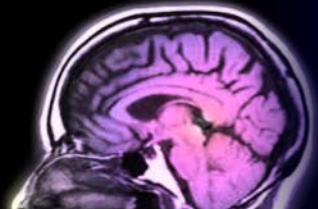
„individual symbols “, Metaphysical -about everything and nothing “,

Paralogia - non-logical combinations of thoughts, Autistic - „own subjective world “, Incoherent thinking - „various topics at once “,

Obsessive - compulsive thoughts

3. Content of thinking

Delusions - wrong mindset leads out of objective reality; person believes without hesitation about correctness of these outcomes



Psychosis

- **Definition:** Psychosis is a group of acute symptoms characterized by „loss of contact with reality“ featuring hallucinations, delusions, disorganized thought processes, abnormality of person's perceptions, impaired reasoning, emotional regulation, and social functioning,
- Primary psychiatric conditions: **schizophrenia, bipolar disorder, or severe mood disorders, neurodevelopmental disruptions, substance-induced states** (amphetamines or cannabis), **traumatic brain injury, or infections** affecting cerebral function.
- Genetic factors > 80% (twin studies of schizophrenia-spectrum psychoses),
- **Epidemiology:** prevalence of psychotic disorders ~ 3%; incidence rates for first-episode psychosis ~ 20-30 / 100,000 persons per year, Early-onset episodes - late adolescence or early adulthood
- **Manifestations:** DSM-5 psychosis requires at least 2 characteristic symptoms (one being delusions, hallucinations, or disorganized speech) persisting for a significant duration,
 - **delusions**—fixed, false beliefs held with conviction despite contradictory evidence, such as persecutory ideas that others intend harm;
 - **hallucinations**—sensory experiences without corresponding external stimuli, most commonly auditory voices commenting on or commanding the person;
 - **disorganized thinking and speech** - tangential, incoherent, loose associations;
 - **disorganized or catatonic behavior**, ranging from unpredictable agitation to stupor.



Schizophrenia

Def: Chronic disease with onset early in life and significant deterioration in the content of thought (shattered mind) mixture of signs & symptoms very incapacitating

- **Various symptoms** suggest possible involvement of a variety of cortical and subcortical areas
- Anatomical abnormalities include **enlargement of ventricles and prominent sulci due to abnormal brain development**

Epi: 1% of the population. It typically starts between ages **15-35** in men and late **20s** to early **30s** in women.

Etio: Mixture of genes and environment

Genetics heritability of schizophrenia **80%**

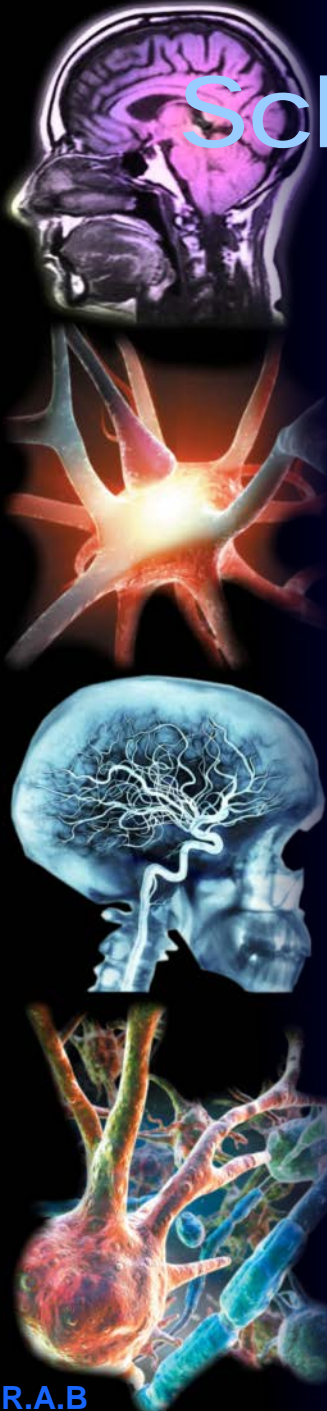
- Concordance in monozygotic twins- **40 - 50%**
- Concordance in dizygotic twins- **10 - 15%**

Non genetic factors

- poor nutrition
- infections during pregnancy or childhood
- toxins-damage neurons or affect NT systems
- radiation-mutations

Exaggerated dopamine activity (working hypothesis but is oversimplified) at key sites- limbic areas, language areas dopamine receptor blockers (type 2) increased dopamine receptors; L-dopa causing schizophrenic symptoms increased levels of dopamine metabolites

Schizophrenia – Environmental



Factor	Description	Proposed Role in Schizophrenia
Prenatal infection (e.g. T. gondii, viruses)	Maternal illness during pregnancy	Alters fetal brain development
Childhood trauma/stress	Abuse, neglect, maltreatment	Increases susceptibility
Early drug use	Cannabis, LSD, other substances	Highest risk during adolescence
Malnutrition	Low Vitamin D, choline, maternal stress	Disrupts brain development
Immune activation	Inflammation, gut microbiome changes	Potentially causal in some cases

Schizophrenia - Etiology

Schizophrenia: Gene X Environment

Brain Chemistry

Dopamine, Glutamate, GABA -
both excess and deficient
Neuroinflammation, immune
activation

Neuronal Changes

Dendritic apoptosis
Decreased neuronal plasticity
Synaptic pruning

Symptoms

Hallucinations, delusions,
disorganized thinking, lack of
motivation, anhedonia

Genetic Susceptibility

DISC1, Dopamine Receptors,
RELN, Glutamate receptors, GABA
NRG1, Immune system genes

Environmental Triggers

Infections (e.g. Toxoplasmosis)
Childhood & adolescent stressors
Malnutrition
Cannabis or drug abuse at a
young age

Genetic Lifehacks
Learn. Experiment. Optimize.

<https://www.geneticlifehacks.com/schizophrenia-genetic-and-environmental-factors/>

Schizophrenia - Notes

- Etiology:
- **Genetics: role in susceptibility to schizophrenia, but genetics alone doesn't cause schizophrenia** (2022) GWAS - the polygenic nature of psychosis; hundreds of common variants with small effect sizes. **287 independent genomic loci** associated with disease severity, implicating pathways in synaptic plasticity, neuronal development, and dopamine signaling; deletions on 22q11.2 bring a higher individual risk (probability ratio up to 20-fold),
- **Pregnancy:**
- **Obstetric complications**, including hypoxia, preeclampsia, maternal bleeding or diabetes and low birth weight, are consistently associated with heightened psychosis risk, 1.5- to 2-fold
- **Neurodevelopmental**: subtle deviations in neuronal migration, connectivity, and cortical organization during **gestation and infancy**, detectable through markers like **delayed motor milestones**
- Findings
- **Functional MRI studies: reduced brain connectivity in at-risk youth** (exacerbated by cannabis, 70-80%) impair thalamic and cortical development

Schizophrenia - symptoms

Positive symptoms

- **distortions of normal cognitive or emotional functions**
 - delusions
 - hallucinations
 - disorganized speech
 - bizarre behavior
- **Mesolimbic loop**
 - ventral tegmental area to many areas of limbic system

Negative symptoms

- **loss or decrease of normal functions**
 - alogoria - poverty of speech or empty content
 - flat emotions
 - anhedonia-inability to experience pleasure
 - avolition - inability to initiate or persist in goal directed behavior
 - attentional impairment
- **Mesocortical loop**
 - ventral tegmental area to neocortex

tend to impair the persons ability to function in daily life more so than positive symptoms

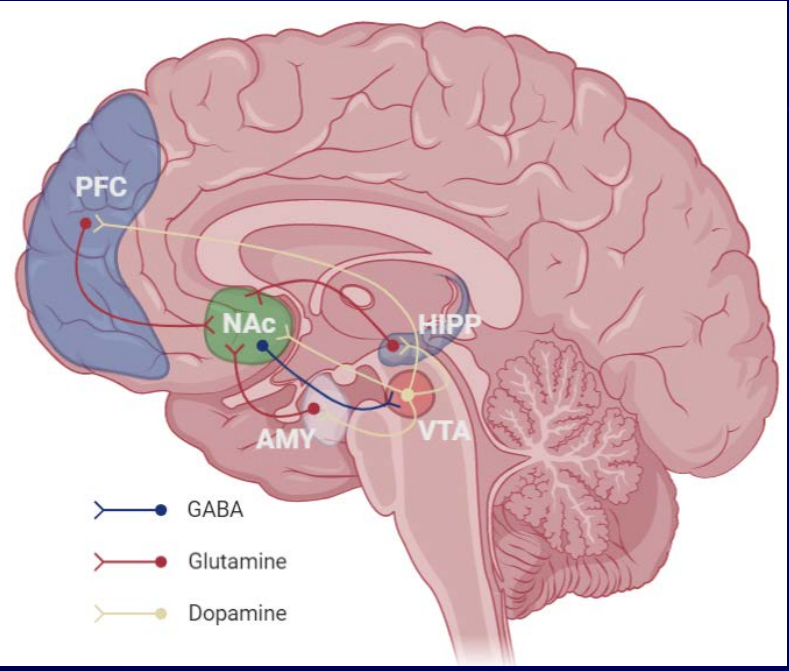
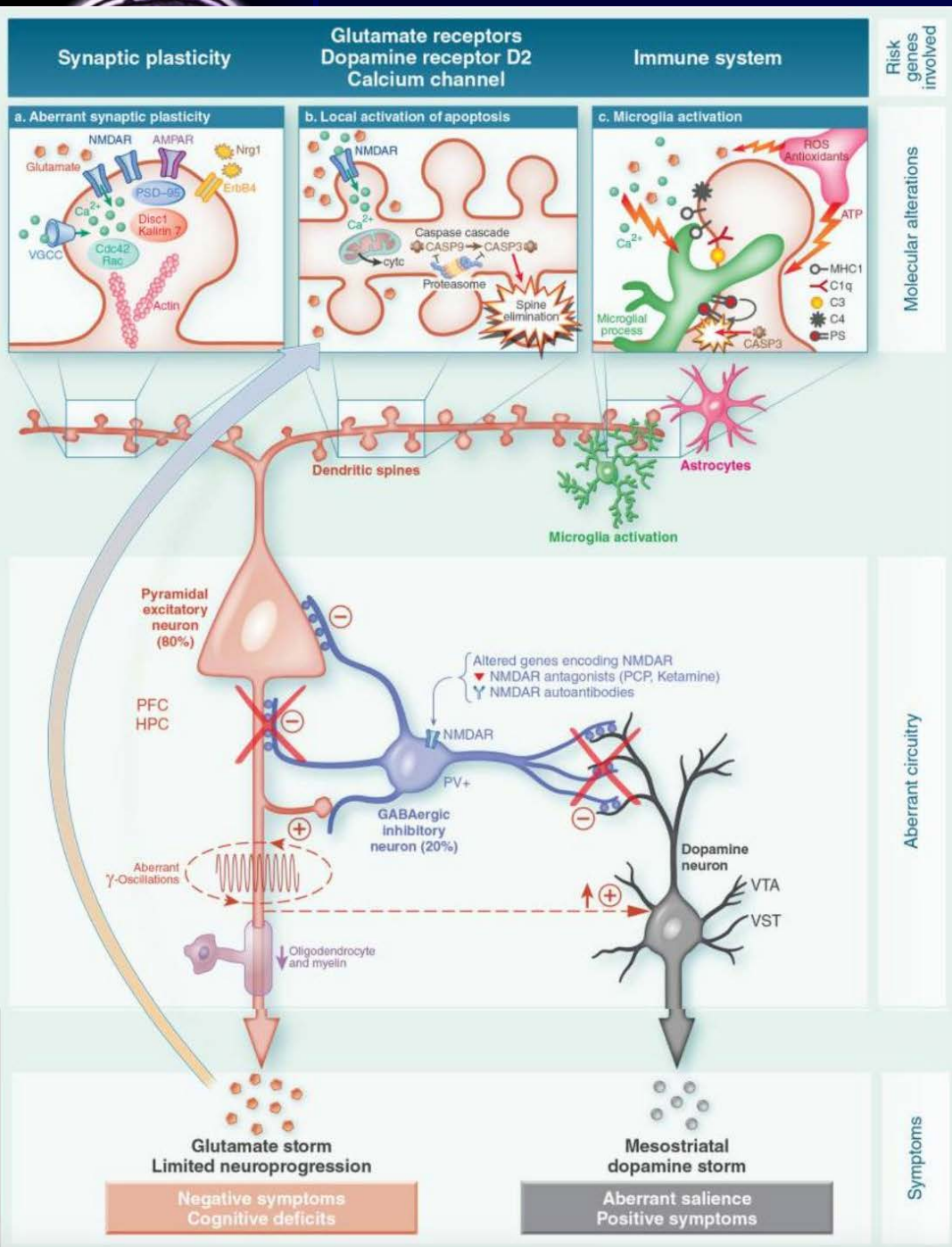
Schizophrenia - Notes

Overview of changes in schizophrenia

Neurotransmitter	Normal Role	Change in Schizophrenia	Impact on Symptoms
Dopamine	Movement, motivation, learning	Imbalances: ↑ some regions, ↓ others	Hallucinations, delusions, anhedonia
Glutamate	Memory, learning, mood	NMDA receptor dysfunction; ↓ function	Cognitive deficits, psychosis
GABA	Main inhibitory neurotransmitter	Reduced GABA levels	Disinhibition, emotional/cognitive changes
Serotonin	Mood regulation, perception	Hyperactive pathways in some cases	May affect a subset of patients

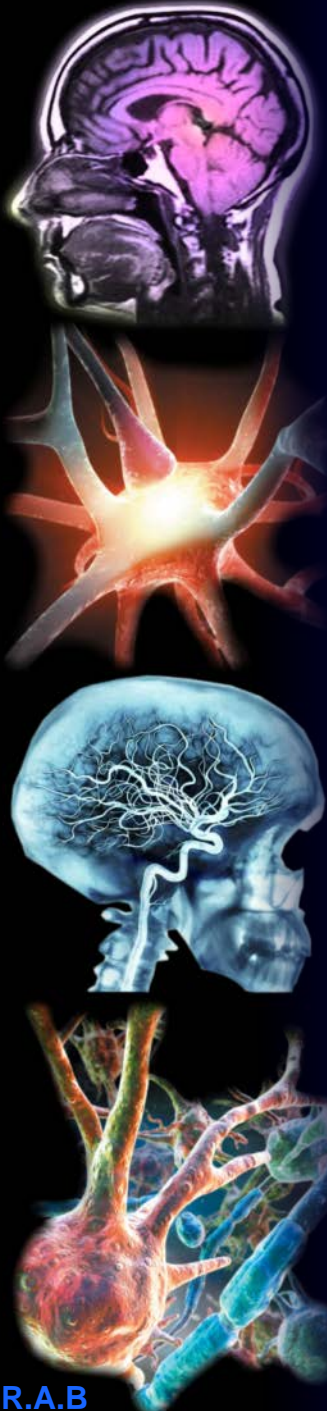
Drugs that are NMDA antagonists, like ketamine, can imitate some symptoms of schizophrenia.

Insufficient GABA in frontal cortex, → increase in dopamine and a dysregulation of NMDA receptors. GABA is synthesized from glutamate using the GAD67 enzyme, and postmortem studies show reduced GAD67 in the prefrontal cortex in schizophrenia patients
hyperactivity in serotonergic pathways



Positive symptoms: dopaminergic overactivity in mesolimbic pathways
 The mesocorticolimbic pathway: originates in VTA, amygdala, nucleus accumbens, hippocampus.
 These functions are relative to memory, emotional regulation, motivation, and reward.

Schizophrenia - Genes



Gene	Function/Pathway	Associated Risk Change	Notable Research Highlights
NRG1	Neuronal development, plasticity	↑ susceptibility (when altered)	White matter changes, animal models
DISC1	Neurogenesis, stress response	↑ susceptibility	Interacts with mood, stress regulation
C4	Synaptic pruning, immune system	↑ risk (overactivity)	Over-pruning in adolescence
RELN	Neuron migration, plasticity	↑ risk (mutations/epigenetics)	Linked to schizophrenia/autism
Dopamine-related (COMT, MAO)	Dopamine metabolism	↑/↓ risk, depending on variant	Influences neurotransmitter balance

Schizophrenia - Epigenetics

Mechanism	Example/Note	Impact on Schizophrenia Risk
DNA methylation	RELN gene hypermethylation	Gene silencing, ↑ risk
Histone modifications	Transcription regulation changes	Alters gene/protein expression
Gene-environment interaction	Polygenic risk + environment “hits”	Determines overall susceptibility

