Neuropsychiatric disorders

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STROKE
(BRAIN ATTACK)

- Focal ischemia
- Global ischemia

1. **Ischemic**: 80% of all strokes (mortality 20%)

2. **Hemorrhagic**: 20% of all strokes (mortality 80%)

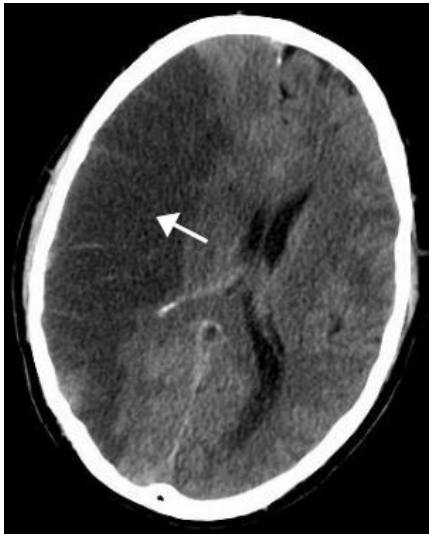
Silent stroke – without any symptoms (brain - damaged)

Transient ischemic attack (deficits - less than 1 h) – zone of penumbra without central infarction

Causes

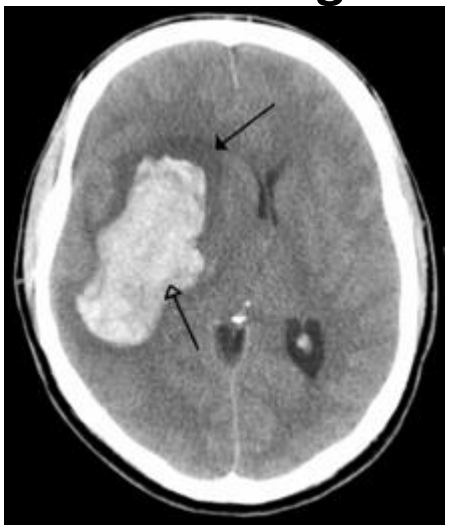
- thrombosis (50%)
- embolism (30%)
- cerebral hypoperfusion
- cerebral venous thrombosis
- intracerebral hemorrhage

Ischemic



CT scan of the brain showing a right-hemispheric ischemic stroke

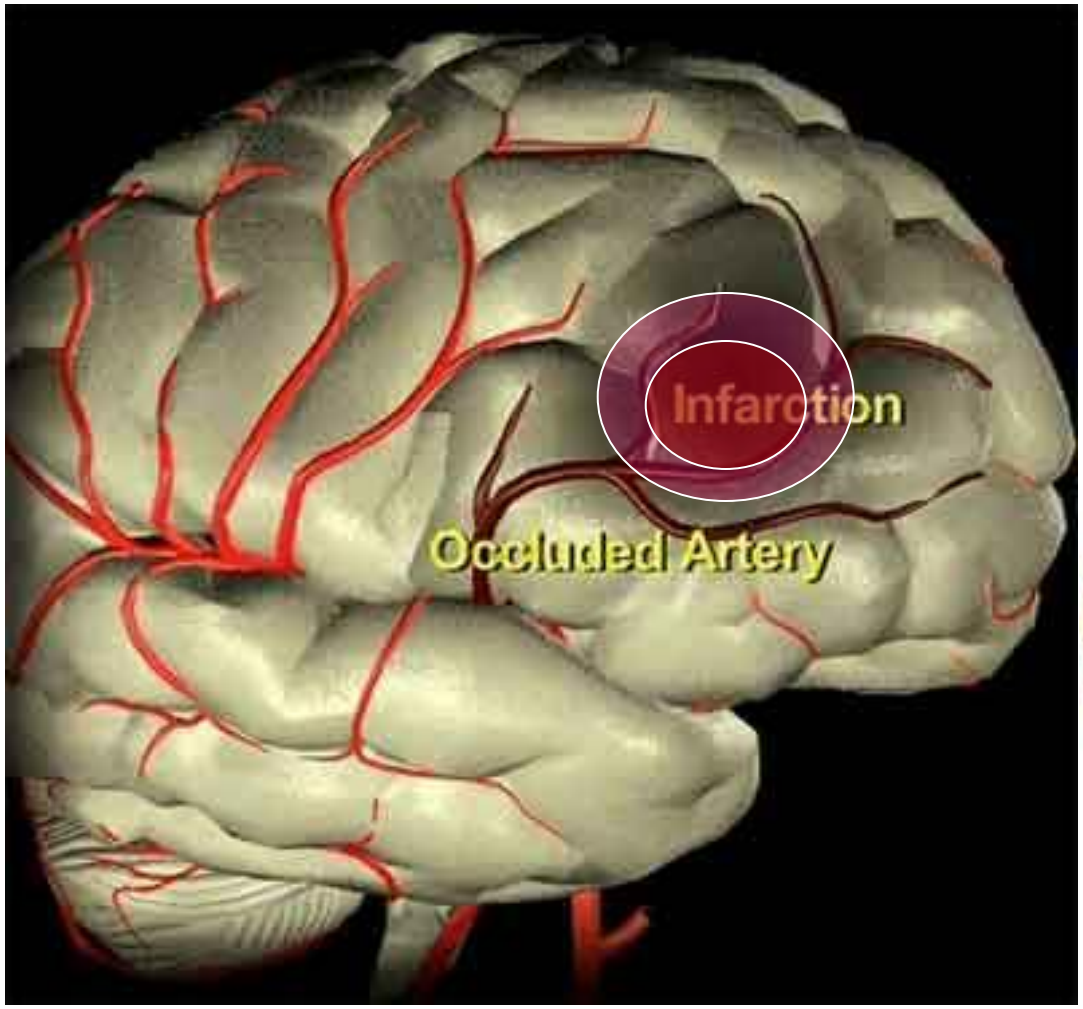
Hemorrhagic

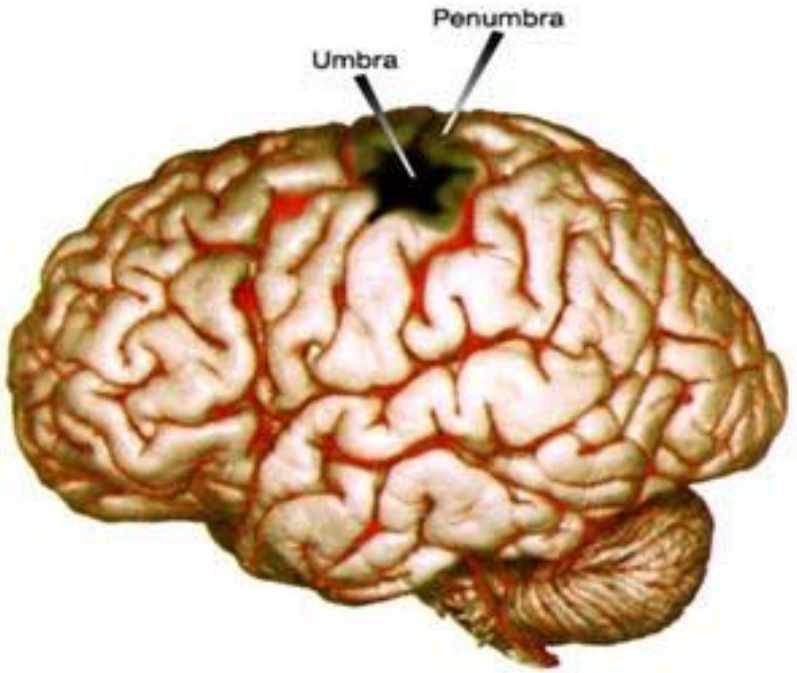


CT scan of an intraparenchymal bleed (bottom arrow) with surrounding edema (top)

- **Umbra**

- **Penumbra**



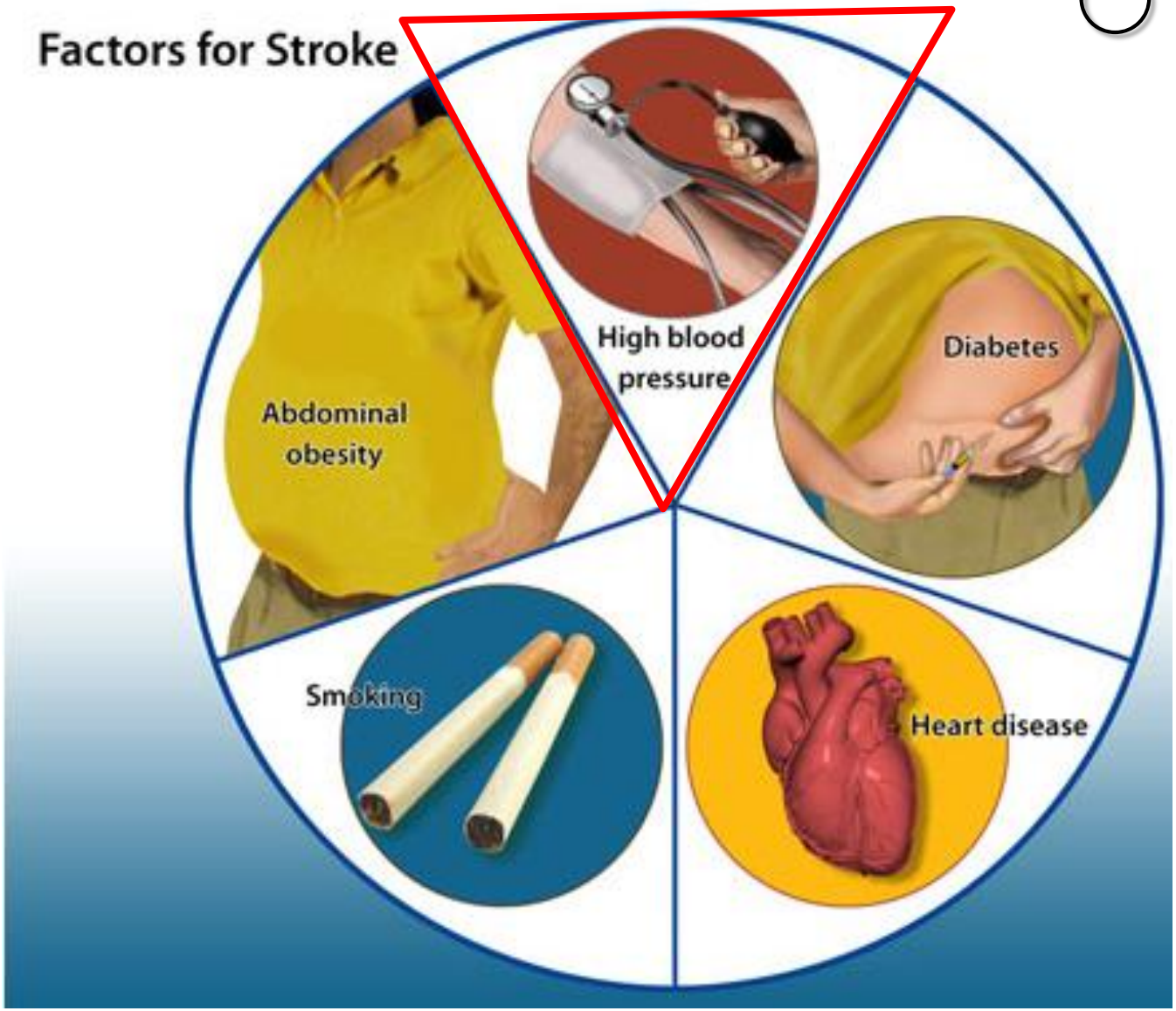


Symptoms

- sudden onset – over seconds to minutes
- **face weakness**
- **arm weakness**
- **speech difficulties**
- **vision, smell, taste, hearing impairment**

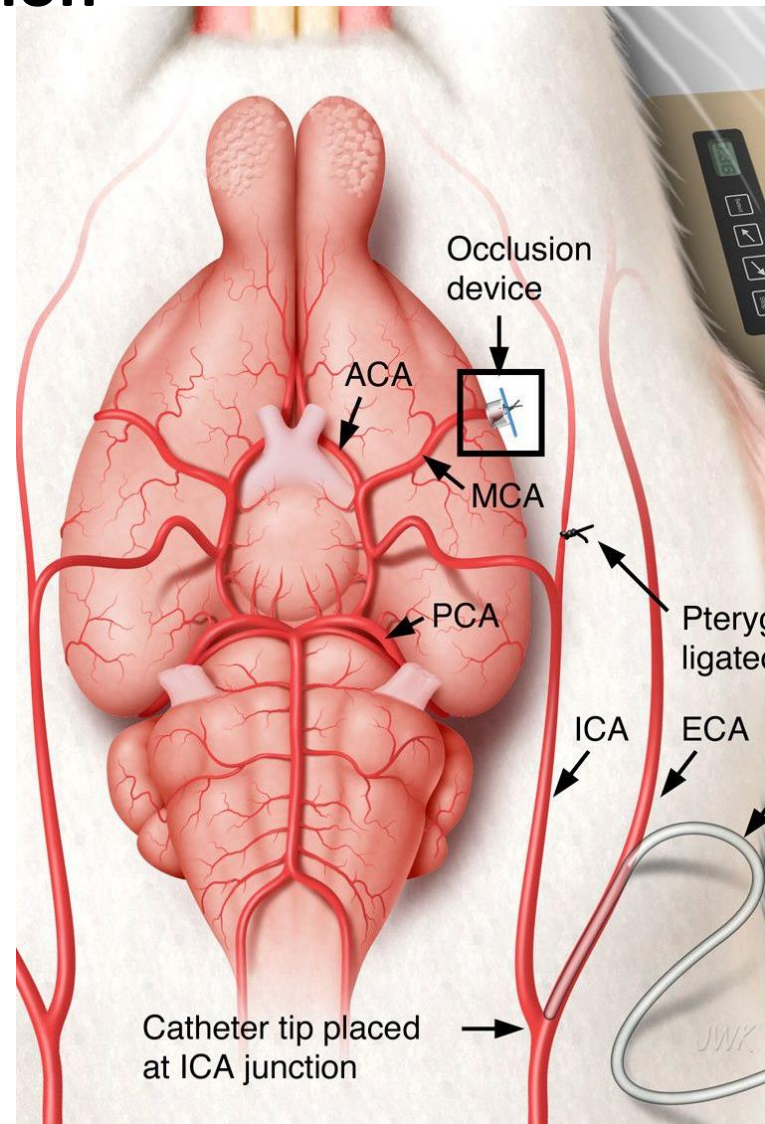
Etiology

♂ > ♀


Factors for Stroke
High blood pressure
Diabetes
Abdominal obesity
Smoking
Heart disease

Stroke – animal models

- **Endothelin-1 induced vasoconstriction**
- **Middle cerebral artery occlusion**
- **Permanent transcranial middle cerebral artery occlusion**



https://www.youtube.com/watch?v=VMGoUGE5_ok

Epilepsy

- group of neurological disorders
- recurrent seizures
- seizures =
  - **spontaneous, abnormally synchronous electrical discharges from collections of neurons in the cerebral cortex.**
  - are thought to result directly or indirectly from **changes in excitability** of single neurons or groups of neurons
- predisposition :1-3% of population

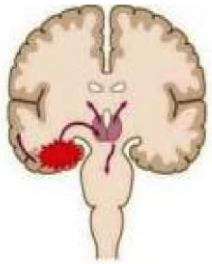
Seizure type:

- **Partial (focal) seizures** (simple partial, complex partial, secondarily generalized)
- **Generalized seizures** (absence, atonic, tonic, clonic, tonic-clonic)

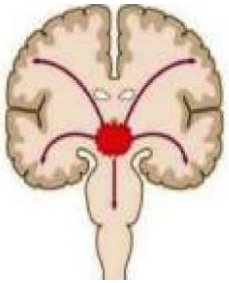
Partial seizures

- beginning in one hemisphere with secondary spread of seizure activity to other parts of the brain

- **simple partial**



- **complex partial** – temporal lobe
  - automatism

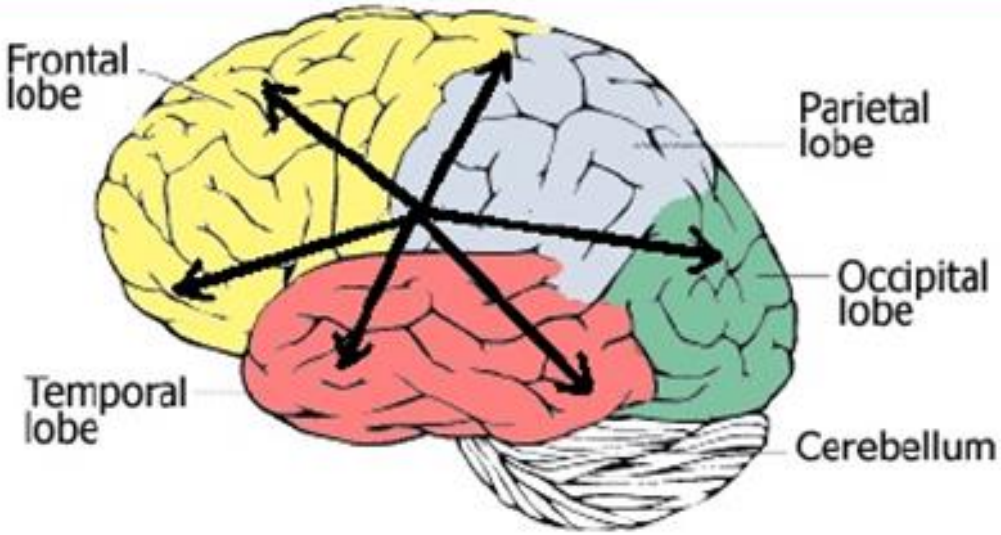


- **secondarily generalized partial** – deeper structures of the brain
  - **aura**

Generalized seizures

simultaneous disruption of normal brain activity in **both hemispheres from the onset**

Seizure involves whole brain & consciousness is affected



Tonic Clonic	Absence	Atonic / Tonic	Myoclonic
"grand-mal" or convulsion	"petit mal" or staring fit	"drop attack"	Sudden muscle jerks
Tonic: constant contractions of the muscles Clonic: shaking of the limbs in unison	**brief periods of unconsciousness**	**sudden, split-second loss of muscle tone/constant contractions of the muscles**	**spasms of muscles in either a few areas or all over**

Etiology

- **unprovoked** - no identifiable cause (genetic)

- **provoked –** febrile seizures in children or metabolic disturbances (electrolyte imbalances, hypoglycemia, hypoxia, hypocalcemia and rapid withdrawal of sedative drugs)

Cause:

- unknown... brain injury, stroke, brian tumors, infections, birth defects

Difference between epilepsy and seizure

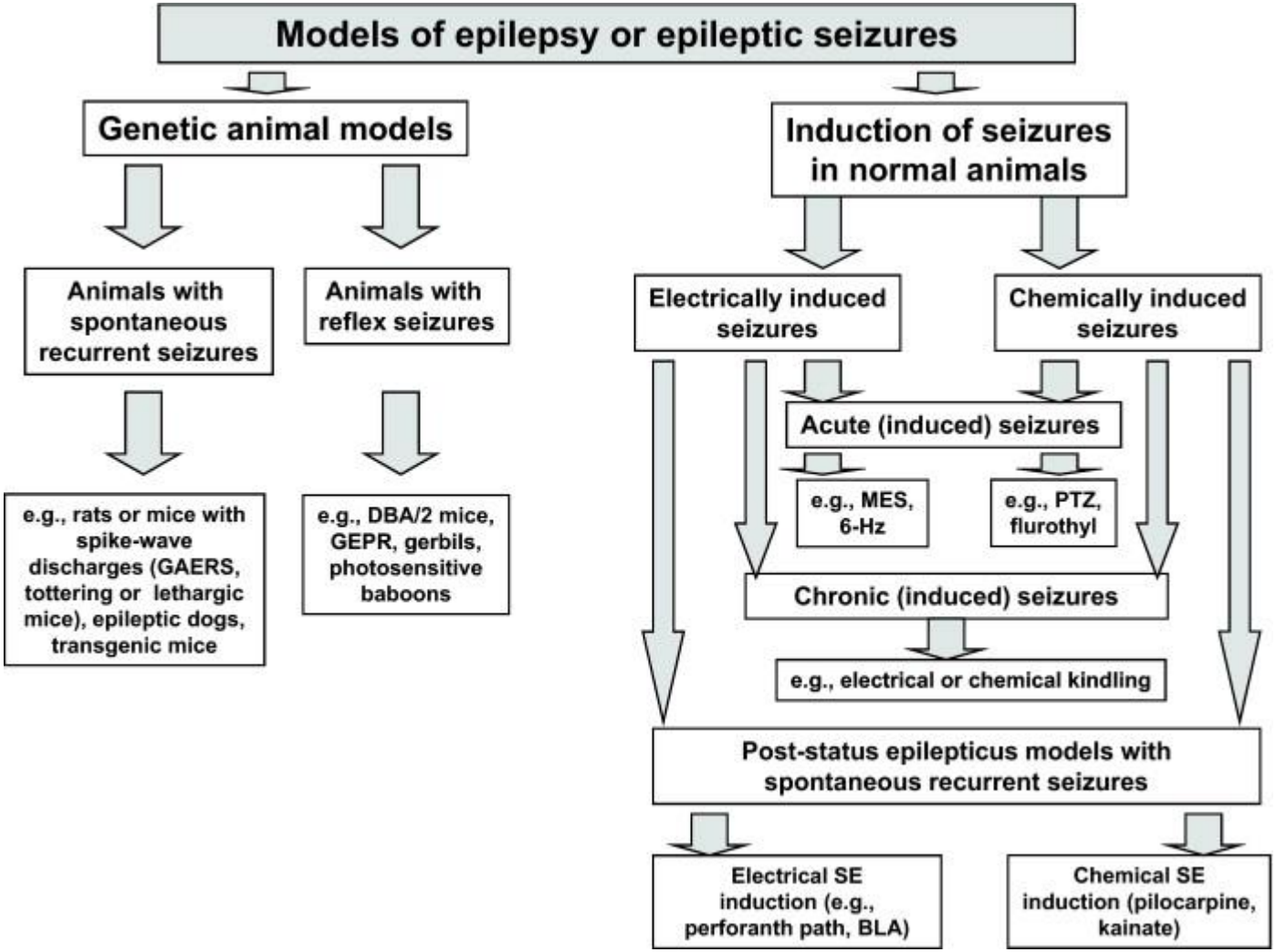
- **Epilepsy -** a disorder (recurring seizures)

VS

- **Seizure -** a brief, temporary disturbance in the electrical activity of the brain

Animal models

Models of epileptic seizures rather than epilepsy



Seizure testing

1. **“Tail twisting”** – **twisting movements of the tail beginning at the tip and gradually involving entire tail to its base**, frequently including the hind limbs. The tail bends in an abnormal way, initially sideways and later in a spasmic movement. Movement continues during the whole seizure testing period.
2. **Arching** – which is an introduction to flexion spasms, the **rat is curled in an upright position.**
3. **Emprosthotonus** – a tetanic spasm in which **the head and feet are drawn forward and the spine arches backward**. Finally, the rat loses righting ability, and arching turns into fully flexed position while lying on one side (flexion spasms, emprosthotonus). Flexion spasms last >10s with multiple recurrences, usually after interictal running or walking behavior.

- **[21^{10}, LLS]** – long lasting seizure – >1 min.
- **[WDS - 10^{14}] –** wet dog shake. The whole body shakes.
- **Scr -** = scratching – doesn´t count as a seizure – just phenotype

Tailing

Arching

Full emprosthotonus

Headache

- **Pain**
- **Brain - no pain receptors**

- Pain receptors:
  - extracranial arteries
  - large veins
  - venous sinuses
  - cranial and spinal nerves
  - head and neck muscles
  - eyes, ears, teeth and lining of the mouth

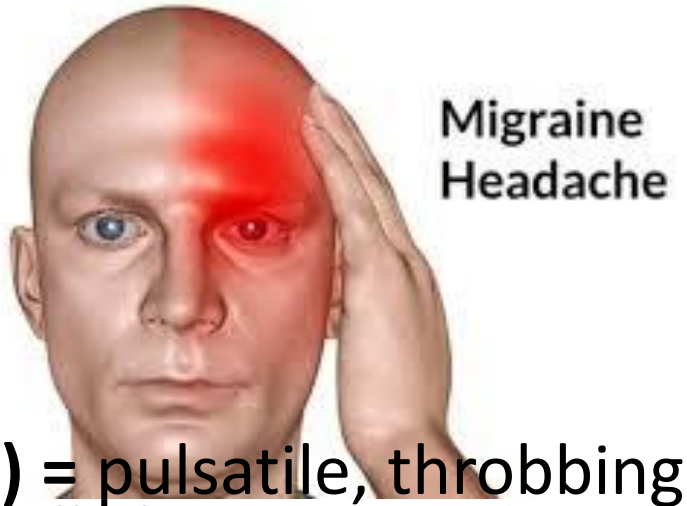
Headache

- secondary vs primary (90%)
- **Tension-type headache =** non-pulsing "bandlike" pressure on both sides of the head
- **Migraine =** pulsing head pain, nausea, photophobia, phonophobia
- **Cluster headache =** short episodes (15–180 minutes) of severe pain, usually around one eye – same time every day
- **Chronic daily headache =** headaches that occur 15 days or more a month

Tension type headache

- **most common type**
- not sufficiently severe to interfere with daily activities
- dull, aching, diffuse, hatband distribution of the pain around the head
- infrequent, episodic or chronic
- **unknown cause**
  - **Theory: sustained tension of the muscles of the scalp and neck**
  - **by psychogenic stress, anxiety, depression, and muscular stress**
  - **overuse of analgesics or caffeine**
- **treatment:** more responsive to nonpharmacologic techniques (massage, acupuncture, relaxation, imagery, and physical therapy)

Migraine



- **Without aura (85%) =** pulsatile, throbbing, unilateral headache that typically lasts 1 to 2 days
- nausea and vomiting,
- sensitivity to light and sound

- **With aura (15%) =** similar symptoms, but with the addition of visual or neurologic symptoms that precede the headache = aura
- the aura usually develops over a period of 5 to 20 minutes and lasts less than an hour.

- Affects more women than men

Causes of migraine

- result from a primary disorder in the brain related to **episodic changes in neural hyperexcitability** → dilation of **blood vessels → pain and further nerve activation**

Treatment:

- **Non-pharmacological -** regular eating and sleeping habits, quiet, darkened room
- **Pharmacological:** ibuprofen, etc.

Chronic daily headache

- 15 or more days a month

- **Unknown cause:**
  - transformed migraine headache?
  - evolved tension-type headache?
  - post-traumatic headache?

- **Manifestations:** from migraine to chronic tension-like headache

- **Treatment:** pharmacologic and non-pharmacologic, behavioral interventions

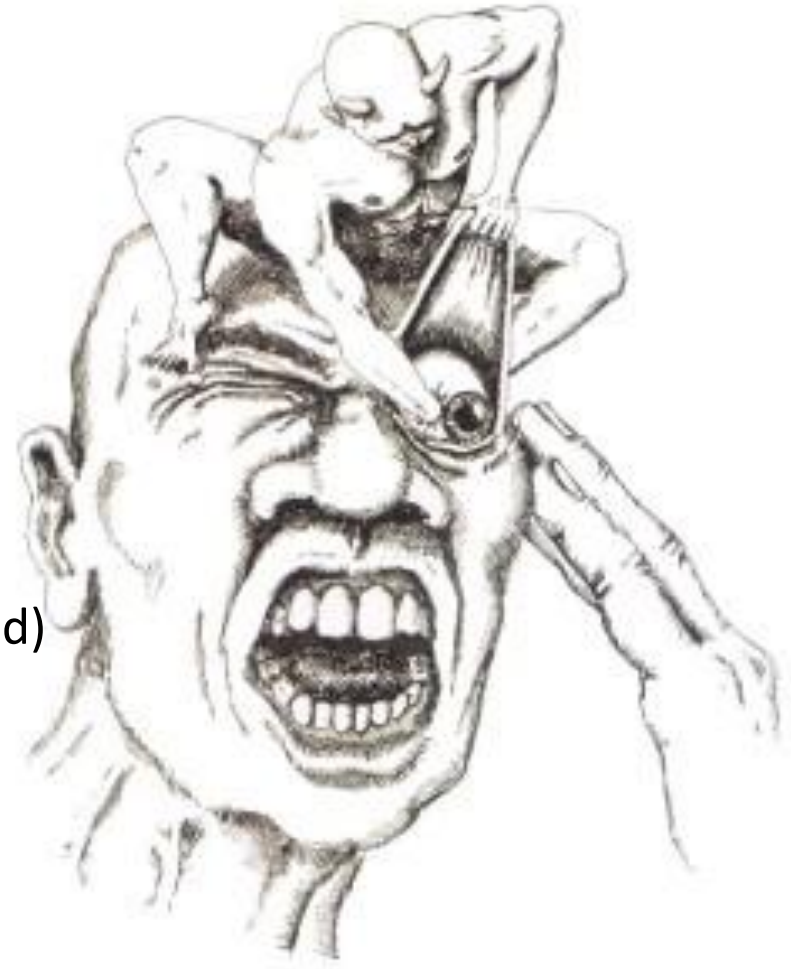
Cluster headache

- in clusters over weeks or months
- long, headache free remission phase
- rapid onset (duration 15-180 min)

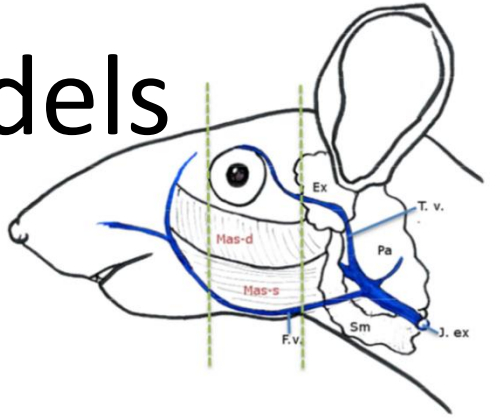
- **Symptoms:**
  - restlessness
  - conjunctival redness,
  - lacrimation, nasal congestion, rhinorrhea,
  - ptosis (drooping or falling of the upper eyelid)
  - eyelid edema

- **More common in men!**

- Treatment: quickly acting medications



Headache – animal models



- **Trigeminal autonomic cephalgia:**
- primary headache
- with pain on one side of the head in the trigeminal nerve area
- symptoms in autonomic systems on the same side, such as eye watering and redness or drooping eyelids.

Headache. 2013 January ; 53(1): 137–151. doi:10.1111/j.1526-4610.2012.02226.x.

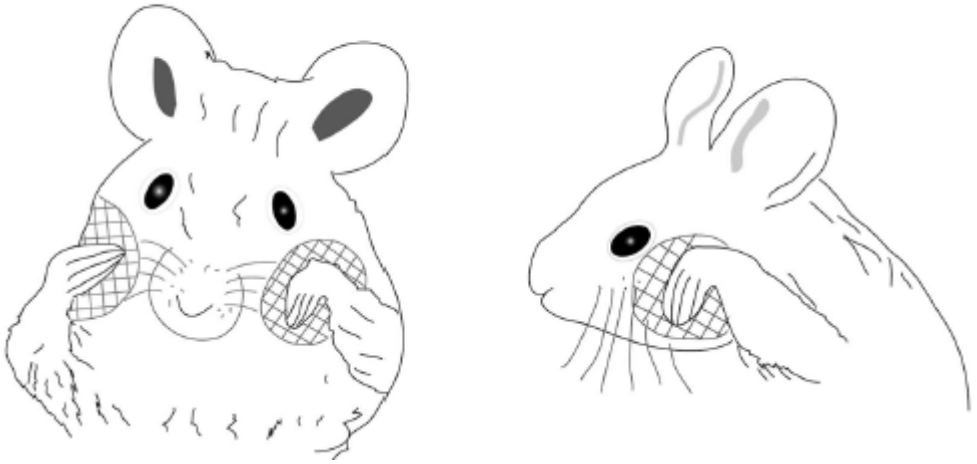
Spontaneous behavioral responses in the orofacial region: A model of trigeminal pain in mouse

Marcela Romero-Reyes, DDS, PhD[1,2,*], Simon Akerman, PhD[3], Elaine Nguyen, BS[2], Alice Vijjeswarapu, BS[2], Betty Hom, BS[2], Hong-Wei Dong, MD, PhD[2,4], and Andrew C. Charles, MD[2]

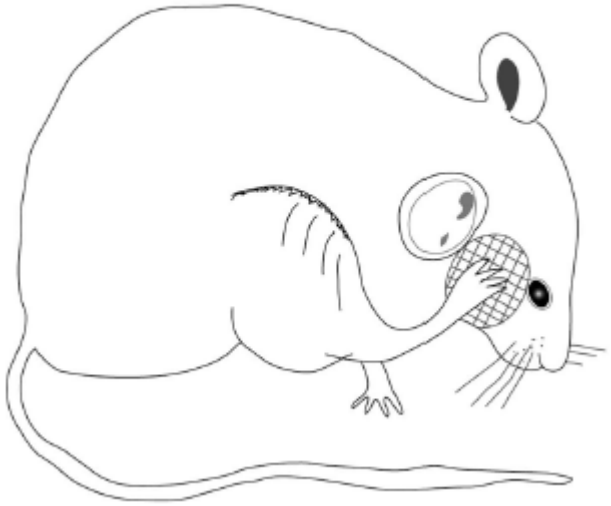
- Freund's adjuvant (CFA) into the right masseter muscle – unilaterally

- fore-paw rubbing, lower lip skin/cheek rubbing against enclosure floor and hind paw scratching.

A). Forepaw face rubbing



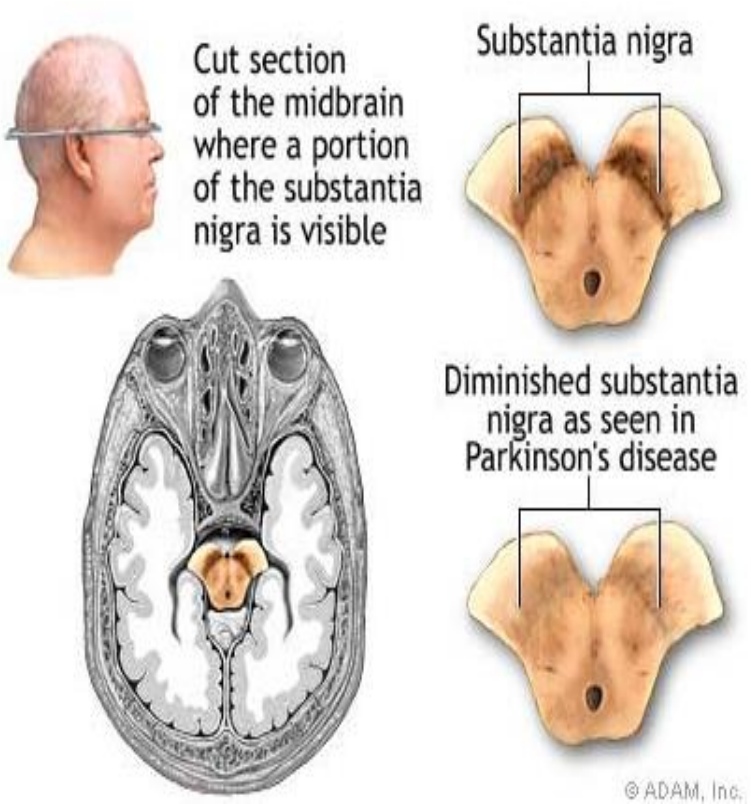
C). Hindpaw face scratching

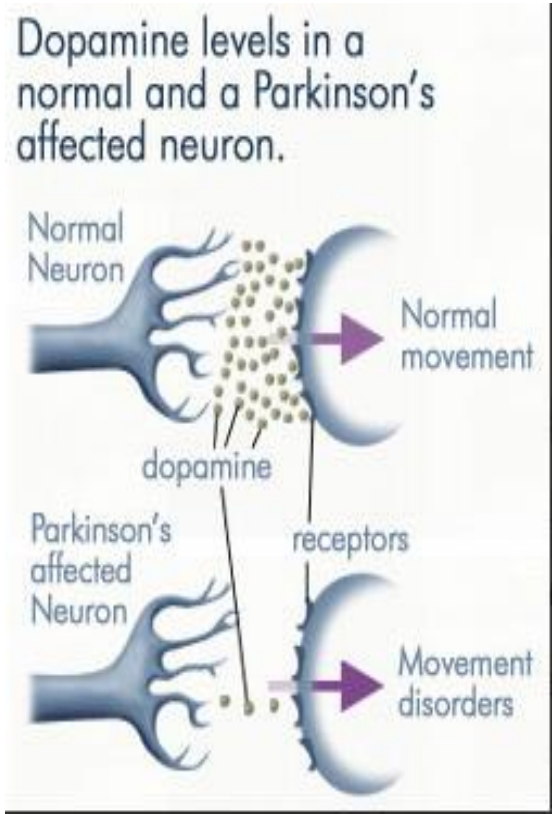


B). Lower lip skin/cheek rubbing against cage surface

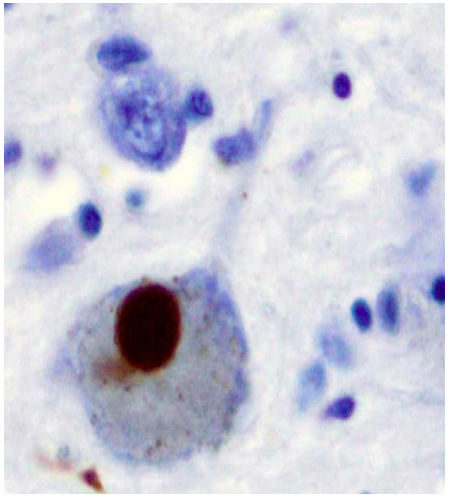
Parkinson‘s disease

- degenerative disorder of the basal ganglia CNS
- mainly affecting the motor system
- degradation of dopaminergic neurons in substantia nigra (↓ dopamine)





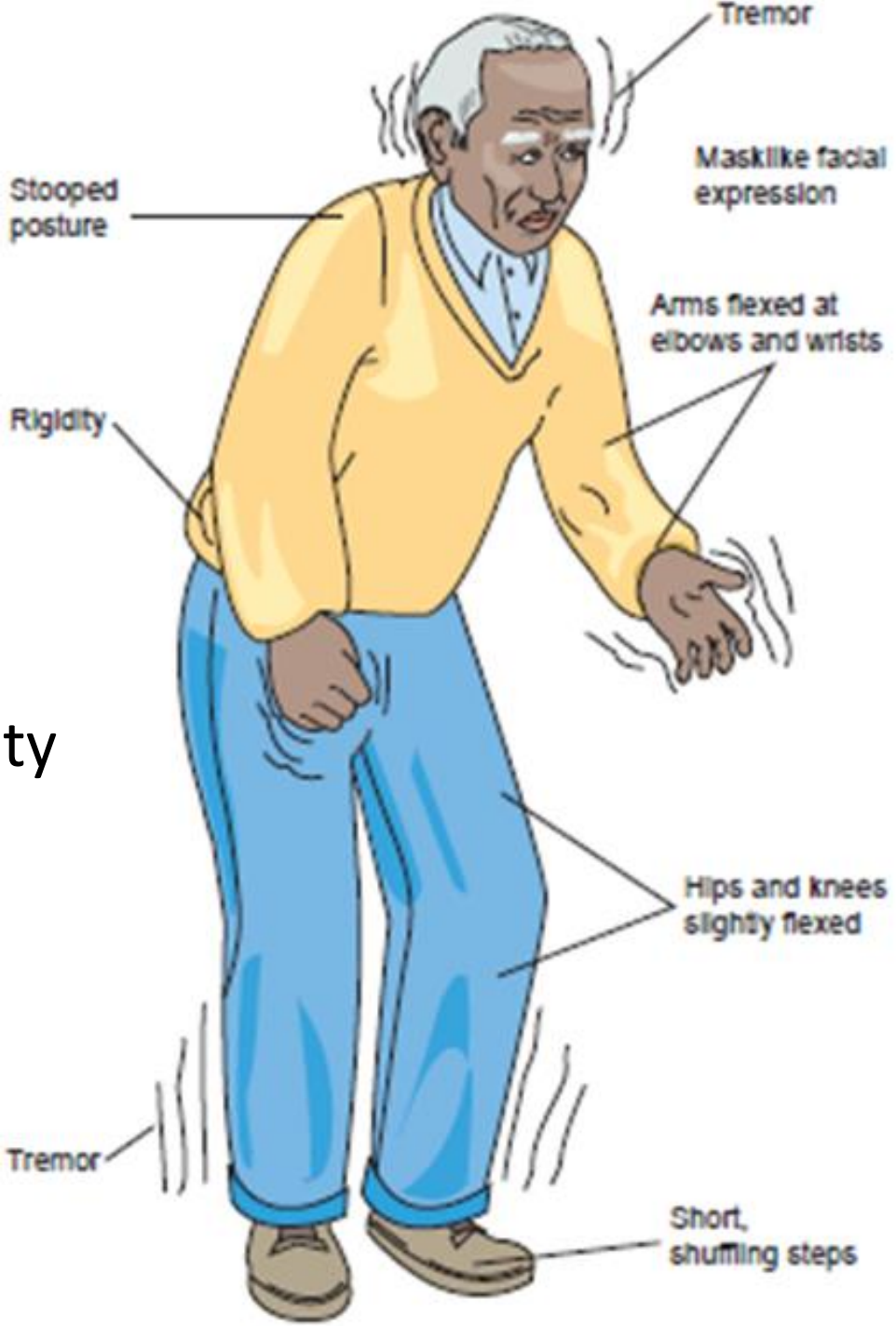
Lewy bodies = intracytoplasmic inclusions found in the substantia nigra neurons



Symptoms:

- **shaking**
- **rigidity**
- **bradykinesis**
- **postural instability**

- dementia, depression, anxiety
- sleep difficulties



- **Etiology**

- cause – unknown
- genetic and environmental factors
- pesticides, head injuries
- tobacco smoke, coffe or tea - protective?

- **Treatment**

- no cure
- treatment - symptomatic

Pharmacologic:

- levodopa = L-DOPA (early) (antiparkinson medication)
- dopamine agonists (later)

Non-pharmacologic:

- education, daily exercise, and adequate nutrition

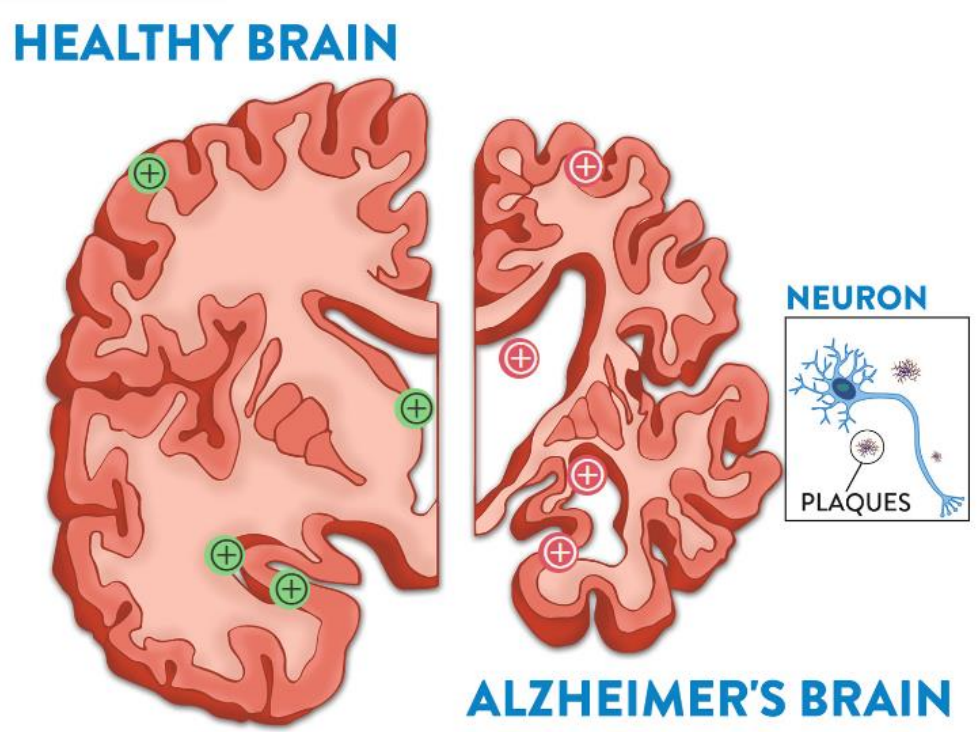
Parkinson‘s disease – animal models

- **Toxin-based models**:
  - rotenone (pesticide)
  - paraquat (herbicide)
  - maneb (fungicide)
  - commonly used in **primates**

- **6-hydroxydopamine (neurotoxin)**
- **intrastriatal administration of 6-OHDA in rats**
- a massive destruction of nigrostriatal dopaminergic neurons
- motor and biochemical dysfunctions

Alzheimer's disease

- **chronic neurodegenerative disease – slow onset**
- **cortical atrophy and loss of neurons** – parietal and temporal lobes → ventricular enlargement
- **hydrocephalus**



cortical atrophy = slender gyri and prominent sulci

Alzheimer‘s disease

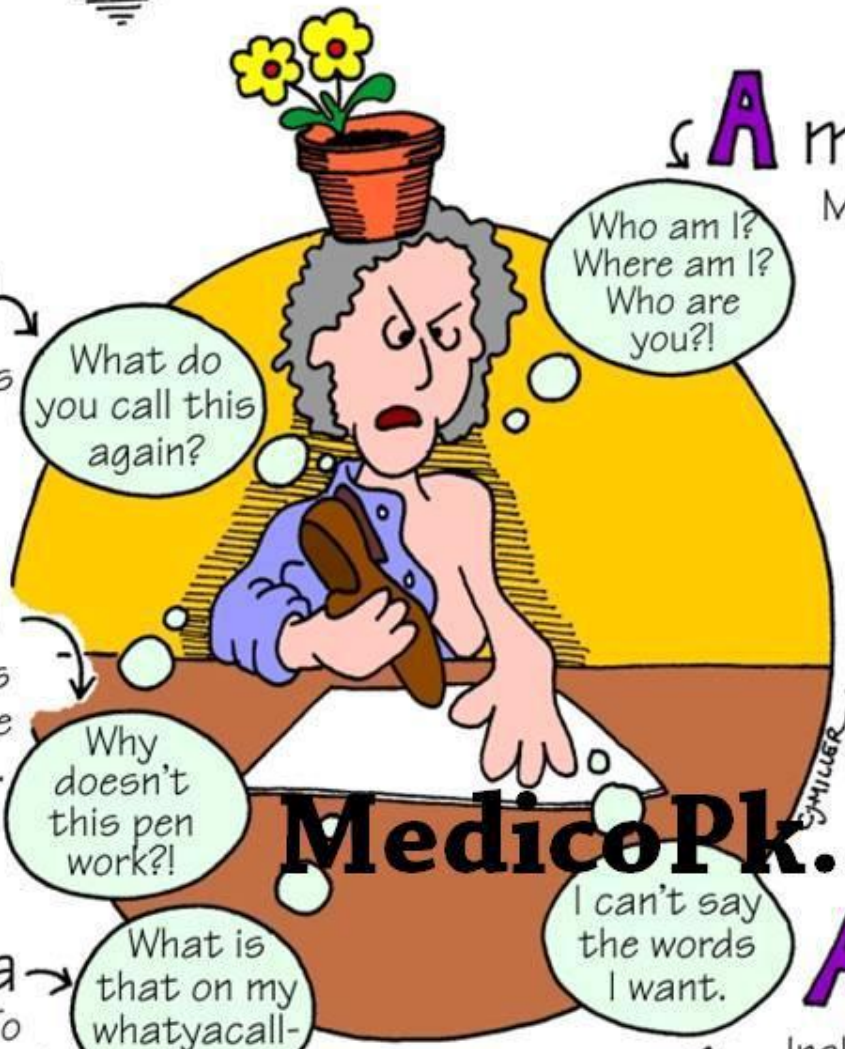
1. **Pre-dementia stage**: short-term memory loss = difficulty in remembering recently learned facts and inability to acquire new information, apathy, depressive symptoms, irritability and reduced awareness

2. **Early stage:** aphasia (speech), apraxia (movement coordination), agnosia (perception)

3. **Moderate stage:** hindered independence, paraphasias, long-term memory impairement, irritability, labile mood – outburst, aggression, crying...

4. **Advanced stage**: completely dependent upon caregivers, apathy, exhaustion

5 As to Alzheimer Diagnosis



Amnesia
Memory Loss...

Anomia
Inability To Remember Names of Things...

Apraxia
Misuse Of Objects Because Of Failure To Identify Them...

Agnosia
Inability To Recognize Familiar Objects, Tastes, Sounds, And Other Sensations...

Aphasia
Inability To Express Oneself Through Speech...

Judgment

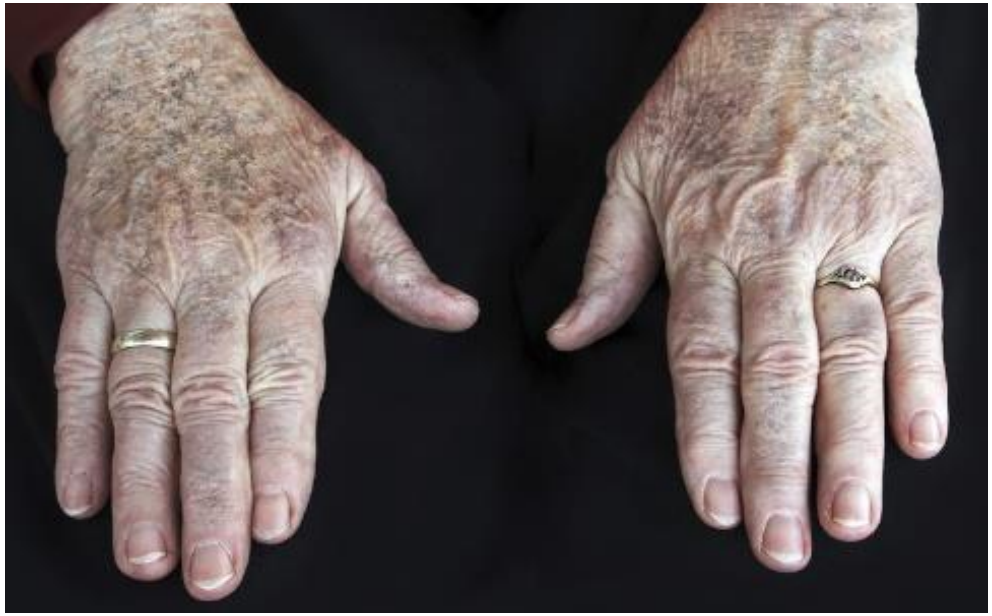
Concentration

Attention

Cause:

- **inherited (genetic):** mutations in 1 of 3 genes:
  - amyloid precursor protein (APP)
  - presenilins 1
  - presenilins 2

  → ↑ amyloid β – **senile plaques**



- **sporadic**: mutations in apolipoprotein E (APOE)

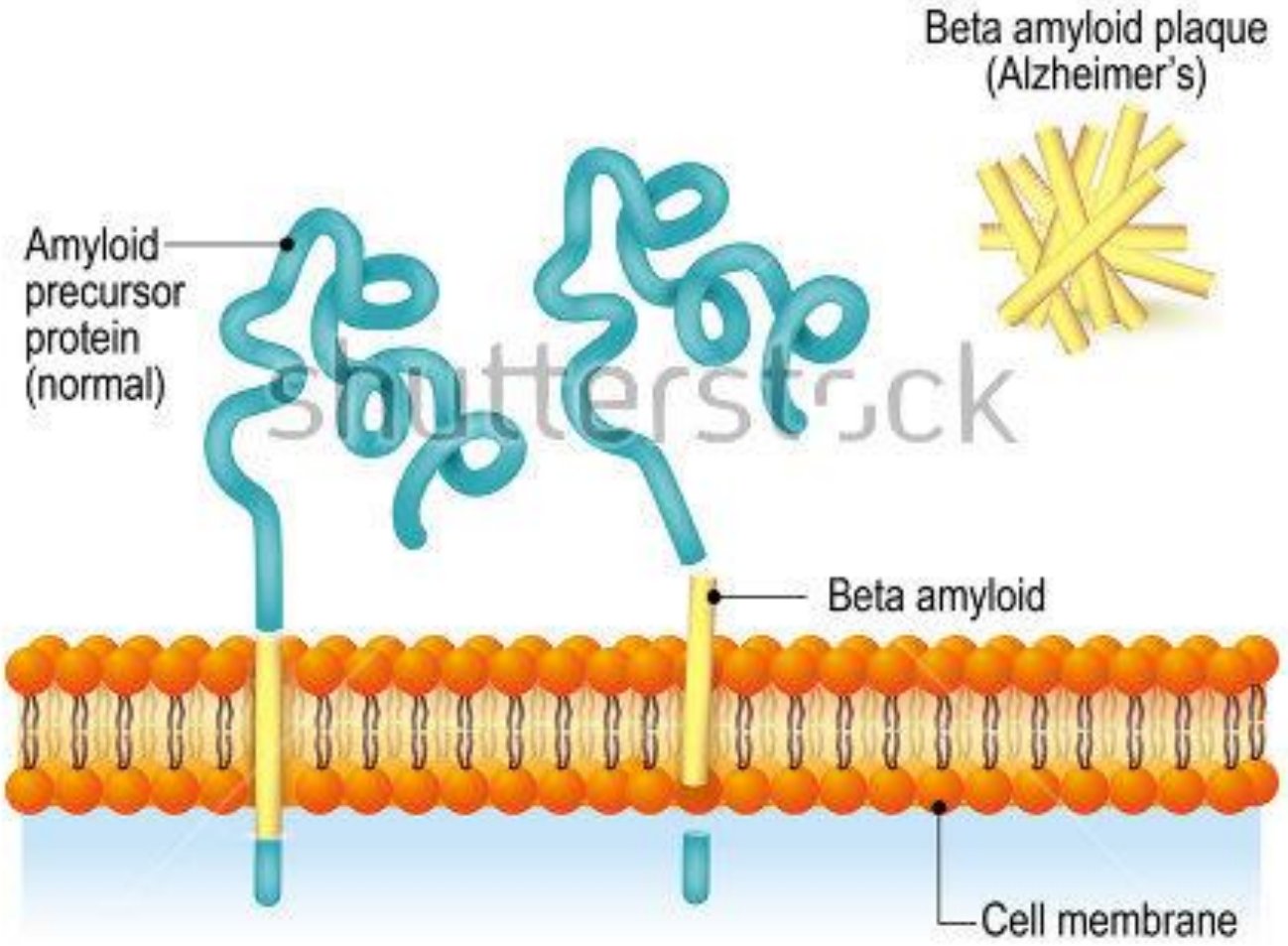
- **Cholinergic hypothesis**

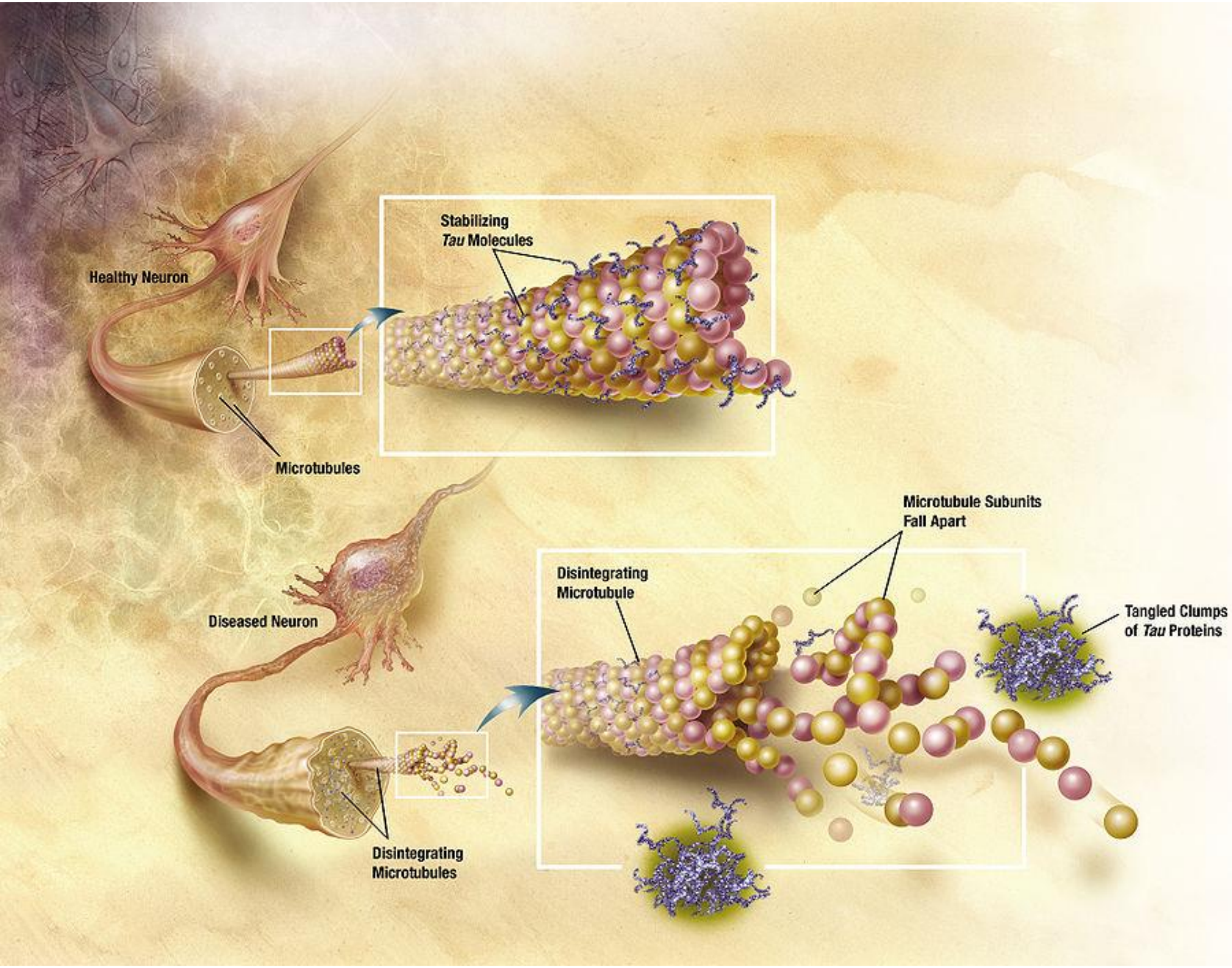
- Deficit in synthesis of the neurotransmitter acetylcholine

- **Amyloid hypothesis** – pieces of beta amyloid forms clusters = oligomers, after chains of clusters = fibrils and ,,mats,, of fibrils = beta sheets → **plaque** → disruption of cell to cell communication

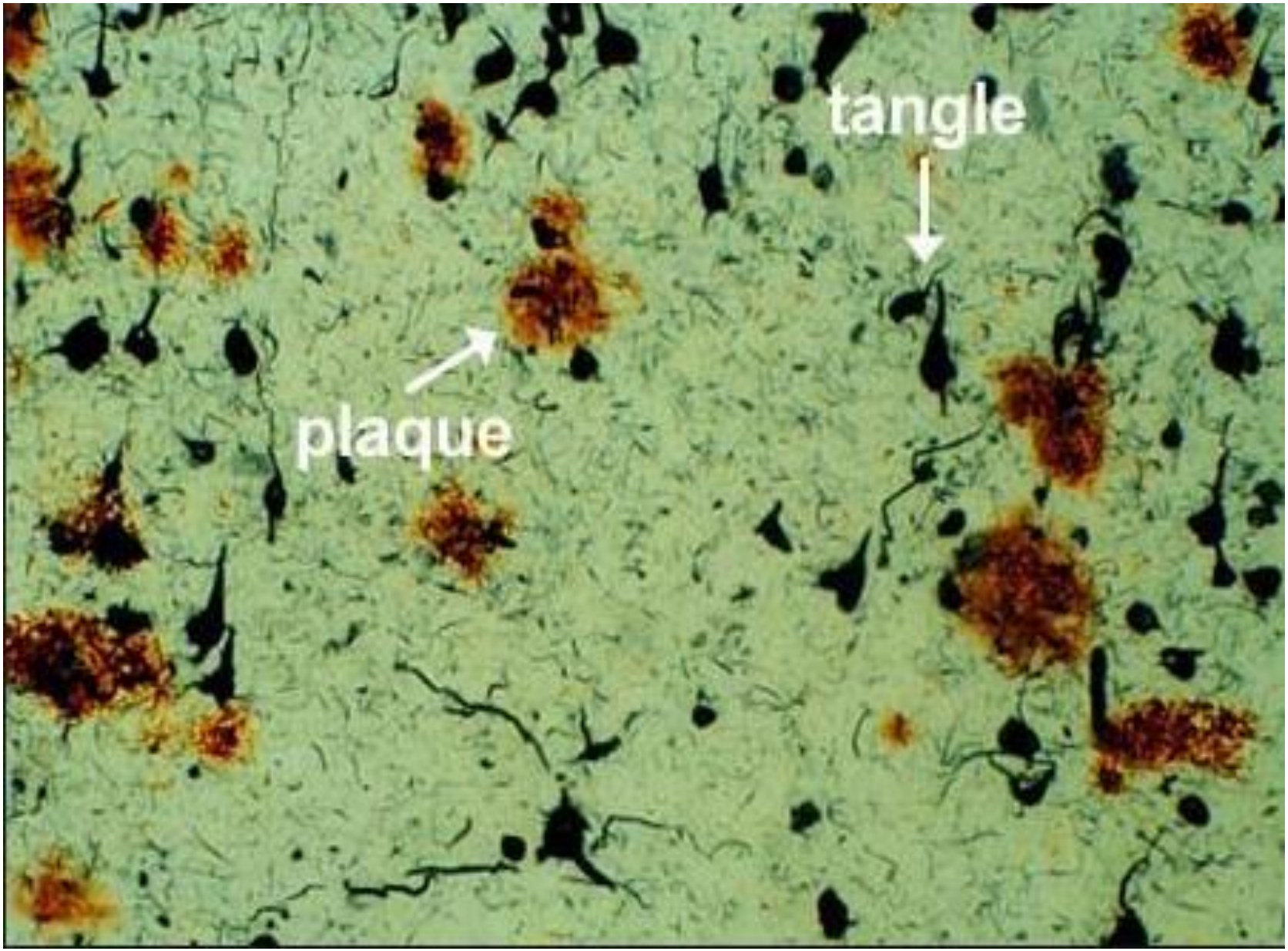
- **Tau hypothesis** (hyperphosphorylated tau – **neurofibrillary tangles**)

Amyloid-plaque formation




Healthy Neuron
Stabilizing
Tau Molecules
Microtubules
Diseased Neuron
Microtubule Subunits
Fall Apart
Disintegrating
Microtubule
Tangled Clumps
of *Tau* Proteins
Disintegrating
Microtubules

Alzheimer‘s disease



Treatment

- No cure

- Medications (for cognitive problems):
  - acetylcholinesterase inhibitors
  - **small benefit**

Animal models

- APP and PSEN mutants

APP/PS1 are double transgenic mice expressing a chimeric mouse/human amyloid precursor protein (Mo/HuAPP695swe) and a mutant human presenilin 1 (PS1-dE9), both directed to CNS neurons. Both mutations are associated with early-onset Alzheimer's disease.

- **Double-Tg mice =**
- over-express human mutant APP and tau
- deposition of Aβ, hyperphosphorylation of Tau
- progressive hippocampus- dependent memory impairment

Schizophrenia

- mental disorder
- abnormal social behavior
- failure to understand reality

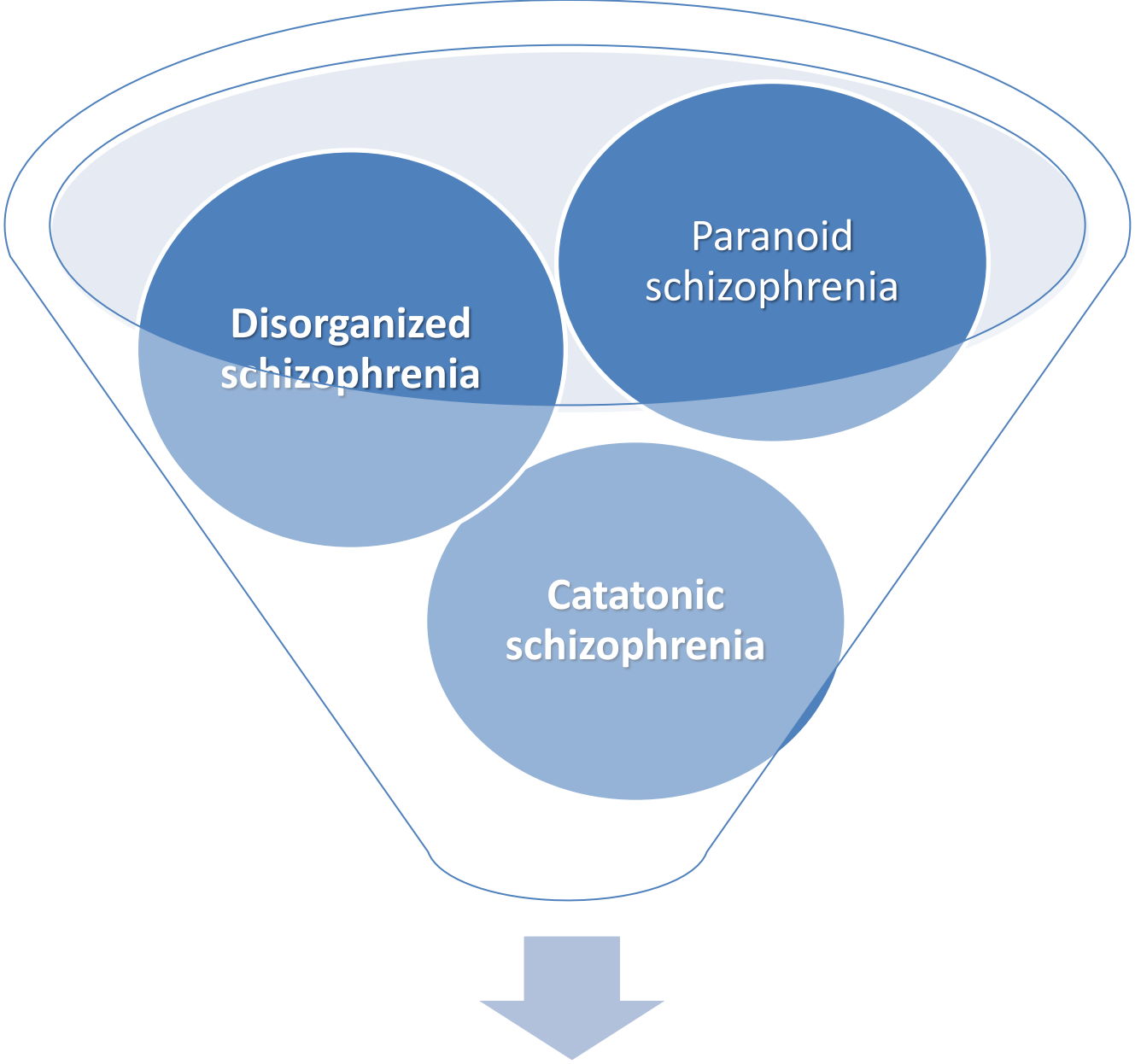
- disorder of thought and language

- Onset: 17 – 25 years of age
  - Men: 18 – 25 years of age
  - Women: 25 – 35 years of age

- invented words (neologisms)
- derailment (loose associations)
- incoherence (loss of logical connections),
- word salad (groups of disconnected words)

- **Positive**
  - Disorganized, incomprehensible speech
  - Delusion
  - Hallucinations (mostly auditory)
  - Disorganized catatonic behavior
  - Impaired ability to respond to environment
  - Ehancement or blunting of senses in the early stage

- **Negative**
  - Alogia
  - Avolition (lack of motivation)
  - Apathy
  - Affective flattening
  - Anhedonia



Schizophrenia

Paranoid schizophrenia

- grandiose **delusions**
- **auditory hallucinations** are common
- interactions with others: rigid, intense, and controlled
- sudden onset
- **negative symptoms are not prominent**
- prognosis of this form of schizophrenia seems to be better, with less evidence of disturbance in the anatomy of the brain and less cognitive deficits

Disorganized schizophrenia

- disintegration of the personality and a **predominance of negative symptoms**
- socially, the person is withdrawn and inept
- speech often is disorganized and incoherent
- personal grooming is neglected
- behavior is aimless = the person with this disorder often is not able to complete activities of daily living
- cognitive and psychomotor deficits
- prognosis is not as good as that for the paranoid schizophrenic type

- **Etiology - unknown**

- Abnormalities in brain anatomy at the onset

- Combination of environmental and genetic factors

- **Genetic factors:** variety of common and rare genetic variants

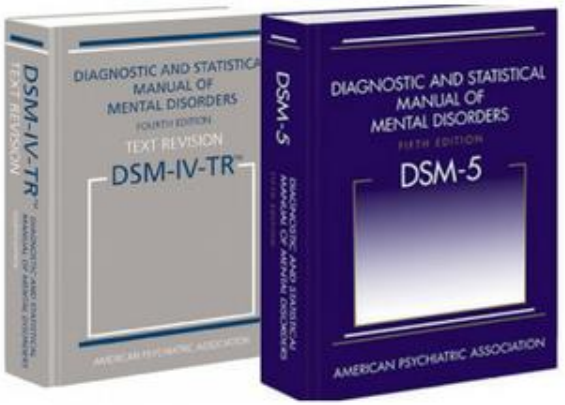
- **Environmental factors**: being rised in a city, cannabis use, parental age, poor nutrition during pregnancy, certain infections

- High rate of substance abuse

Schizophrenia

Diagnostic criteria (Diagnostic and Statistical Manual of Mental Disorders - DSM-5)

- At least **two** of the following symptoms are present during 1 month:



1. delusions,
2. hallucinations,
3. disorganized speech,
4. grossly disorganized or catatonic behavior.

Treatment

- Goals: restore behavior, cognitive or psychosocial functions
- Pharmacological & non-pharmacological (family)

Schizophrenia – animal models

- Developmental models - manipulations of environment, or drug administration **during the sensitive perinatal period, to produce irreversible changes in CNS development**
- Pharmacological models: drug – induced (amphetamine)
- Lesion models – neonatal lesion in hippocampus
- Genetic models

	Methods	*DA-related behavior*	*Gating*	*Cognitive Behavior*	*Social Behavior*	*Molecular/Morpho-logical Signature*
1	Maternal Deprivation		Disrupted PPI, Effect develops after puberty Disturpted Latent Inhibition), Audiotory sensory gating (N40) and startle habituation	Increased impulsivity, depressive-like responses		altered cannabinoid receptor expression in hippocampus; increased plasma glucocorticoid levels
4	Maternal Malnutrition	Enhanced amphetamine- but not MK-801-induced locomotion and apomorphine-induced stereotopy; (females only with post-pubertal onset)	Disrupted PPI (females only with post-pubertal onset)	Decreased learning and memory		Increases in NMDA receptor binding (sex- and region-specific); increased DA receptor binding and decreased DA transporter binding in striatum (females only), decreased LTP,

5	Prenatal Immune Challenge: LPS	Increased amphetamine-induced locomotion	Enhanced acoustic startle; disrupted PPI (worse in males)		Reduced social interaction, possibly due to increased anxiety	Reduced dendritic complexity in PFC and hippocampus; increased accumbal and stria terminalis DA; elevated serum cytokine levels;
6	Prenatal Variable Stress	Increased response to amphetamine and PCP with post-pubertal onset	Disrupted PPI and N40 AMPH-induced locomotor activity	Impaired object, social recognition and social memory	Impaired social interaction present in adolescent and adult rats;	NMDA, GABAergic and presynaptic protein dysregulation Reduced weight of hippocampus, increased levels of CORT, changes in gene expression in the frontal lobe

Depression

- Mood disorder
- Disorder of emotions rather than a disturbance of thought
- Common & underdiagnosed & undertreated
- **Major depressiom: 20 % of population**

➢ unipolar (persistant unpleasant mood) 2xF>M

➢ bipolar (alternating periods of depressions and mania) F=M

Etiology

- **Genetic predisposition**
- **Life events** – physical abuse, sexual abuse, unequal parental care of siblings
- **Medical treatments** – drug induced depression
- **Substance induced** – alcohol, sedatives, opioids, hallucinogens
- **Non-psychiatric illnesses** – result of other diseases

DEPRESSION

SIGNS AND SYMPTOMS

HELPLESSNESS

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GUILT

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ANGER

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WITHDRAWING FROM FRIENDS & FAMILY

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NO CONCENTRATION

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THOUGTS OF DEATH

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CHANGES IN APPETITE

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ENERGY LOSS

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SLEEP PROBLEM

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ALCOHOL AND DRUG ABUSE

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Unipolar depression

- melancholic – **depression is worse in the morning**, **insomnia** with early morning awakening, **anorexia** with significant weight loss, psychomotor retardation or agitation, excessive or **inappropriate guilt**, loss of interest in activity, inability to respond to pleasurable stimuli, and a complete loss of capacity for joy.

- atypical – becomes worse as the day progresses, overeating, and hypersomnia

- depression with psychotic features – delusions or hallucinations

- depression with catatonic features - excessive mobility or motoric immobility, extreme negativism, repetitive speech, strange voluntary movements.

Bipolar depression

- manic – depressive illness
- **periods of elation or irritability (mania) with or without (unipolar mania) episodes of depression**

- <u>manifestations of mania:</u>

1. ↓ need for food and sleep
2. labile mood
3. irritability
4. rapid and pressured speech
5. excessive involvement with pleasurable activities

- rapid cycling – four or more mood shifts during 1 year F>M

MANIC

- Onset between 18-30 yrs old
- Mood:
  - Elevated
  - Expansive
  - Irritable
- Speech:
  - Loud-Rapid
  - Punning
  - Poor Judgment
  - Clanging
  - Vulgar
- ? Wt. loss
- Grandiose delusions
- Distracted
- Hyperactive
- ↓ Need for sleep
- Inappropriate Dress
- Flight of ideas

DEPRESSIVE

- Previous manic episodes
- Feelings of
  - Worthlessness
  - Guilt
  - Hopelessness
- ↑ Anger & Irritability
- ↓ Interest in pleasure
- Negative views
- Fatigue & ↓ Energy
- ↓ Appetite
- Constipation
- Insomnia
- ↓ Libido
- Suicidal preoccupation
- May be agitated or have movement retardation

Depression - treatment

- antidepressant drugs

- psychotherapy

Depression – animal models

Assessment of various animal models and their advantages and disadvantages.

Animal model	Emulated MDD characteristics
Learned helplessness (LH)	Hopelessness, decreased motor activity, weight loss/ lack of weight gain, decreased reward sensitivity
Early life stress (ELS)	Anxiety, down-regulated BDNF expression
Social defeat	Anxiety, anhedonia
Olfactory bulbectomy (OBX)	Anhedonia, reduction of serotonin and 5-HIAA in the brain
Unpredictable chronic mild stress (UCMS)	Anhedonia, decrease in reward sensitivity
Chronic restraint stress (CRS)	Atrophy in hippocampal CA3 pyramidal cells, increased corticosteroid levels
Glucocorticoid/corticosterone (CORT)	Anxiety, dysregulation of HPA Axis
Transgenic models	Dependent upon brain area and targeted genes

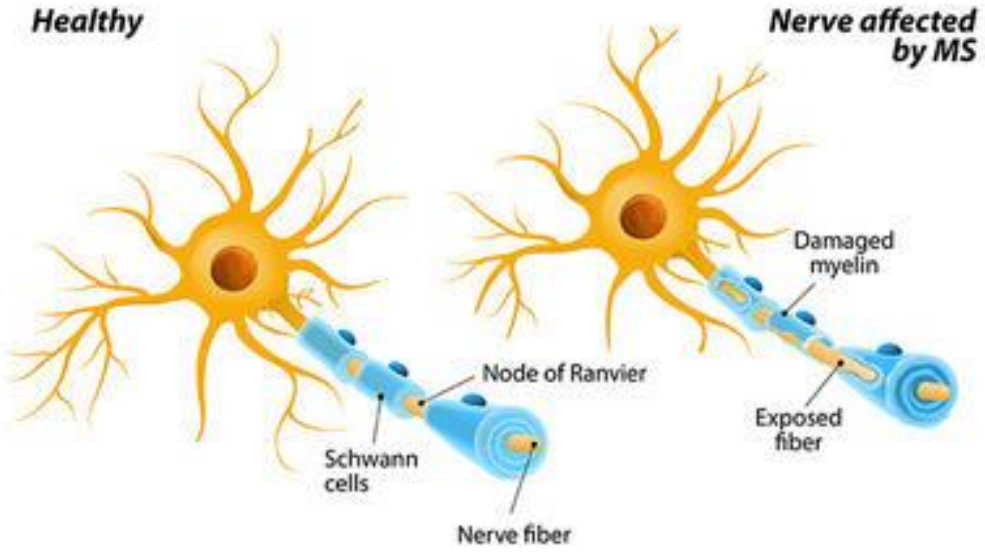
Multiple sclerosis

- Demyelination of neurons in the white matter of the brain, spinal cord and optic nerve => conduction abnormality

- Destruction by IS or fail to produce myelin

- **formation of lesions in the central nervous system (also called plaques), inflammation, and the destruction of myelin sheaths of neurons**

- First symptoms 20-40 years, **F>M**



Etiology

- Prevalence – varies around the world
- 2xF>M
- Not directly inherited – familiar predisposition
- genetic and environmental factors
- Infections
- Smoking
- Stress …

Symptoms

➢depends on the location and extent of the lesion

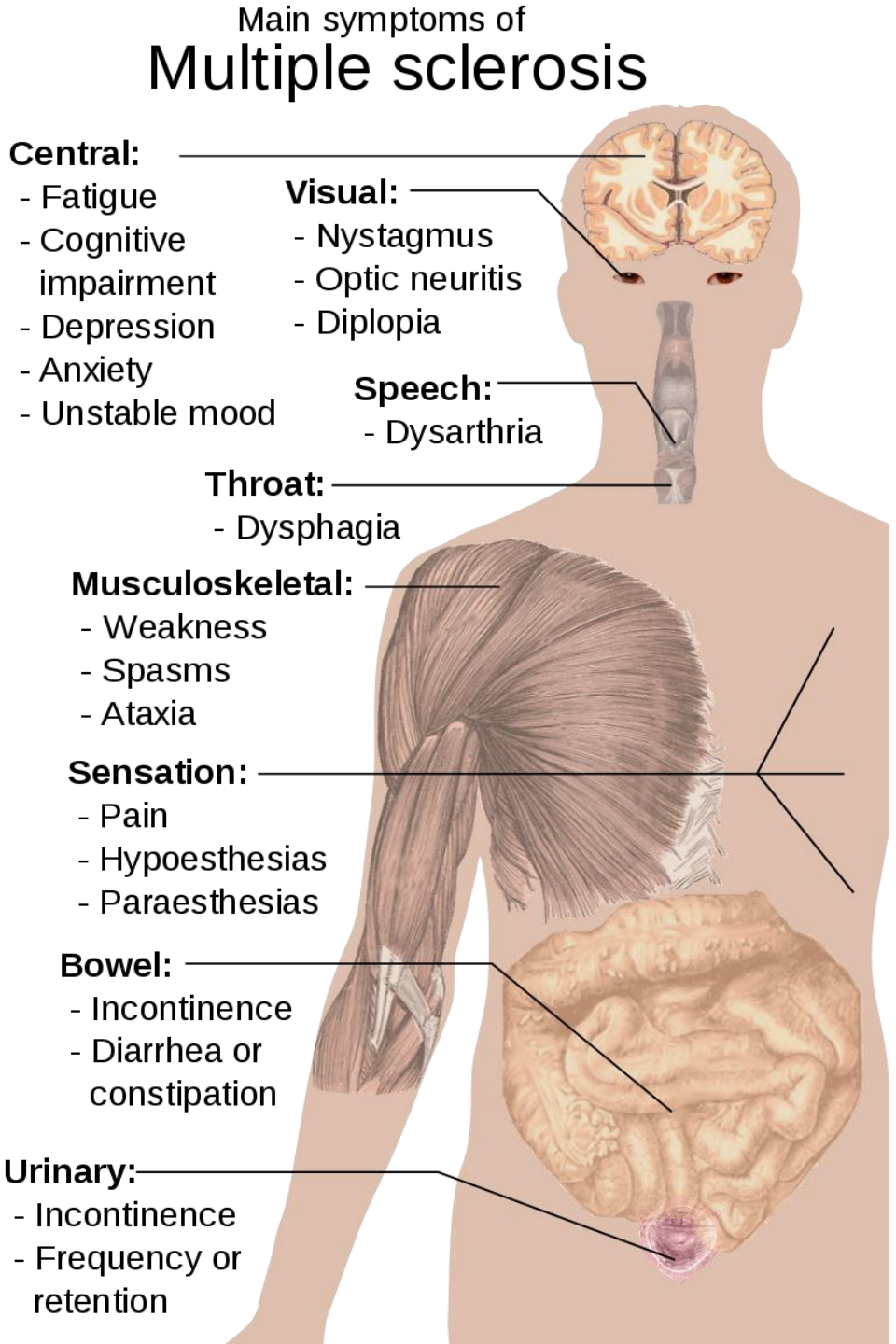
Treatment

•to treat acute symptoms of the disease – corticosteroids

•those used to modify the course of the disease - interferon-beta

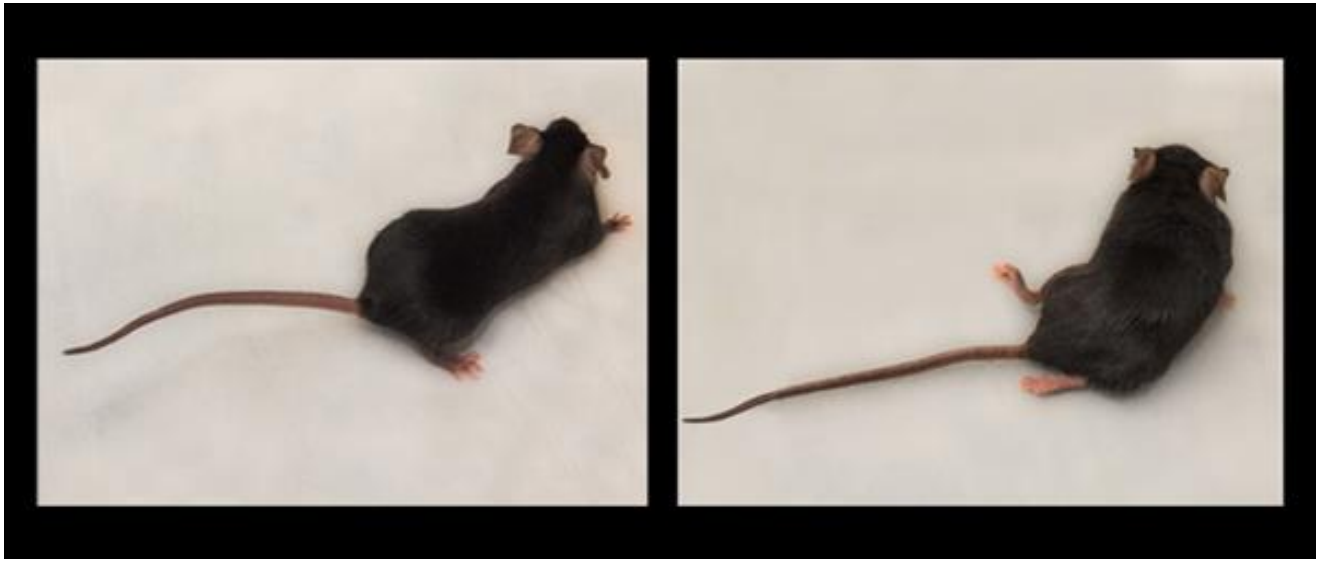
•those used to interrupt progressive disease – cyclosporine

•those used to treat the symptoms of the disorder - diazepam



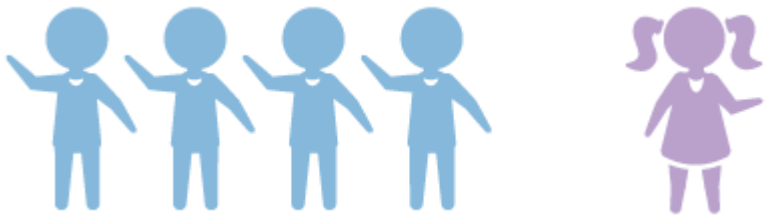
Multiple sclerosis – animal models

- **Theiler's murine encephalomyelitis virus (TMEV)** – induced animal model of MS
- TMEV = single-stranded RNA picornavirus
- by intracerebral infection with TMEV



- Presence of abnormal or impaired development

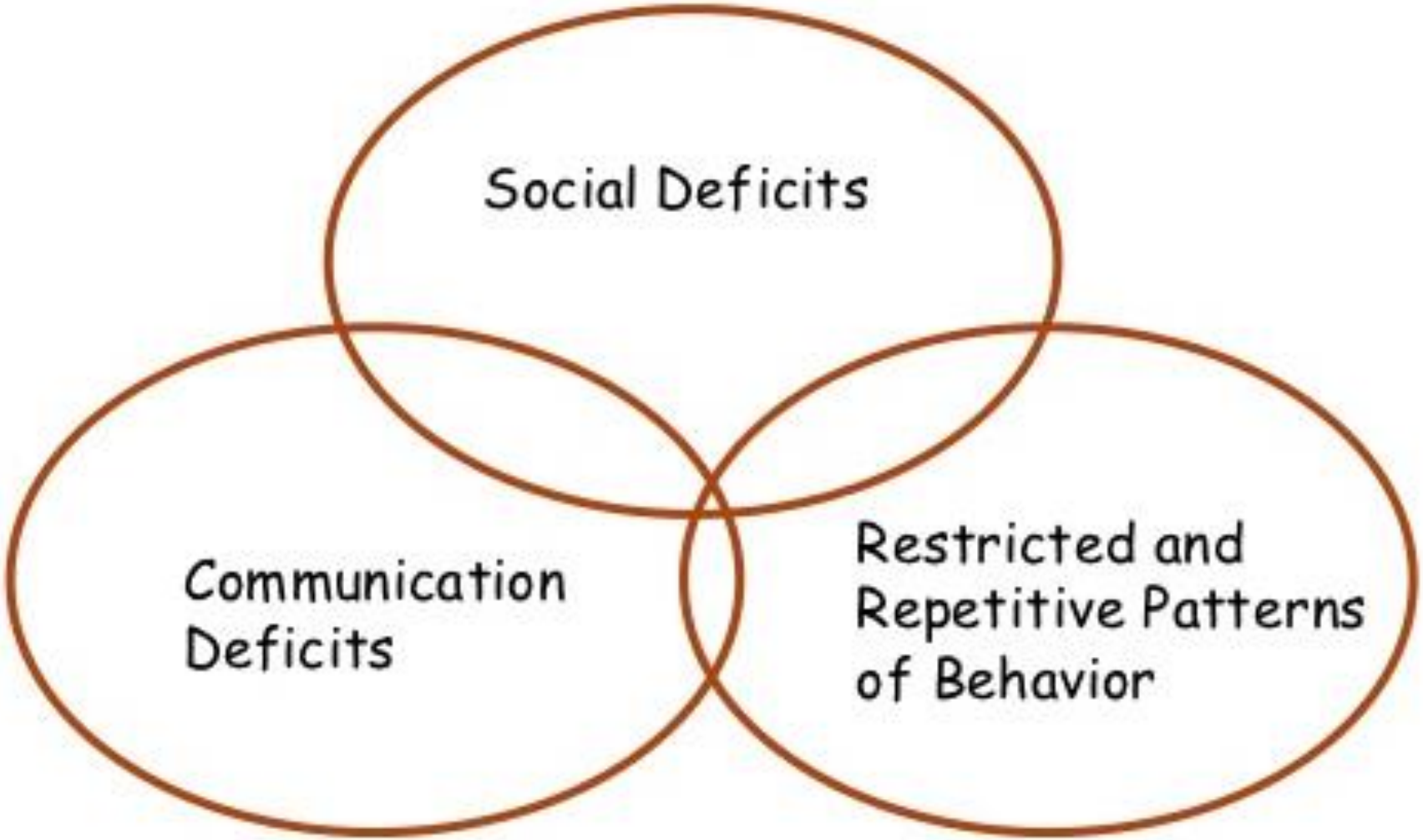
- Onset of symptoms: before 3 years of age



Etiology

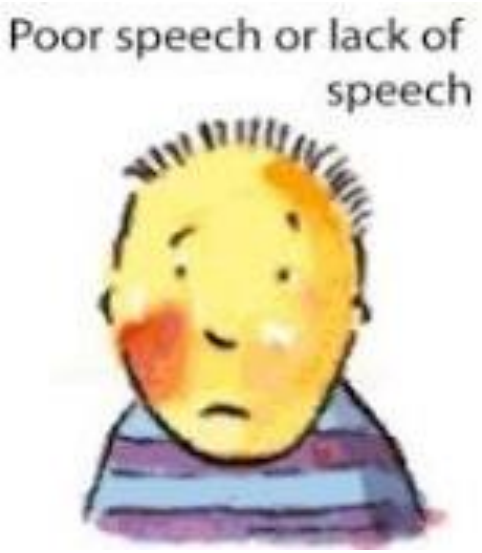
- still unknown
- multiple factors:
  - **genetic** (more than 1000 candidate genes)
  - **environmental (non-genetic)** – environmental chemicals, maternal factors, drugs
  - **advanced age**

Symptoms


Social Deficits
Communication Deficits
Restricted and Repetitive Patterns of Behavior

Communication deficit

- development of spoken language - delayed
- verbal and nonverbal communication - qualitative impairments



Autism – social deficits

Inability to relate to children or adults

Oversensitive or undersensitive to sound

Lack of awareness of Danger

Hyperactivity or Passiveness

Strange attachment to objects

Inappropriate playing with toys

Inappropriate laughter or crying

Oversensitive or undersensitive to touch

Lack of eye contact

Difficulty dealing with changes in routine

Autism – repetitive behavior

- **Motor stereotypes:** repeated non-purposeful movements: hand flapping, head rolling, body rocking

- **Compulsive behavior:** repeated forms of behavior performed according to rules: the arrangement of objects in stacks or lines

- **Sameness behavior:** insistence on sameness: insistence on the position of objects e.g. lining up the toys in a certain order

- **Ritualistic behavior:** performing daily activities in the same manner: a dressing ritual

- **Restricted behavior:** limited range of focus, interest, or activity: preoccupation with a single television program, toy, or game

- **Self-injurious behavior:**eye-poking, skin-picking, hand-biting, head-

Autism - treatment

- Only symptomatic
- Pharmacological: psychoactive drugs, anticonvulsants – antidepressants, antipsychotics
- **Fecal microbiota transplantation (FMT):**

frontiers | Frontiers in Psychiatry

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Effect of fecal microbiota transplantation in children with autism spectrum disorder: A systematic review

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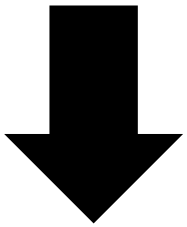
SHANK3 mouse model of Autism
SHANK 3 protein

- scaffold protein at excitatory synapses
- proper synaptic development and function
- functioning of synapses (cell to cell communication)
- formation and maturation of dendritic spines (transmission of nerve impulses)

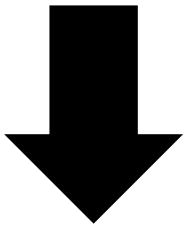
SHANK 3 and ASD

- ~ 43 SHANK3 gene mutations:

1. disruption of the function of the SHANK3 protein
2. prevention of the protein production



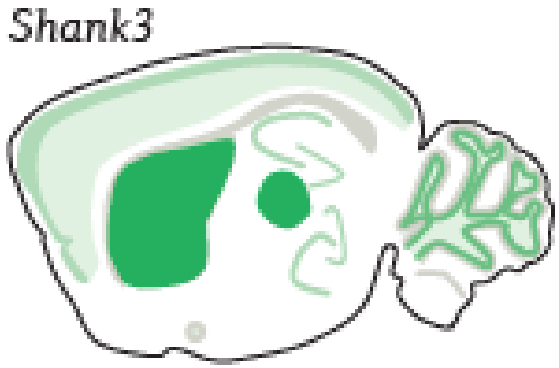
disruption in cell to cell communication



ASD

CNS expression

- **SHANK1** – cortex, thalamus, amygdala, hippocampus (CA1 and CA3), cerebellum
- **SHANK2** – cortex, thalamus, hippocampus (CA1 and CA3), dentate gyrus, cerebellum, (kidney and liver)
- **SHANK3 – heart, spleen, cortex, thalamus, striatum, hippocampus (more in CA3 than in CA1), dentate gyrus, cerebellum**

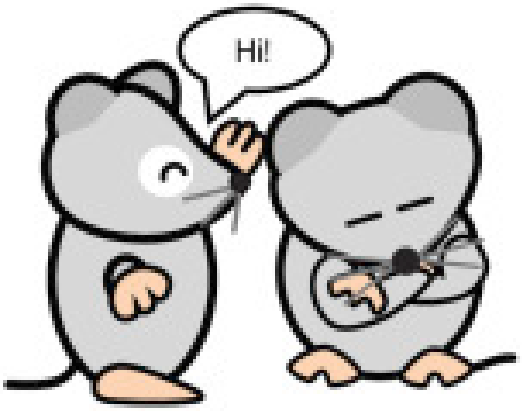


SHANK3 isoforms expression in the brain

Brain region/ cell type	SHANK3 isoform				
	3A	3B	3C	3D	3E
Striatum	Enriched	Low	Low	Low	Enriched
Cortex	Present	Low	Low	Low	Present
Hippocampus	Present	Low	Low	Low	Present
Thalamus	Present	Low	Low	Low	Present
Amygdala	Present	Low	Low	Low	Present
Cerebellum	Low	Low	Enriched	Enriched	Low
Hippocampal neuron	Abundant mRNA	Abundant mRNA	Abundant mRNA	Abundant mRNA	Abundant mRNA
Hippocampal astrocyte	Detectable mRNA	No mRNA detected	Detectable mRNA	Detectable mRNA	Detectable mRNA

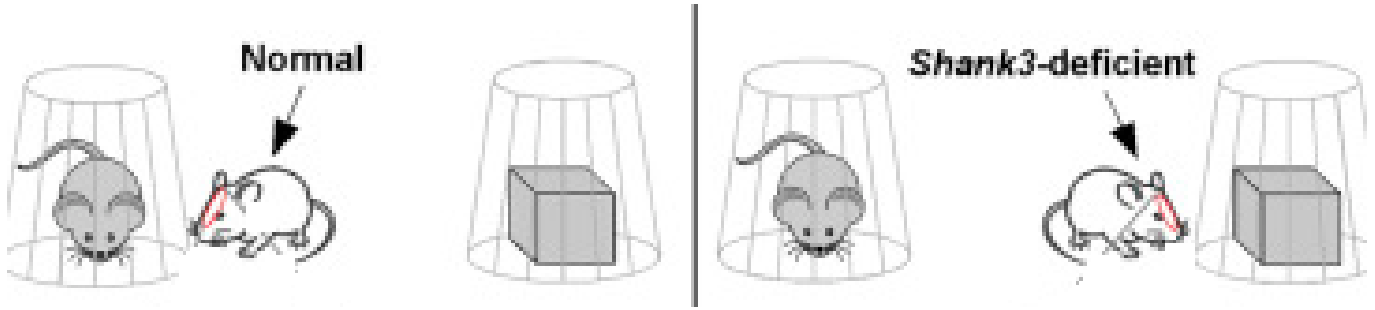
The link between SHANK genes and ASD

- mutations or disruptions in the SHANK gene family account for ~1% of all patients with ASD
- correlation: SHANK1–3 mutations vs degree of cognitive impairment ASD
- patients with SHANK3 mutations - more-severe cognitive deficits than with SHANK1 or SHANK2



↓communication

↑ repetitive behavior



↓sociability

Traumatic brain injury (TBI)

- = intracranial injury
- external force cause brain injury

- **TBI classification:**
  - **severity** (mild, moderate, and severe)
  - **mechanism** (closed or penetrating head injury)
  - **other features** (specific location or over a widespread area)

- **Following TBI:**
- physical, cognitive, social, emotional, and behavioral symptoms
- complete recovery vs permanent disability or death

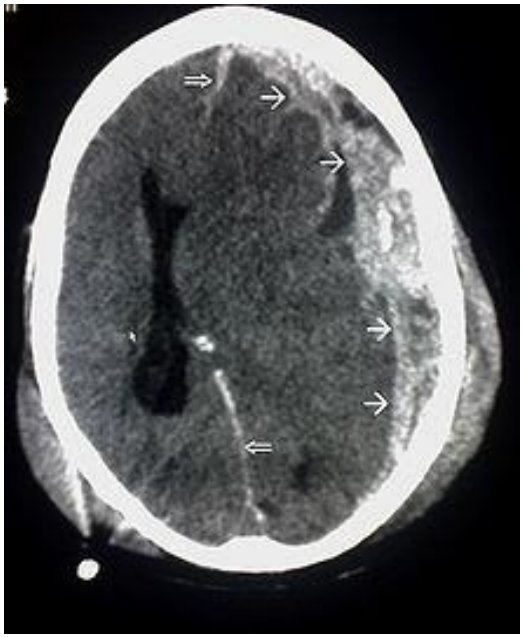
- **Causes**
  - falls
  - vehicle collisions
  - violence

Traumatic brain injury

- sudden acceleration or deceleration within the cranium or complex combination of both

- events leading to further injury:
  - alterations in cerebral blood flow
  - pressure within the skull

- **Diagnosis:**
- computed tomography (CT)
- magnetic resonance imaging (MRI)



CT scan Spread of the subdural hematoma (single arrows), midline shift (double arrows)

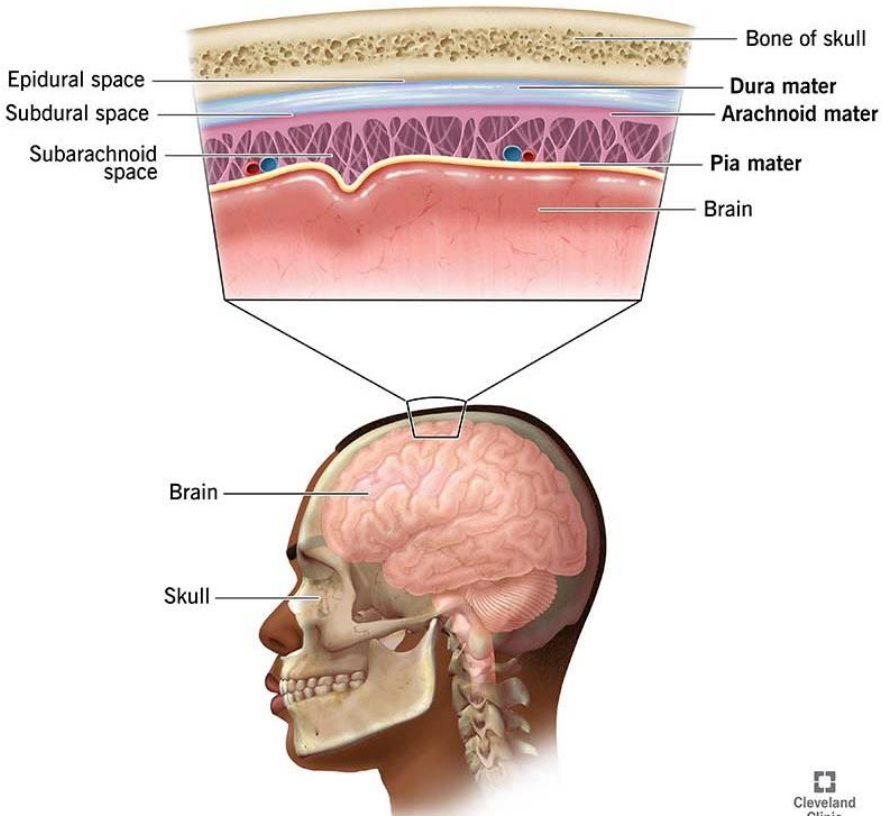
Pathological features

- **Lesions:**
  - **extra-axial** = within the skull but outside of the brain (epidural, subdural, subarachnoidal hematoma)
  - **intra-axial** = within the brain tissue (intracerebral hemorrhage with bleeding in the brain)

- **Damage from TBI:**
  1. **focal** - specific areas of the brain (hematomas)
  2. **diffuse** - distributed in a more general manner:

  ❑ edema (swelling)

  ❑ diffuse axonal injury (a widespread damage to axons including white matter tracts and projections to the cortex)



Symptoms - Mild TBI

- headache
- vomiting
- nausea
- lack of motor coordination
- dizziness
- difficulty balancing
- lightheadedness
- blurred vision or tired eyes
- bad taste in the mouth
- fatigue or lethargy
- sleep problems
- ringing in the ears

- **Cognitive and emotional symptoms:**
- behavioral or mood changes
- confusion
- trouble with memory, concentration, attention, or thinking

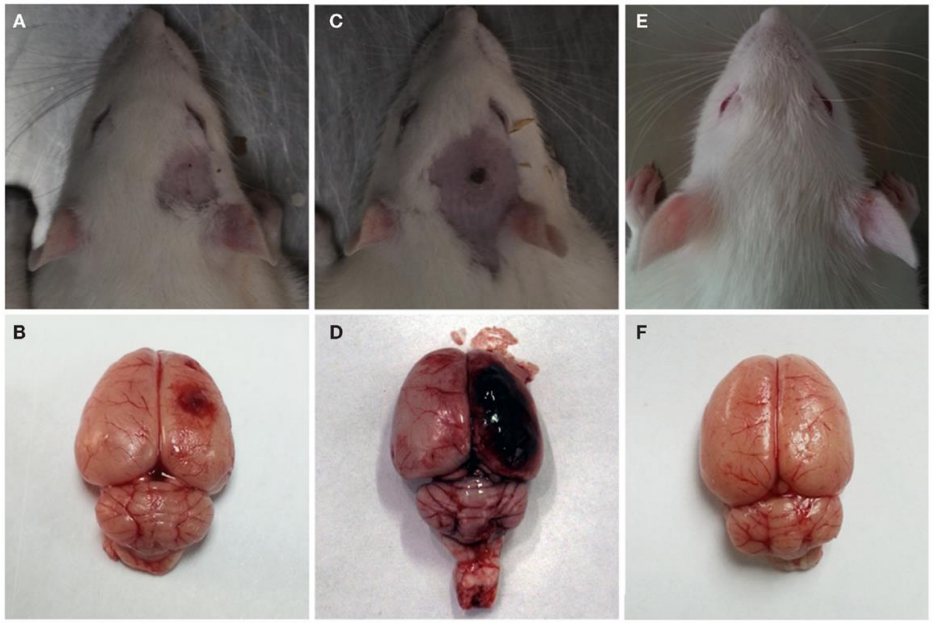
Symptoms – Moderate and Severe TBI

- continuous headache
- repeated vomiting or nausea
- convulsions
- an inability to awaken
- dilation of one or both pupils
- slurred speech
- aphasia (word-finding difficulties)
- dysarthria (muscle weakness that - disordered speech)
- weakness in the limbs
- loss of coordination
- confusion
- restlessness

- **Cognitive and emotional symptoms:**
- changes in appropriate social behavior, deficits in social judgment, and cognitive changes, problems with sustained attention, processing speed
- Alexithymia – 60% of TBI patients

Animal model of TBI

- Under anesthesia using weights (25g)
- Height 50 cm
- Side of the head



Mild TBI | **Severe TBI** | **CTRL – without TBI**