# Extrapyramidal System and its Disorders

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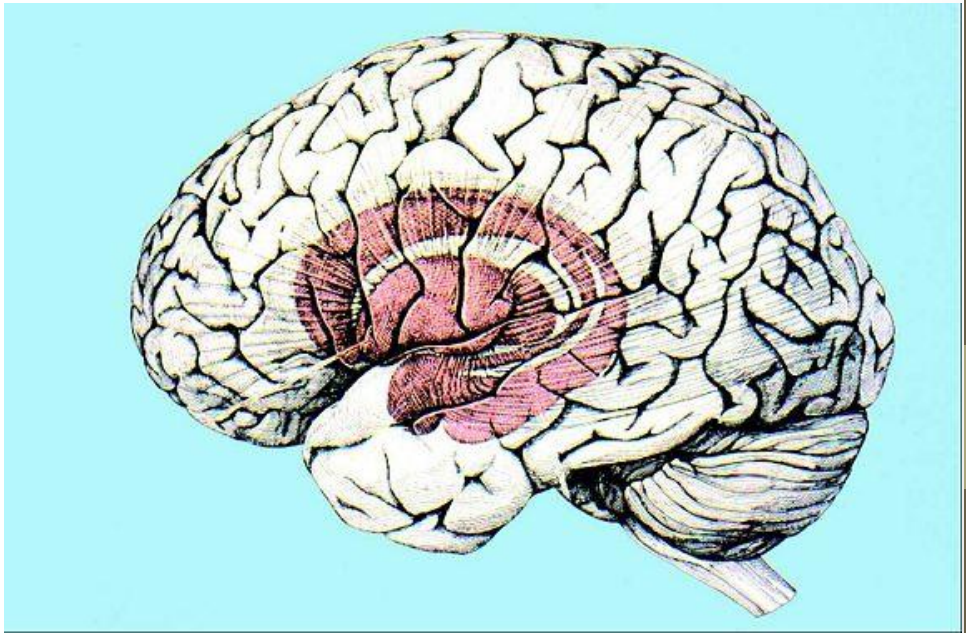

MEDICAL UNIVERSITY - PLEVEN
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DEPARTMENT OF NEUROLOGY AND NEUROSURGERY
DIVISION OF NEUROLOGY

Lecture № 5

# EXTRAPYRAMIDAL SYSTEM AND ITS DISORDERS

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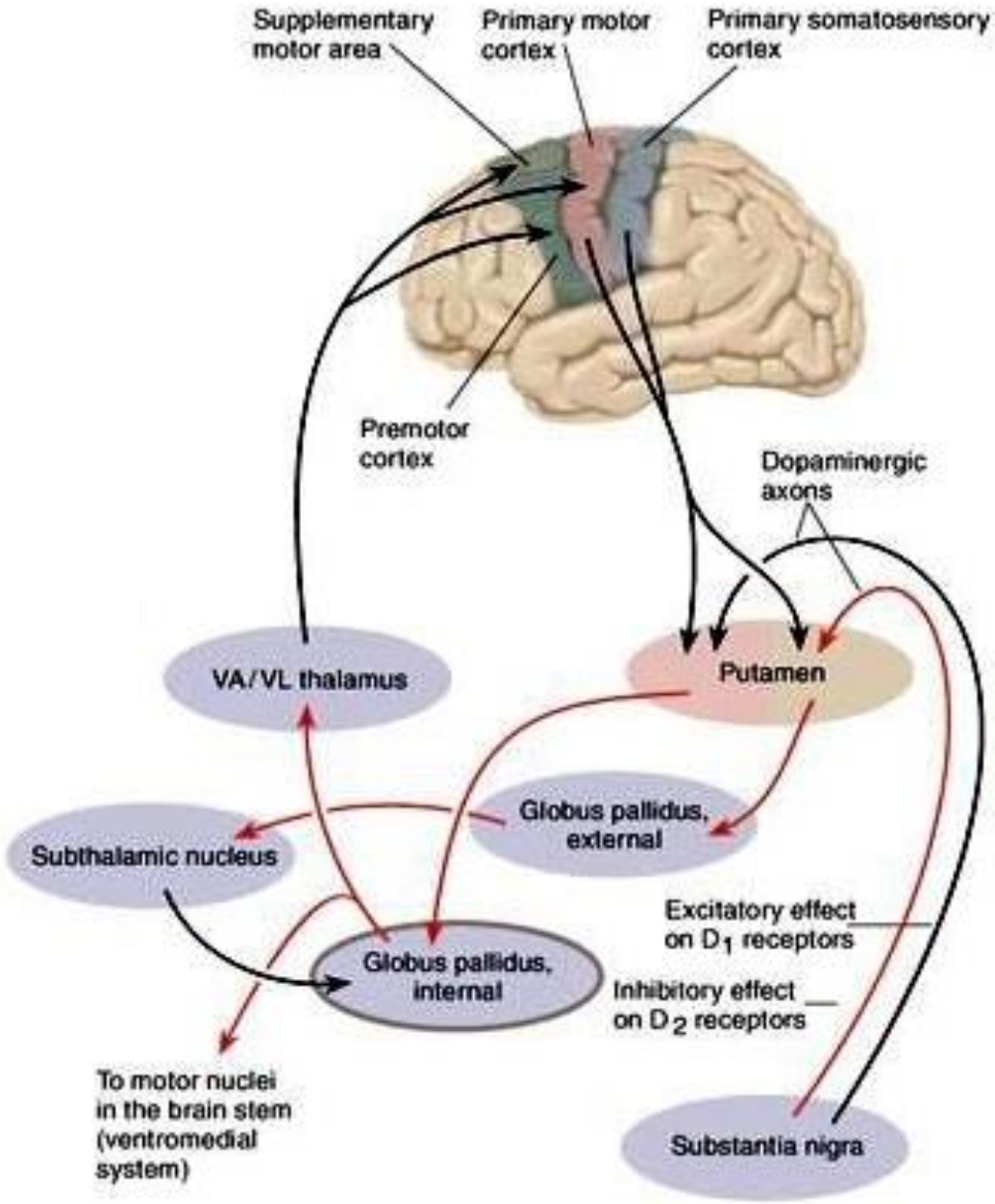
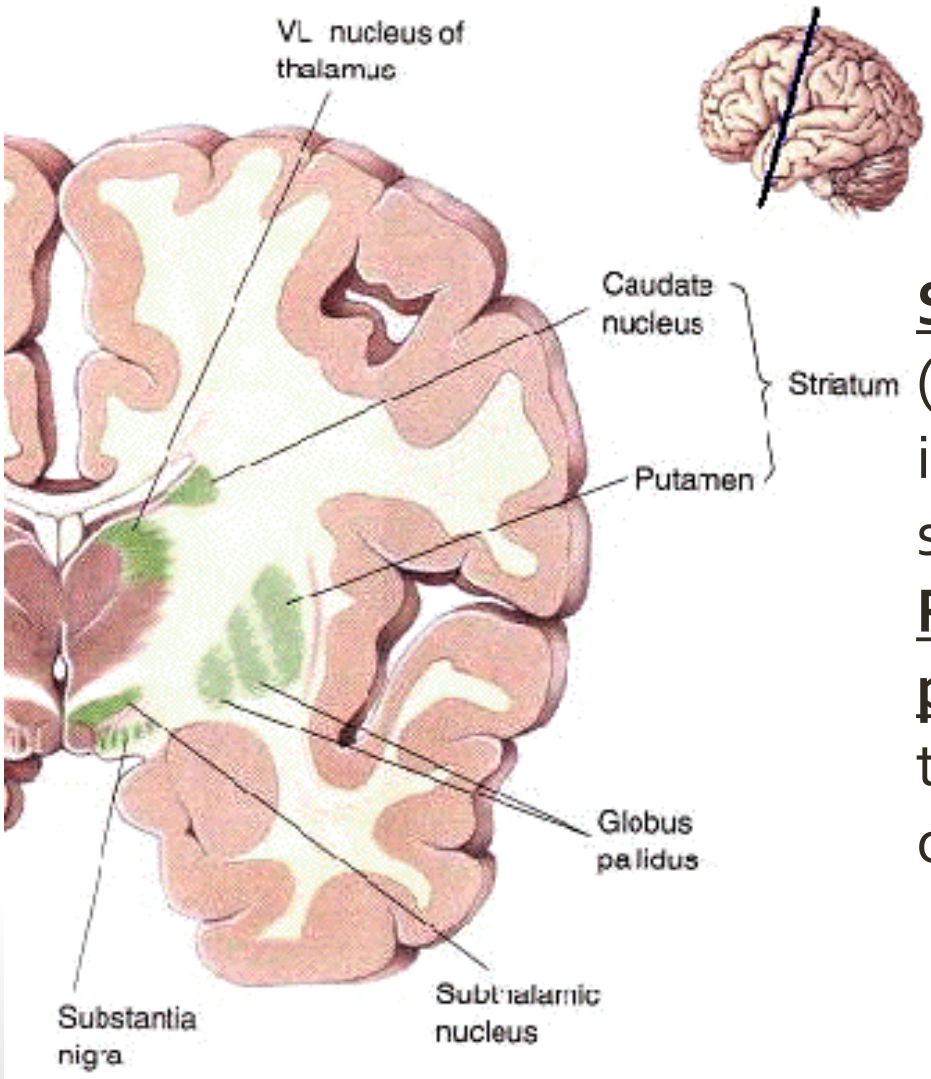
# General considerations

- **Extrapyramidal system:** a set of subcortical circuits and pathways presented by all motor gray structures and pathways that are not included in the **pyramidal system**.
- **Extrapyramidal system consists of:**

1. **Cortical areas 4, 6, 8** /premotor frontal areas, cingulate gyrus/;
2. **The basal ganglia**: caudate nucleus, lenticular nuclei (putamen, globus pallidus);
3. **Thalamus**;
4. **Nuclei of the brain stem** (black substance, red nucleus, vestibular nuclei, reticular nuclei, nucleus of Darkschewitsch, Lui's body, lower olives);
5. **Cerebellum**;
6. **Spinal cord**: γ-motor neurons and α-small motor neurons, located in anterior horns of the spinal cord.


Supplementary motor area
Primary motor cortex
Primary somatosensory cortex
Premotor cortex
Dopaminergic axons
VA/VL thalamus
Putamen
Globus pallidus, external
Subthalamic nucleus
Excitatory effect on $D_1$ receptors
Globus pallidus, internal
Inhibitory effect on $D_2$ receptors
To motor nuclei in the brain stem (ventromedial system)
Substantia nigra

# Basal ganglia




**<u>Striatum = Neostriatum</u>** (**<u>caudate nucleus + putamen</u>**) is the principle receptive structure of the basal ganglia; **<u>Paleostriatum = Globus pallidus + Substantia nigra</u>** is the principle output structure of the basal ganglia.

# Two parts of Extrapyramidal system:

## 1. Pallidum

- globus pallidus
- black substance /substantia nigra/
- red nuclei
- vestibular nuclei
- nucleus of Darkschewitsch
- lower olives
- Lui's body

- **Paleostriatum: globus pallidus & substantia nigra**
- **Pallidum is phylogenetically older then striatum. That's why in new born babies pallidum dominates!**

# Two parts of Extrapyramidal system:

## 2.Striatum

- Cortical areas 4,6,8
- Nucleus Caudatus
- Putamen

- **Neostriatum**: caudate nucleus and putamen
- **Corpus striatum**: n. lentiformis+ n.caudatus

**Only at the age of 4 – 5 months old striatum starts to influence on motor functions**

# Connections of Extrapyramidal system:

Subcortical extrapyramidal nuclei are interconnected directly, reciprocally and by fibre loops:

- The main **afferent** connections terminate in the striatum
  - ✓ **Cortical striate projection - inhibitory**
  - ✓ **Thalamic projection - facilitatory**
- Connections between the **basal ganglia** - Pallidum and striatum are closely connected with each other by means of such pathways:

✓ **Nigro-striatal** (dopaminergic) – black substance – nucleus caudate– it inhibits the neurons of striatum

✓ **Strio-nigral** (GABAergic)- nucleus caudated (GABA)– black substance – it controls production of dopamine.

- The main **efferent** projections: ansa lenticularis /striatum- pallidum/
- The main **reverberating circuits** of the extrapyramidal system:

**Cerebral cortex ⇨ Striatum ⇨ Pallidum ⇨ Thalamus ⇨ Cerebral cortex** /direct motor pathway/.

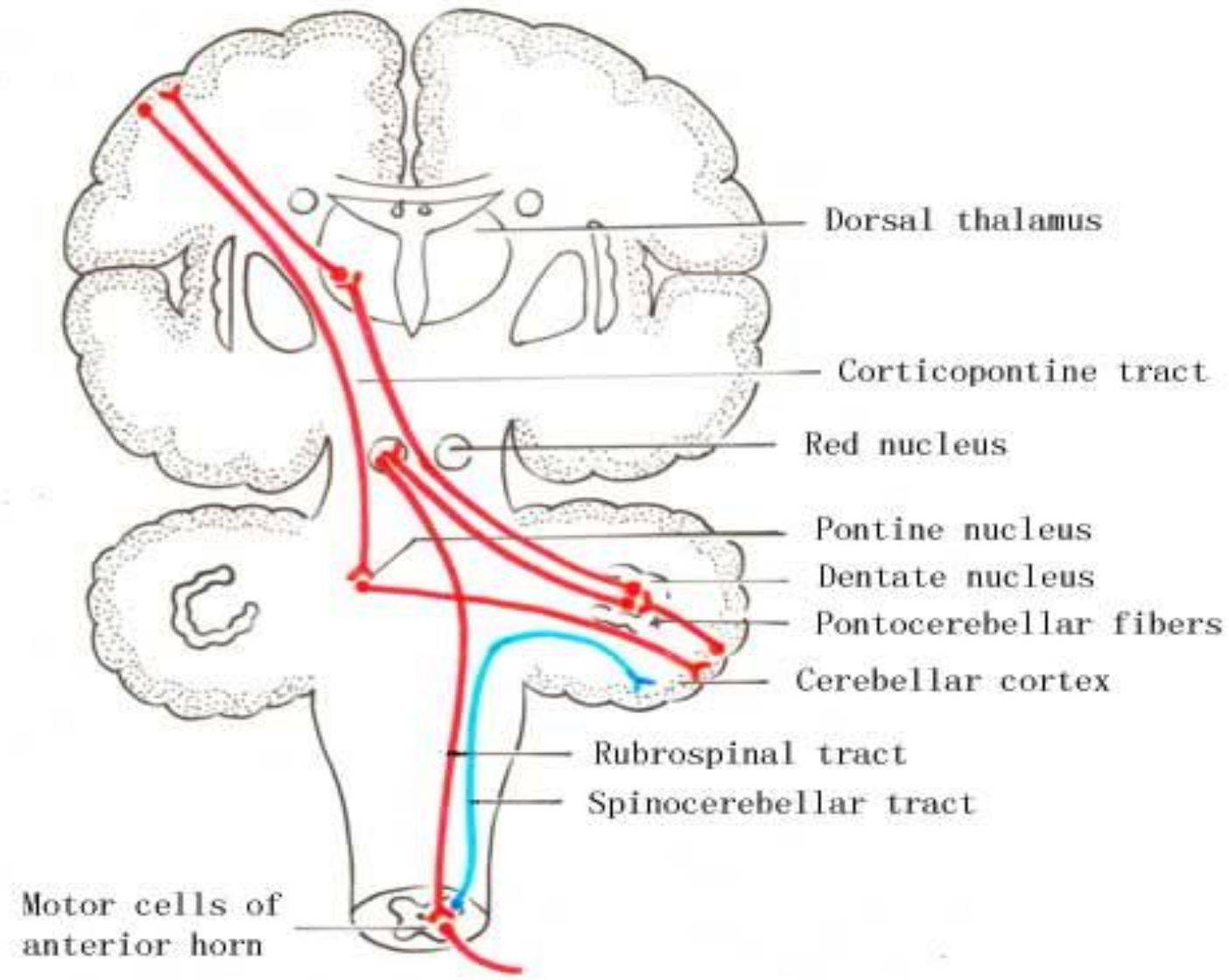



Fig. 15-28 The extrapyramidal system(corticoponto-cerebellar-cortex circuit)

# Connections of Extrapyramidal system:

- **Additional extrapyramidal circuits:**

✓ Striatum Pallidum Thalamus Striatum

✓ Pallidum N. Subthalamic Pallidum

✓ Striatum Substantia nigra Striatum

- **Subcortical descending system- extrapyramidal tracts;**

✓ Corticostriate

✓ Corticorubral

✓ Corticonigral

✓ Corticoreticular

- **Descending pathways from the basal structures via interneurons to the lower motor neurons;**

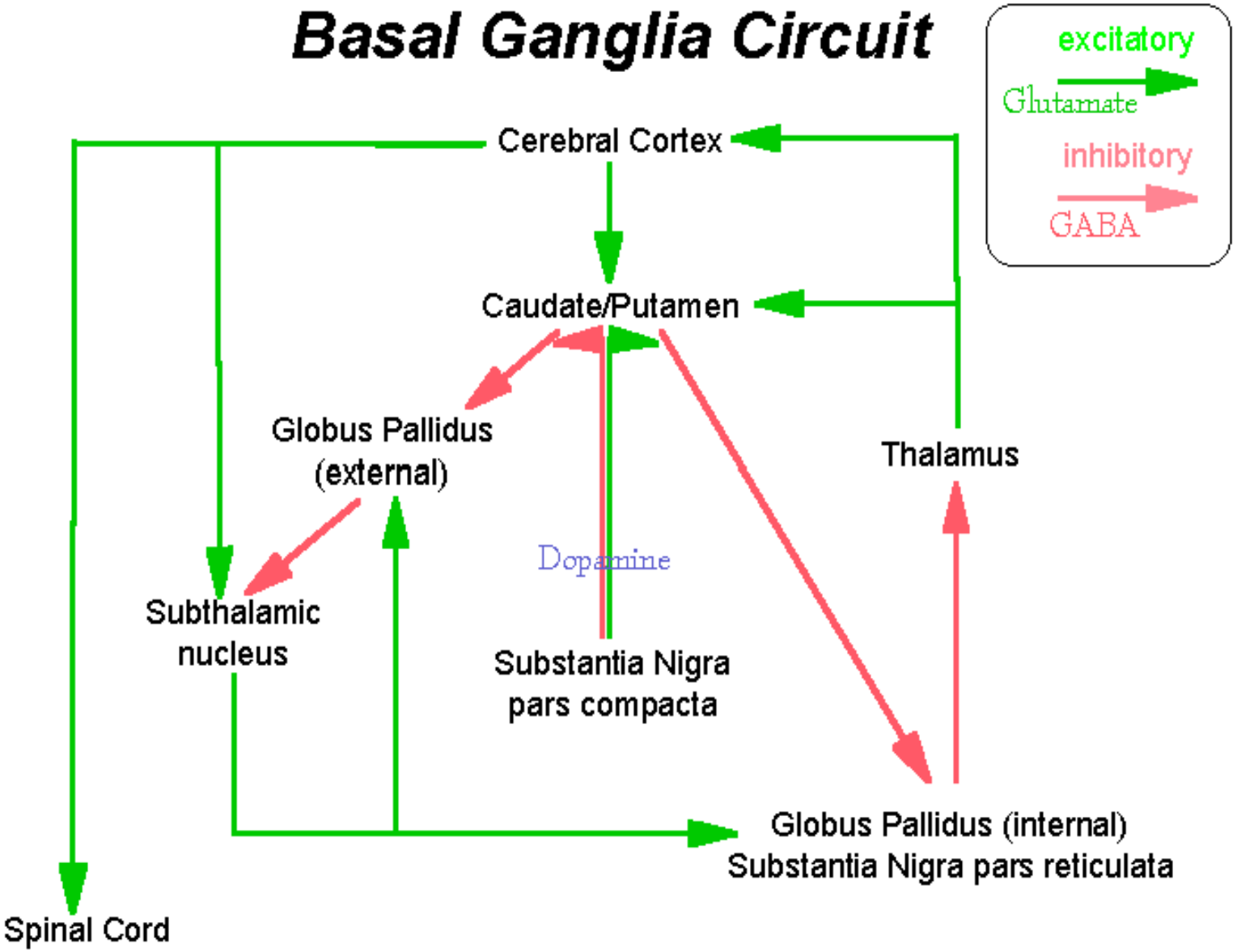
- Tr. olivospinalis
- Tr. rubrospinalis
- Tr. vestibulospinalis
- Tr. tectospinalis
- Tr. reticulospinalis

# Connections of the extrapyramidal system

- **Neurotransmitters in the basal ganglia**
  - ✓Dopamine – nigro-striatal system
  - ✓Acetylcholine- striatum

  **Stimulation of striatal dopamine receptors inhibits release of Acetylcholine and blockade of dopamine receptors causes an increase in the turnover of striatal Acetylcholine**
  - ✓GABA
  - ✓Norepinephrine
  - ✓Serotonin
  - ✓Enkephalin
  - ✓Glutamate

# Basal Ganglia Circuit

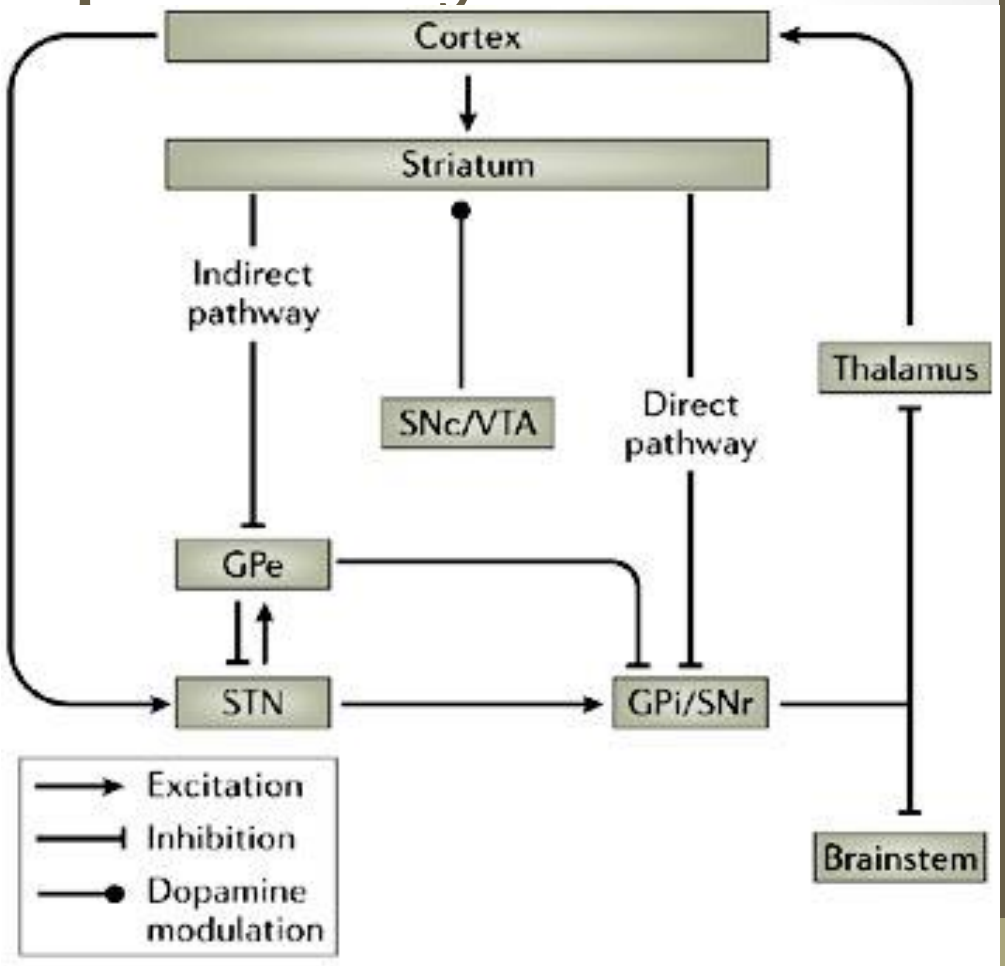


# Functions of Extrapyramidal system

- It prepares muscles to smooth economical movements;
- It determines the posture;
- It makes automatic  involuntary regulation of active conscious movements;
- It provides automatic stereotyped movements and reflector protective movements;
- It provides motor manifestation of emotions.

# Dopaminergic pathways

- functional balance
- cooperation of direct and indirect nigro-striatal pathways



# Extrapyramidal syndromes:

- **Akinetic - rigid  syndrome**: reduction of spontaneous activity, increase of muscle tone, (akinesia/hypo/bradykinesia, rigidity) = **Parkinson's syndrome** (*lesion of pallidum*);
- **Hyperkinetic syndromes**: involuntary and irregular movements  (tremor, chorea, ballismus, dystonia, myoclonus, tic) = **Syndrome of involuntary movements** (*lesion of striatum*)

# Parkinson's disease (PD) pathology

- Progressive degeneration (loss) of dopaminergic neurons in substantia nigra, projecting to the striatum;
- Resulting in decreased level of dopamine (imbalance in the neurotransmitter mechanism)
- Symptoms of PD appear when 70% of nigrostriatal dopamine neurons are lost - presynaptic lesion !
- Postsynaptic dopaminergic receptors D2 are intact

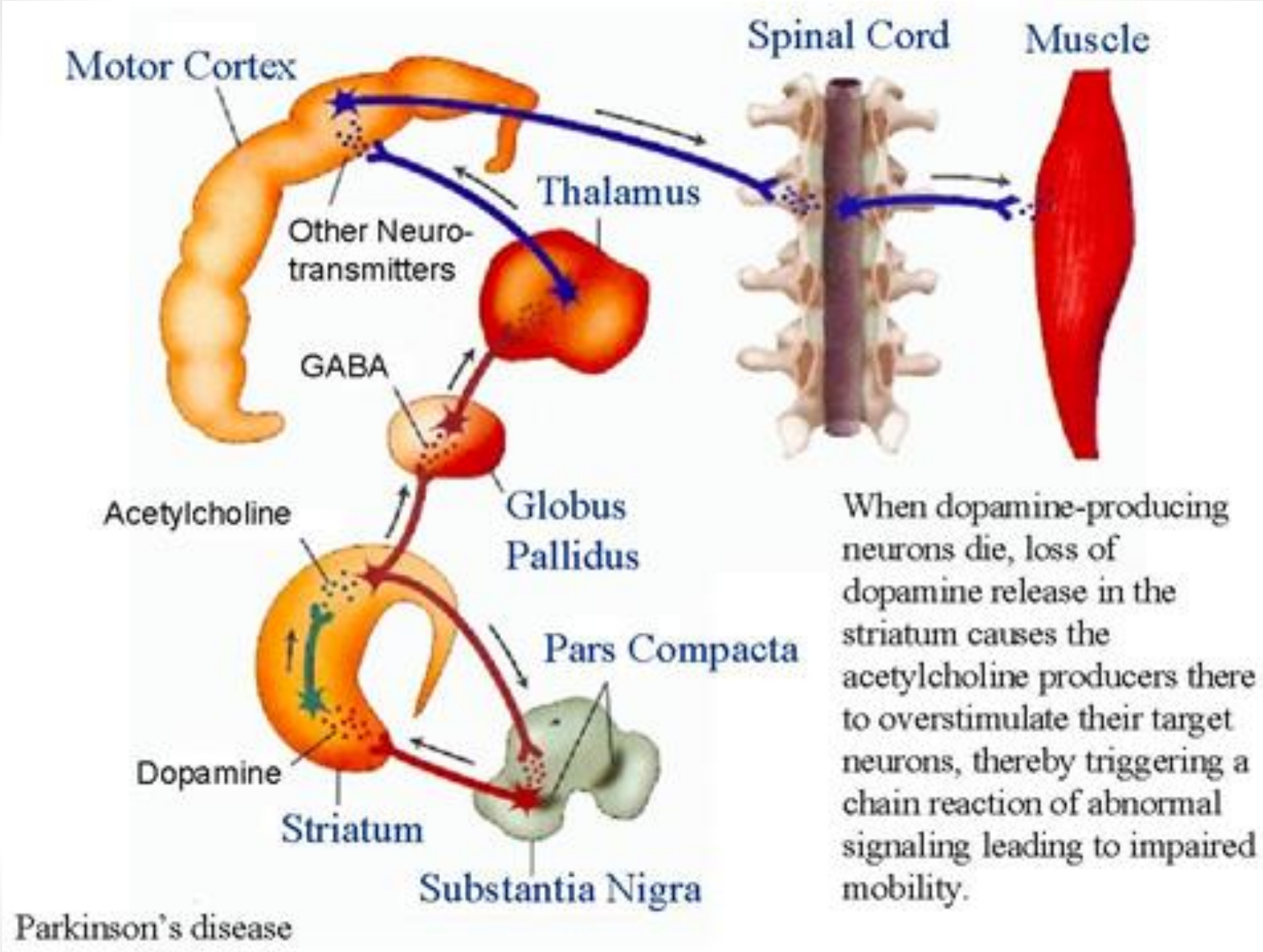
and response to dopaminergic therapy - levodopa is preserved

# Etiology

- The possible role of ageing in the pathogenesis of PD is suggested by its usual occurrence in late middle age, and by marked increases in its prevalence at older ages;
- According to the modern investigations the reason for this disease is inborn deficiency of tyrosinaminotransferase enzyme in dopamine;
- Parkinsonism may be defined in biochemical term as an inborn dopamine deficiency state;
- Another pathologic hallmark of PD is the Lewy body, an eosinophilic inclusion identified within neurons;
- Alfa-synuclein is a component of Lewy bodies;
- Mutations in the Parkin gene were first identified in Japanese families with a unique variant of parkinsonism.

# Basic symptoms of Parkinson's syndrome:

- Hypokinesia (Akinesia)
- Rigidity
- Tremor
- Postural instability


Motor Cortex
Spinal Cord
Muscle
Thalamus
Other Neuro-transmitters
GABA
Acetylcholine
Globus Pallidus
Pars Compacta
Dopamine
Striatum
Substantia Nigra
When dopamine-producing neurons die, loss of dopamine release in the striatum causes the acetylcholine producers there to overstimulate their target neurons, thereby triggering a chain reaction of abnormal signaling leading to impaired mobility.
Parkinson's disease

# Pathogenetic mechanisms:

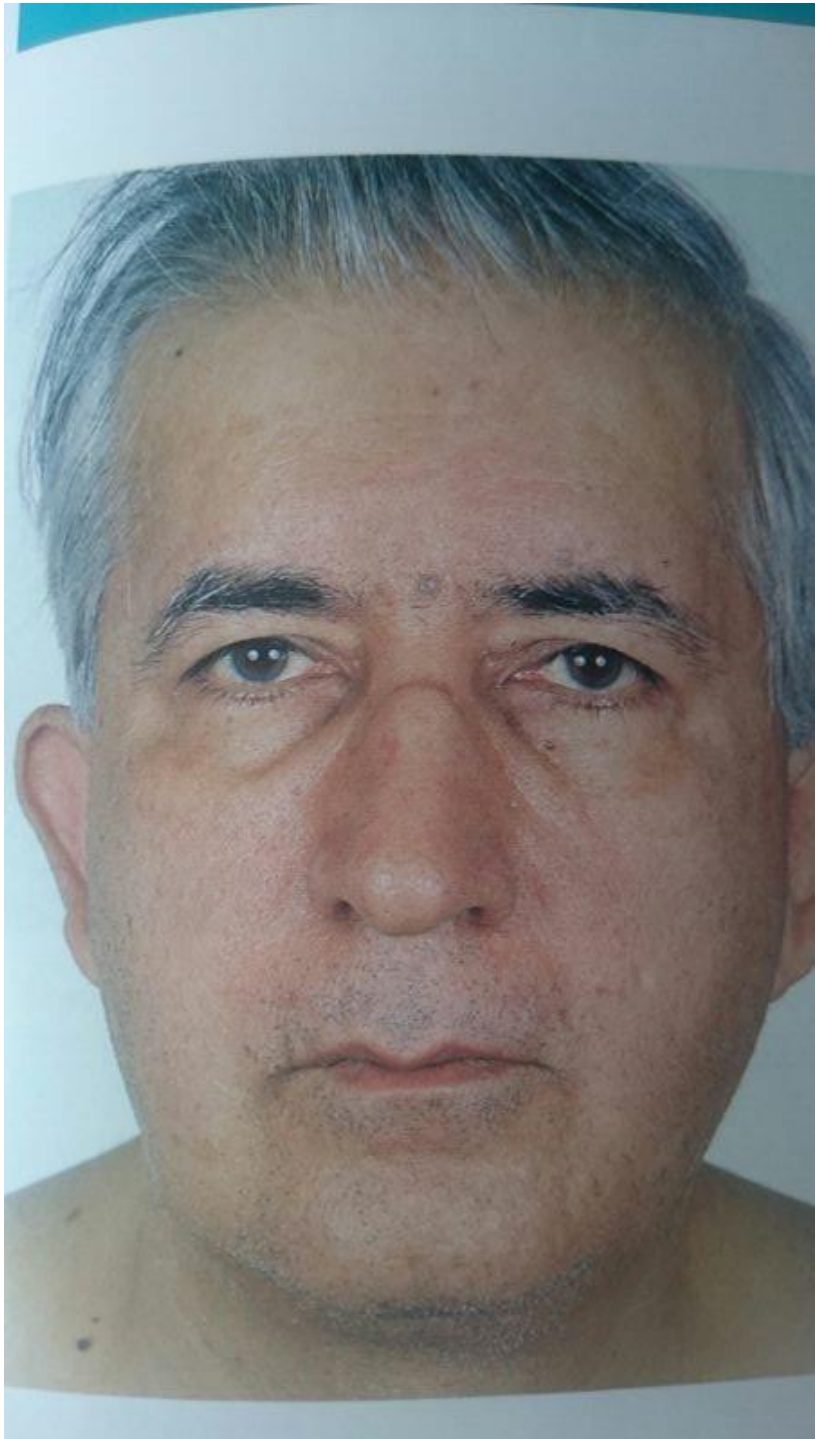
- Great cell loss in the substantia nigra, low concentration of dopamine in striatum and the influence of striatum on pallidum causes akinesia.

- The main cause of rigidity is the increasing of tonic reflex on muscles tension.

- The main source of tremor is the effect of thalamus (its nucleus ventro-lateralis ).

# Hypokinesia (Akinesia)

- Slow movements
- Bradykinetic and akinetic state
- The gait is shuffling and the steps are slight
- Parallel footprints
- The loss of associated swinging of the arm or arms when walking - (acheirokynesis)
- A lack of mobility of facial expression – hypomimic face
- Infrequent blinking of the eyelids (Mary' s symptom)
- Fixed look



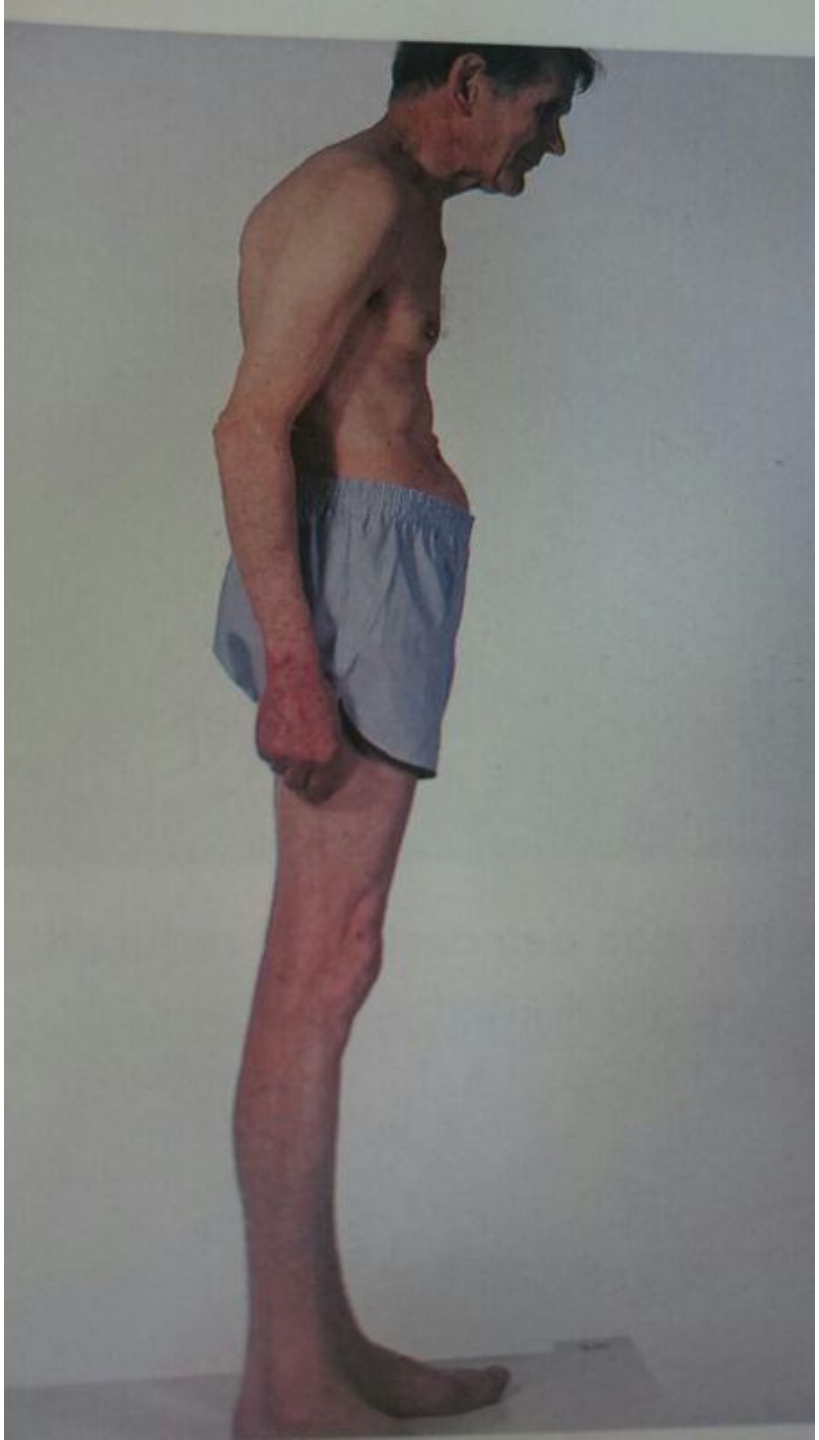
# Hypokinesia (Akinesia)

- **Inertia of rest** (that means it is very difficult for patient to start moving)
- **Inertia of movement** (the so-called propulsive gait, latero-pulsion or retro-pulsion)
- **Micrography** – handwriting is too small
- Speach is quite and inexpressive (**bradylalia**)
- **Paradoxical kynesis** is possible after strong impression or great emotions

# Rigidity

**Plastic type of increased muscle tone**:

- **Cogged-wheel symptom** (in carpal radial joints)
- Tonus increases in course of evaluation of nervous system state
- Tonus is expressed in the same manner in the group of flexors and extensors



# Tremor:

- Much more expressed in the distal parts of extremities, sometimes tremor of lips or lower jaw can occur
- It looks like coins counting
- It is much more expressed while resting. It disappears or decreases while moving
- Its frequency is 3 – 6 times per second

# Other features of Parkinson's disease

- **Bradyphrenia** (thoughts are too slow)
- **Bradymnesia** (recollection is slow,  too)
- While speaking such patients are boring (akairia )
- Usually they are in a bad mood. Depression is very typical for patients with Parkinson disease
- Sometimes they have **autonomic disorders:** Parasympathetic nervous system dominates in such patients – they have running saliva (aeriel symptome), hyperhydrosis, fatty skin and type of hair, bradicardia and arterial hypotension

# Tests:

- **The symptom of air pillow or Vartenberg symptom** – the patient is lying down. One props up his head a little bit and then quickly takes his hand out. Normally the head is falling down. But in patients with Parkinson disease the head stays in the same position for a while.
- **Westfahl's phenomena of paradoxical muscle constriction –** while foot extension it stays in the same position for a while.
- **Hand extension test.**
- **Test of knee flexion** – the patient is lying on his abdomen; his lower extremities are bended in knees. In patients with Parkinson disease the legs are fixed in this position for several minutes.

# Clinical forms of Parkinson disease:

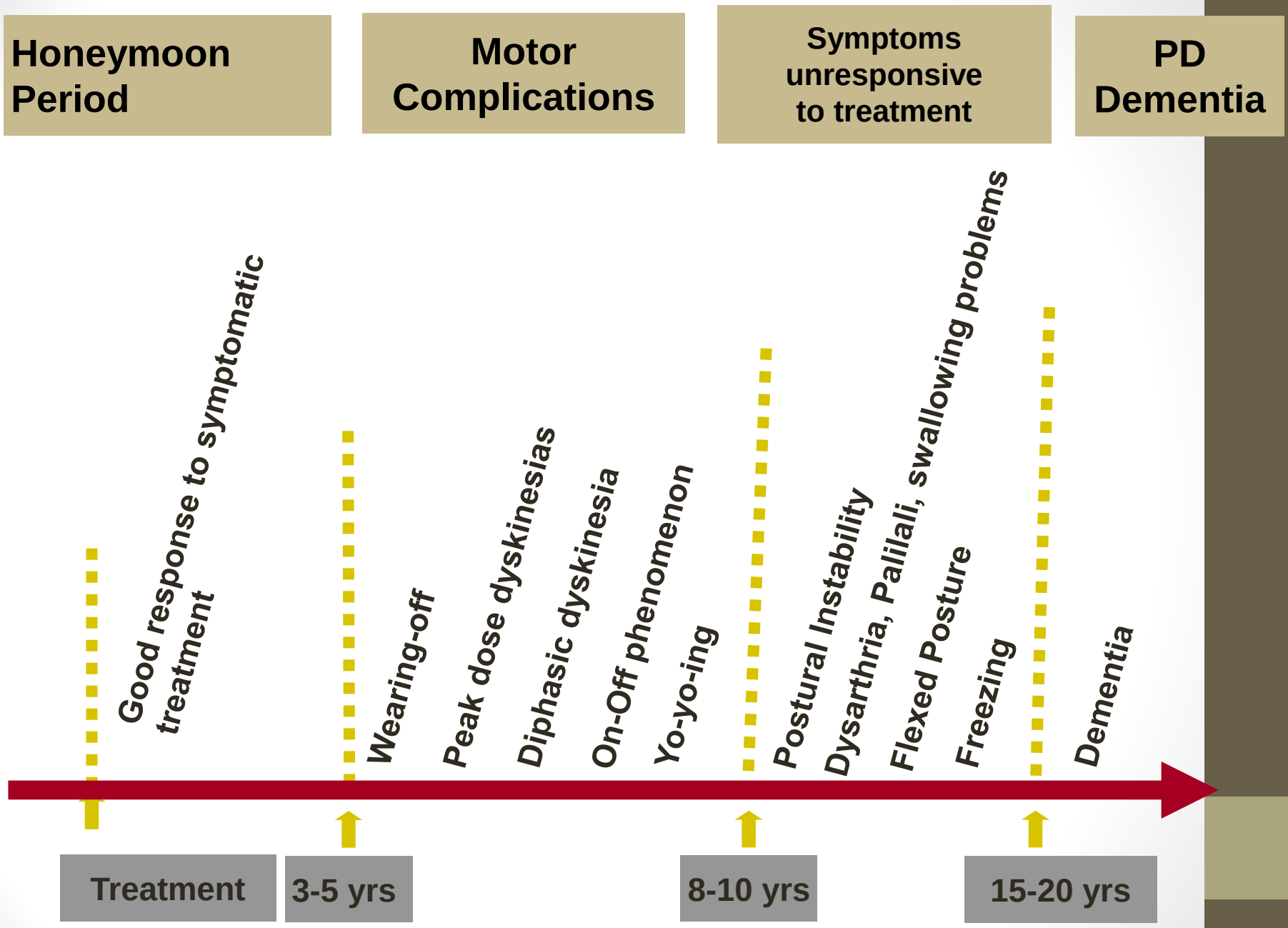
- Rigid (hypokynesia dominates)
- Trembling (tremor dominates)
- Mixed :
  - -rigid – trembling
  - -trembling – rigid

# Degree of severity :

- **The first degree** - expressed one or two main symptoms. The patient preserves professional and home activity
- **The second degree** – The patient is disabled professionally
- **The third degree** – The patient cannot take care of himself

# Symptomatic Parkinsonism

- Cranio-cerebral trauma ( Muhammad Ally)
- CO, Mn intoxication
- Brain tumor
- Encephalitis (Economo)
- Strokes
- Cerebral atherosclerosis
- Medication induced parkinsonism (reserpinum, neuroleptics)
- Poisoning with heavy metals


Honeymoon Period
Motor Complications
Symptoms unresponsive to treatment
PD Dementia
Good response to symptomatic treatment
Wearing-off
Peak dose dyskinesias
Diphasic dyskinesia
On-Off phenomenon
Yo-yo-ing
Postural Instability
Dysarthria, Palilali, swallowing problems
Flexed Posture
Freezing
Dementia
Treatment
3-5 yrs
8-10 yrs
15-20 yrs

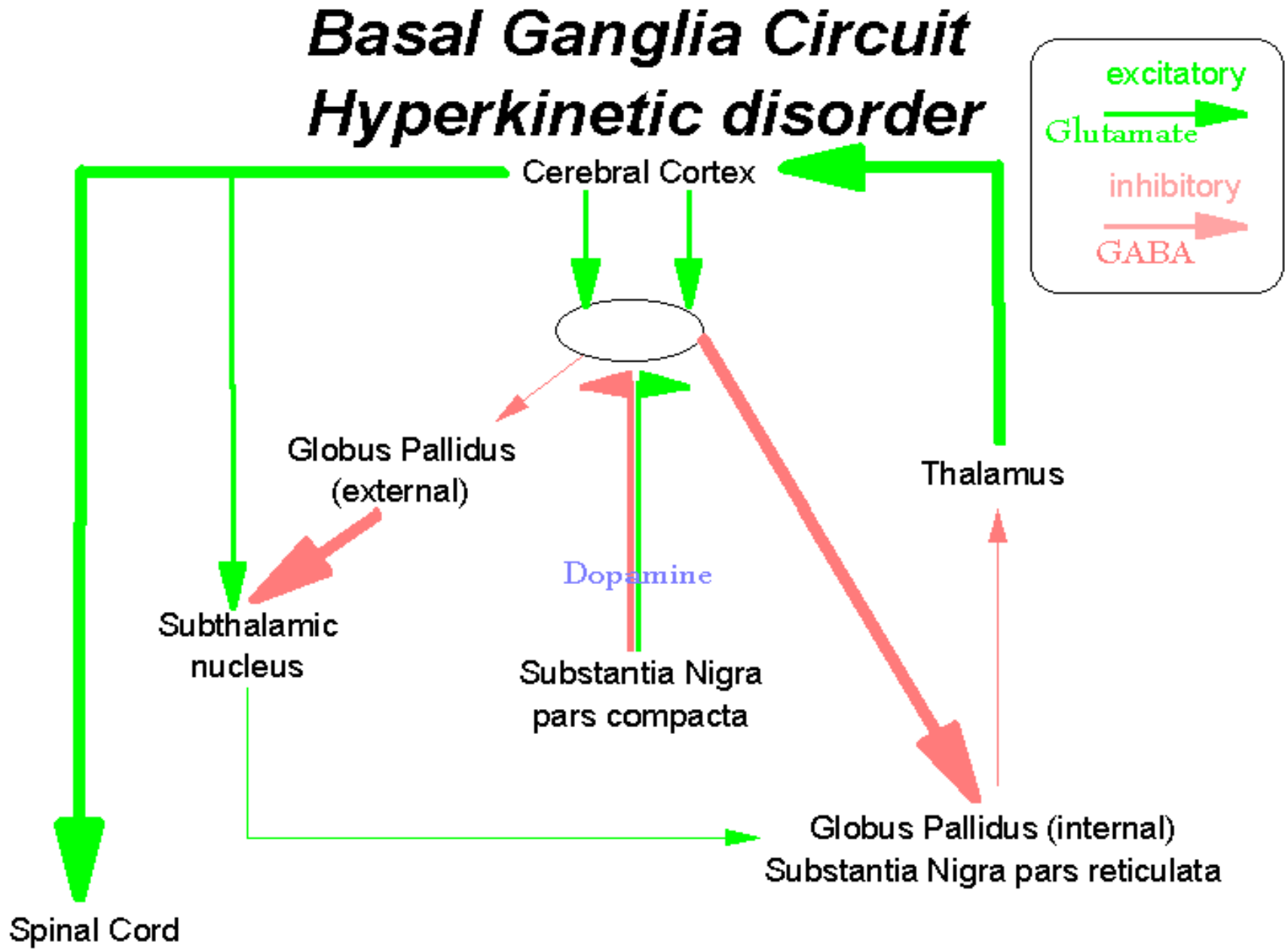
# Hyperkynetic – hypotonic syndrome:

The main **clinical signs** of this syndrome are:

- **Muscular hypotonia**
- Involuntary movements – **hyperkynesis.**

**Involuntary movements** are characterized by:

- the amplitude of the movement
- location of muscle involved
- the rate
- the duration of contraction and relaxation


Basal Ganglia Circuit
Hyperkinetic disorder
excitatory
Glutamate
inhibitory
GABA
Cerebral Cortex
Globus Pallidus
(external)
Thalamus
Dopamine
Subthalamic
nucleus
Substantia Nigra
pars compacta
Globus Pallidus (internal)
Substantia Nigra pars reticulata
Spinal Cord

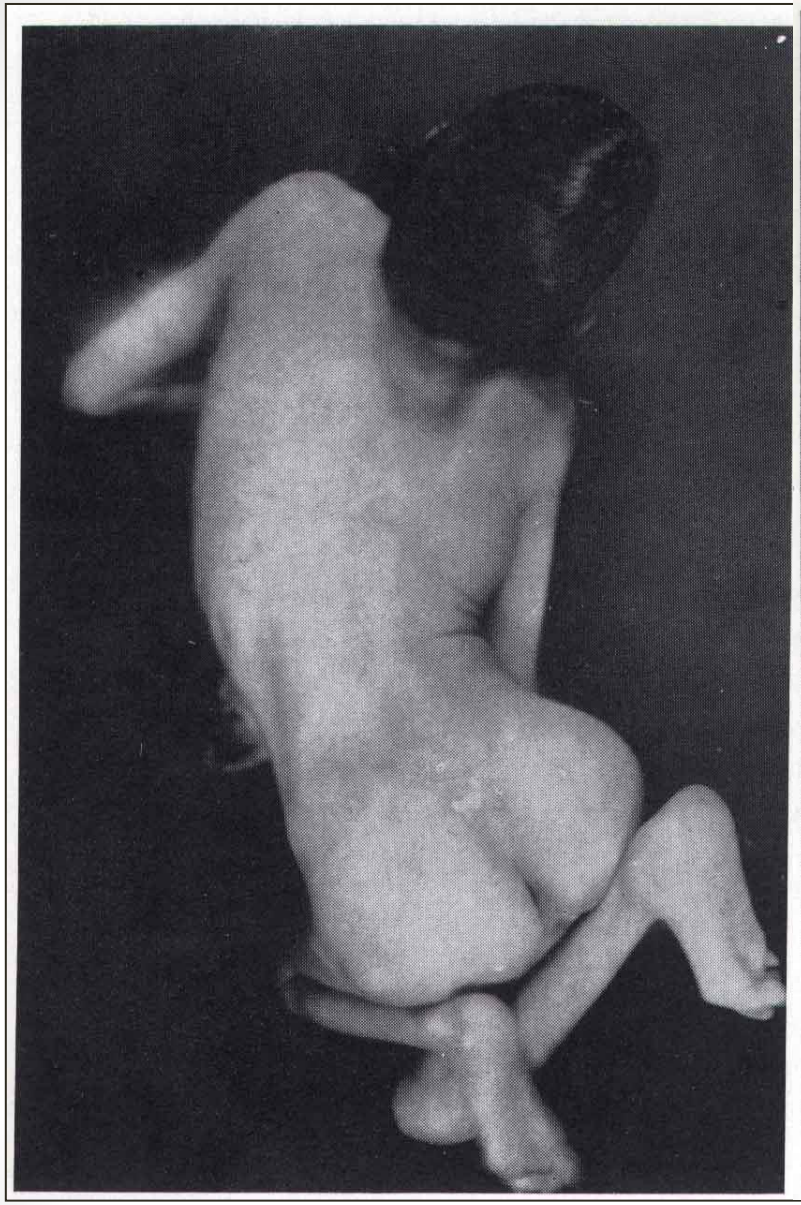
# Hyperkynetic disorders

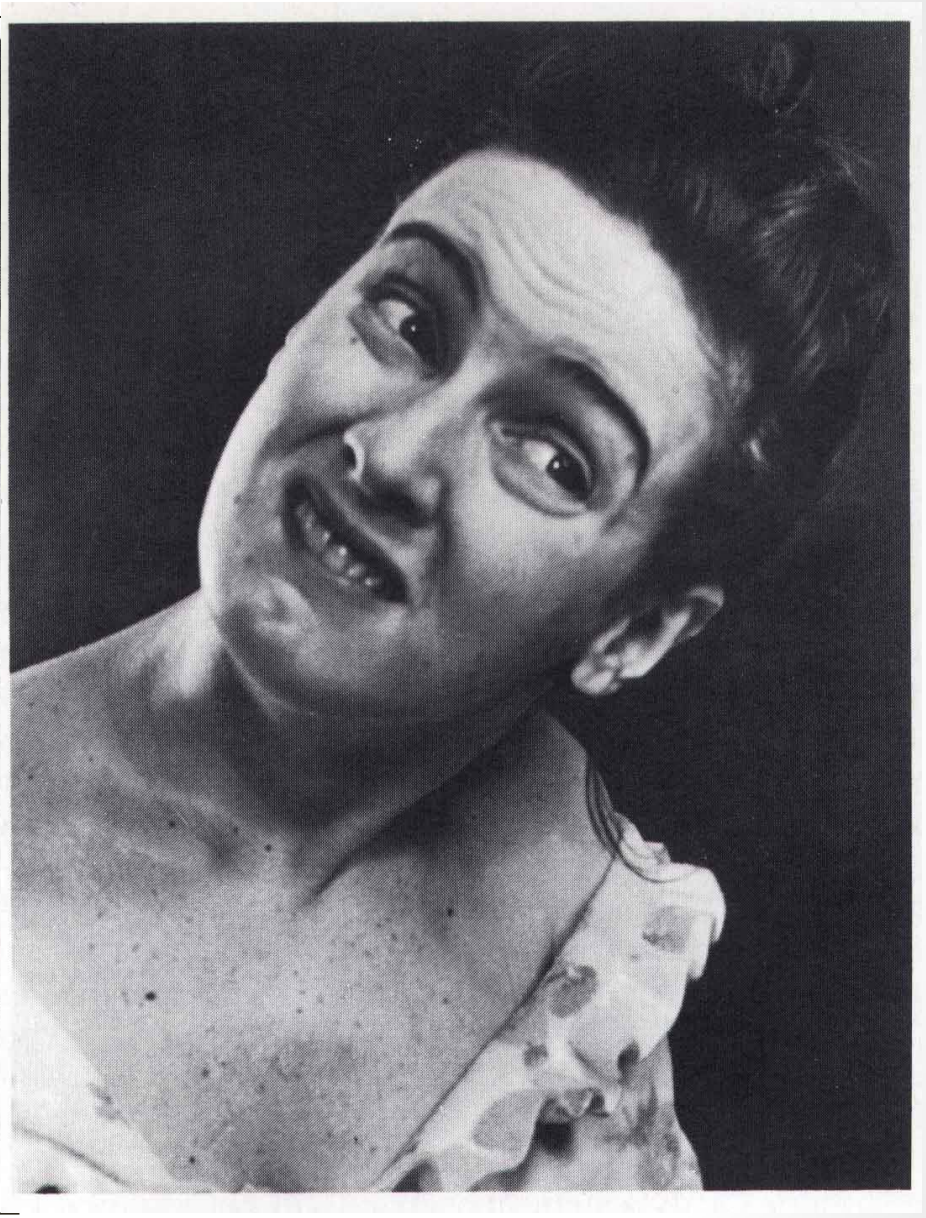
- Chorea
- Athetosis
- Choreo-athetosis
- Ballismus and hemiballismus
- Myoclonus
- Torsion spasm
- Tics
- Tremor
- Dystonia

# C h o r e a /dance/

- Spontaneous, rapid, irregular, purposeless and asymmetric movements that are present at rest and subside during sleep
- “eyes and tongue” symptom - patients are unable to maintain tongue protrusion for more than a few seconds;

- The most common diseases: Huntington’s chorea (inherited disease), rheumatic subcortical encephalitis or chorea of Sydenhams (juvenile disease), atherosclerotic chorea, chorea gravidarum, electric chorea.

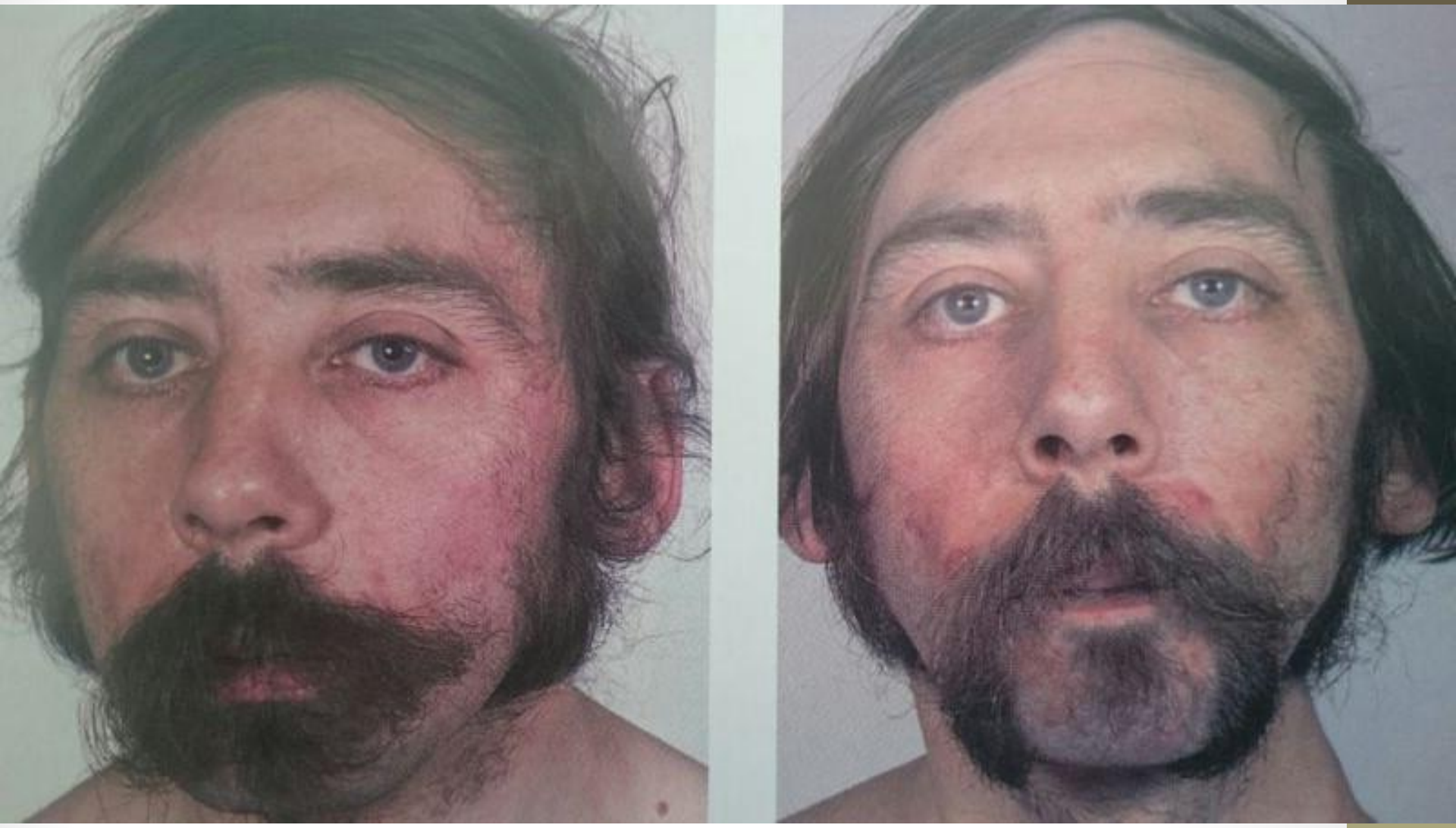




# Athetosis

- Movements are slower and more sustained than chorea movements. They affect primarily the distal portion of extremities with snakelike movements of any combination of flexion,extension, adduction and abduction in varying degrees and are regularly associated with increased muscular tone
- It is supposed that athetosis is the result of **nucleus caudate lesion.**

  **Chorea-athetosis** is a term selected to describe movements that are intermediate between chorea and athetosis.



# Ballismus and hemiballismus

- More or less continuous gross abrupt contractions of axial and proximal muscles of the extremities
- In most of the cases this movement disorder is confined to one side of the body (hemiballismus)
- It may be associated with  muscke hypotonia

# Myoclonus

- Is a jerking movement of one or more muscle groups (for example palate, tongue, pharynx, larynx, diaphragm and skeletal muscles)
- Usually only one muscle group is involved
- They are synchronous in most of cases, but sometimes they may be asynchronous
- The frequency is about 15 – 18 per minute
- They may be induced by visual, tactile, or auditory stimuli (stimulus-sensitive myoclonus) or by the initiation of the voluntary movement (intention myoclonus).

# Tremor

- Defined as a rhythmic, back and forth or oscillating involuntary movement about a joint axis.
- Tremors are symmetric about a midpoint within the movement, and both portions of the movement occur at the same speed

**Tremor types**

- **Tremor in rest-** frequency is about 4 – 6 per second (Parkinsonian)
- **Position tremor** – an action tremor during sustained posture.
  - -Physiological tremor with rate 8-12 Hz
  - -Enhanced physiological tremor
  - -Benign essential tremor
- **Intention tremor** – during activity due to a cerebellar disorders (MS)
- **Flapping tremor** (**Asterixis**) - is characterized by irregular flapping-hand movement, which appears most often with outstretched arms and wrist extension. Individuals with this condition resemble birds flapping their wings

# Tics

- Fast, involuntary compulsive stereotyped movements, localised in particular muscle group;
- Simple or complex
- Tics may involve any portion of the body (they are most common about the face  where they are manifested as blinking, grinning, smirking, lip licking, nose wrinkling)

# Dystonia

- A term given to a syndrome with sustained muscle contraction causing twisting and rotational movements or abnormal postures;
- **Primary and secondary**;
- Abnormal movements disappear during sleep and are enhanced by emotional stress;
- Varieties:

❖ **Focal dystonia**

**-Blepharospasmus**

**-Spasmodic torticollis**

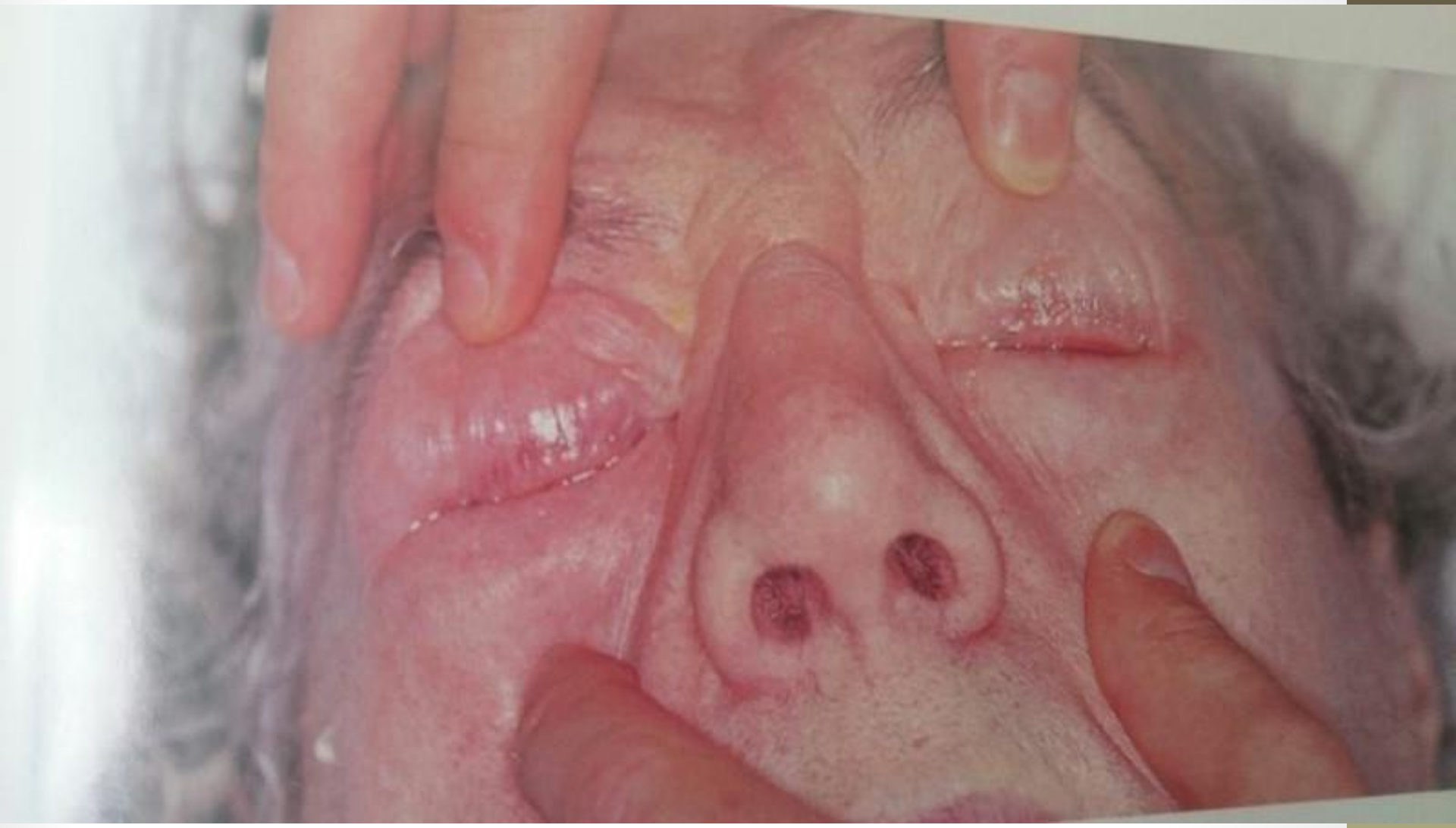
**-Occupational cramps** / writer's cramp, violinist's cramp, telegraphist's cramp/

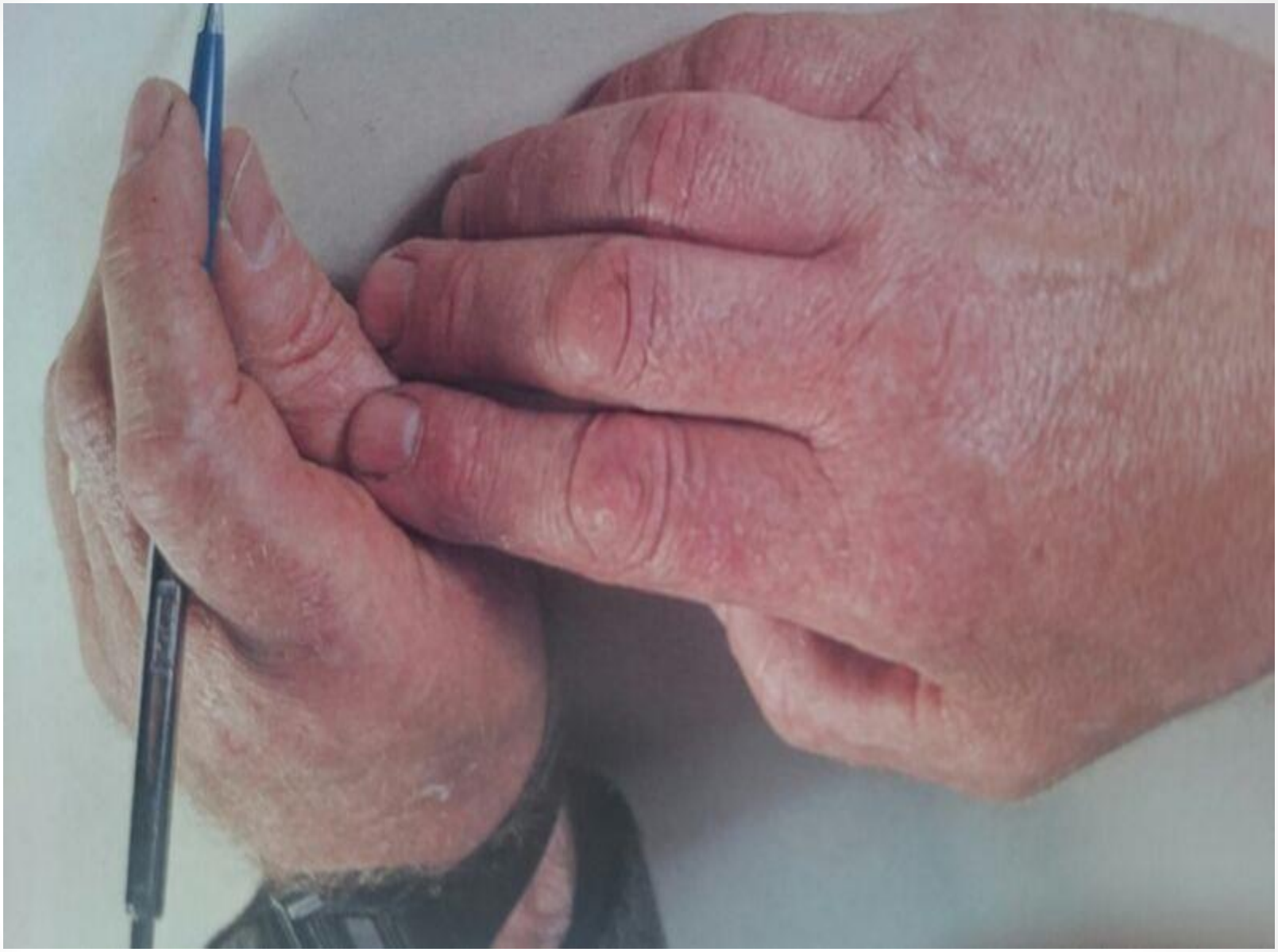
❖ **Segmental dystonia**

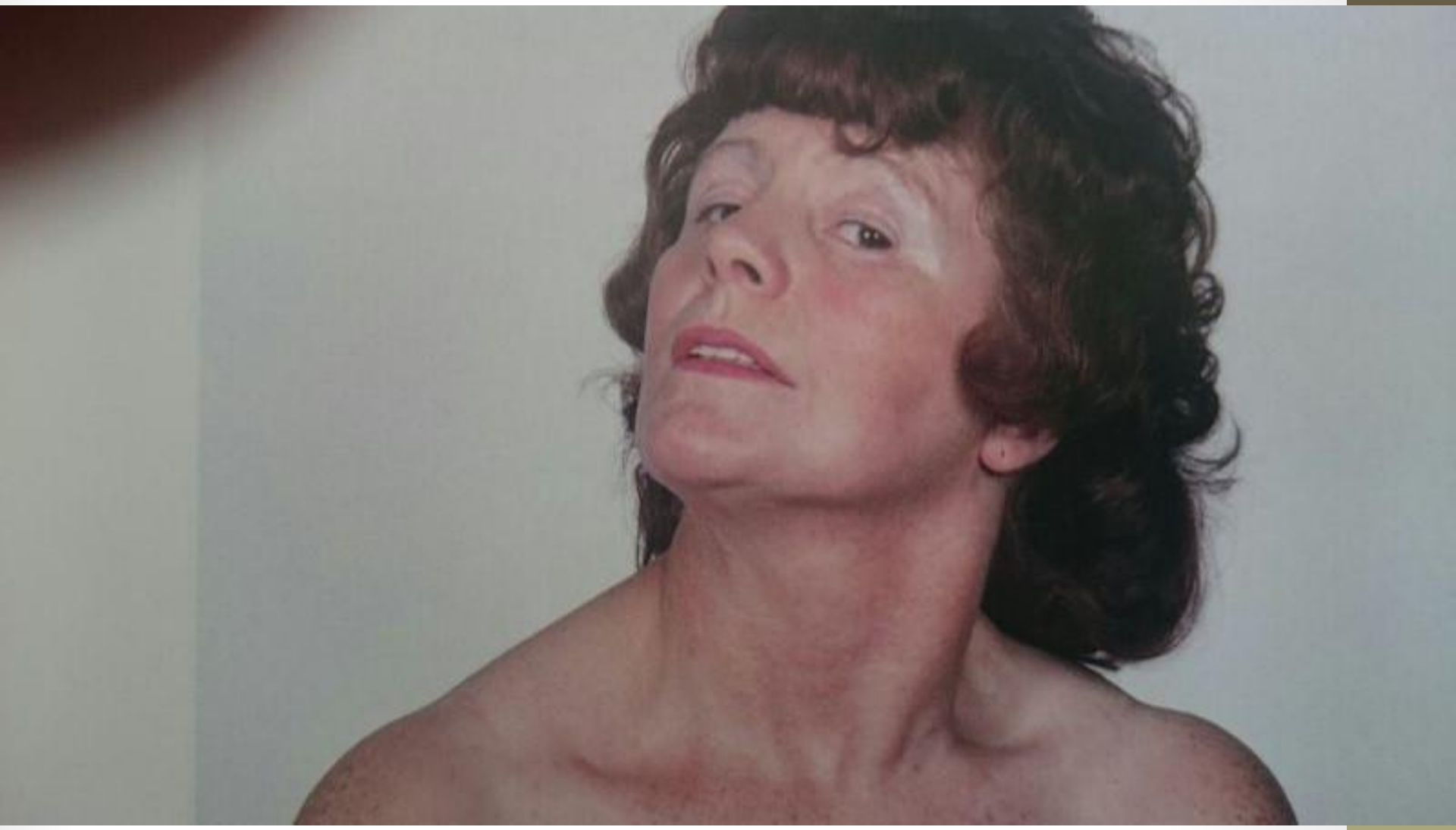
❖ **Multifocal dystonia**

❖ **Generalized dystonia**

❖ **Hemidystonia**







# Torsion spasm

- Twisting or turning movements
- The muscles of trunk and neck are involved
- Sometimes **torticollis** can occur
- Usually it is the result of **putamen lesion**

# Clinical differences between corticospinal and extrapyramidal syndromes

| | CORTICOSPINAL | EXTRAPYRAMIDAL |
|---|---|---|
| Character of the alteration of muscle tone | Clasp-knife effect (spasticity) | Plastic, equal throughout passive movement (rigidity), or intermittent (cogwheel rigidity) |
| Distribution of hypertonus | Flexors of arms, extensors of legs | Generalized but predominates in flexors of limbs and of trunk |
| Involuntary movements | Absent | Presence of tremor, chorea, athetosis, dystonia |
| Tendon reflexes | Increased | Normal or slightly increased |
| Babinski sign | Present | Absent |
| Paralysis of voluntary movement | Present | Absent or slight |