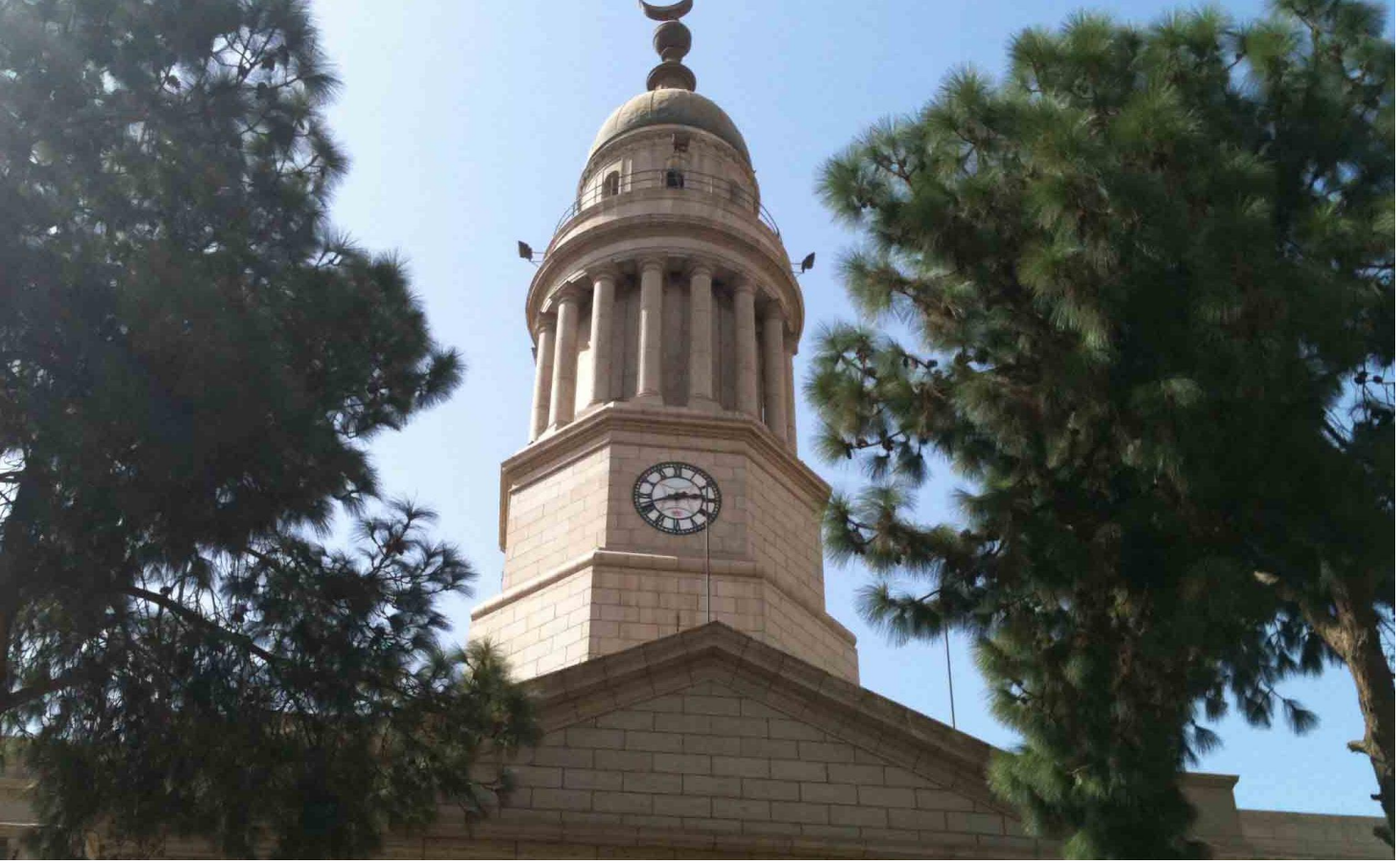


Childhood and Juvenile Movement Disorders

Amr Hassan, M.D,FEBN

Associate professor of Neurology

Cairo University

وحدة الحركات اللاإرادية والتيبس قصر العيني

Movement Disorders & Spasticity Clinic
Kasr Al-Ainy

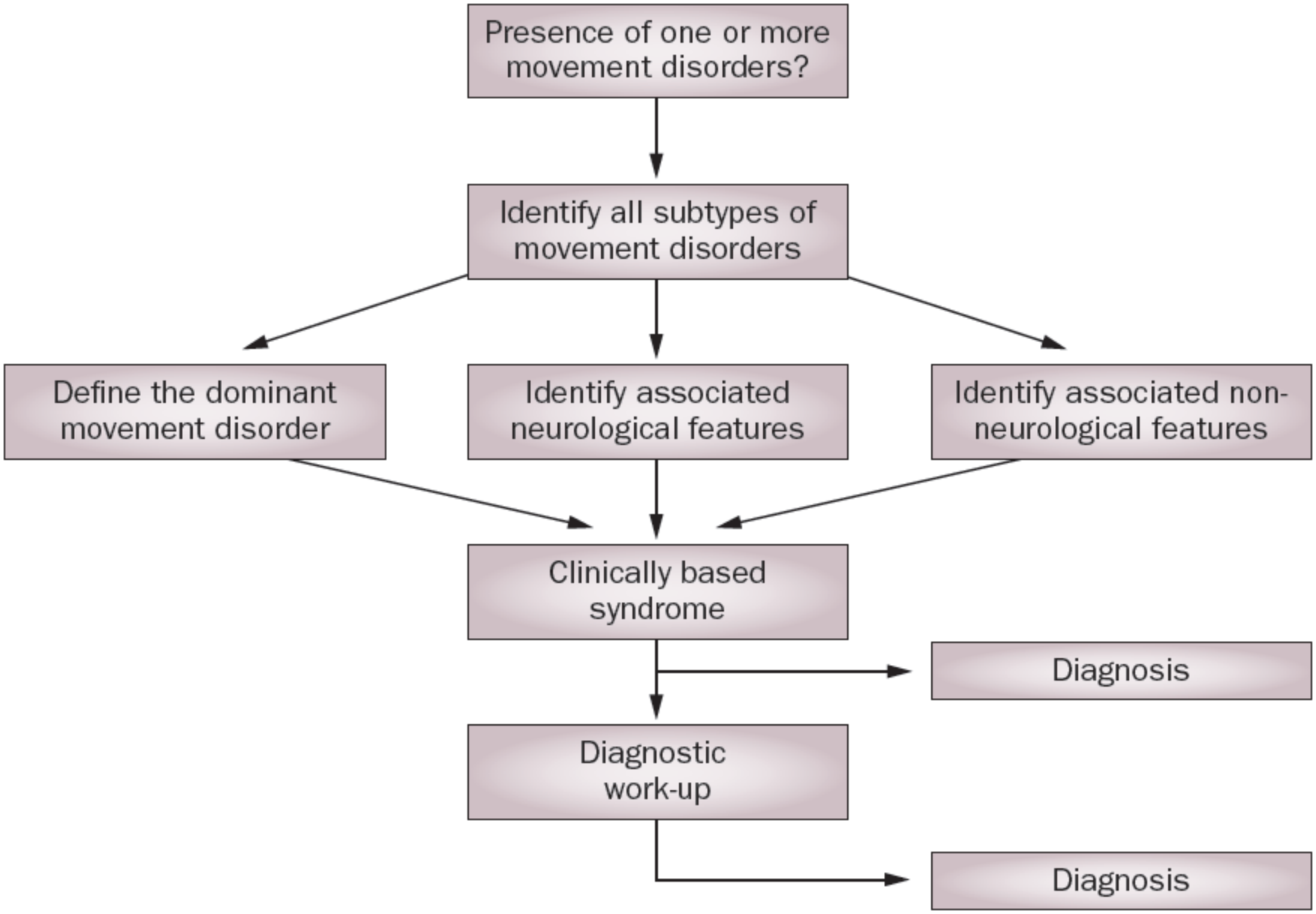
Any approach begins with . . .

A good history

A good physical exam

Keen sense of observation

A systematic differential diagnosis


Presence of one or more movement disorders?
Identify all subtypes of movement disorders
Define the dominant movement disorder
Identify associated neurological features
Identify associated non-neurological features
Clinically based syndrome
Diagnosis
Diagnostic work-up
Diagnosis

Childhood and Juvenile movement disorders

- Parkinsonism
- Tics
- Tremors
- Chorea
- Dystonias
- Ataxia
- Myoclonus
- Mixed

Clinical assessment of AIM

- **D**escribe the movement
- **D**ifferentiate from other MD
- **D**istribution
- **D**ecreased by , Increased by
- **D**iurnal variation
- **D**uration
- **D**istinguished phenomenon

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Clinical assessment of AIM

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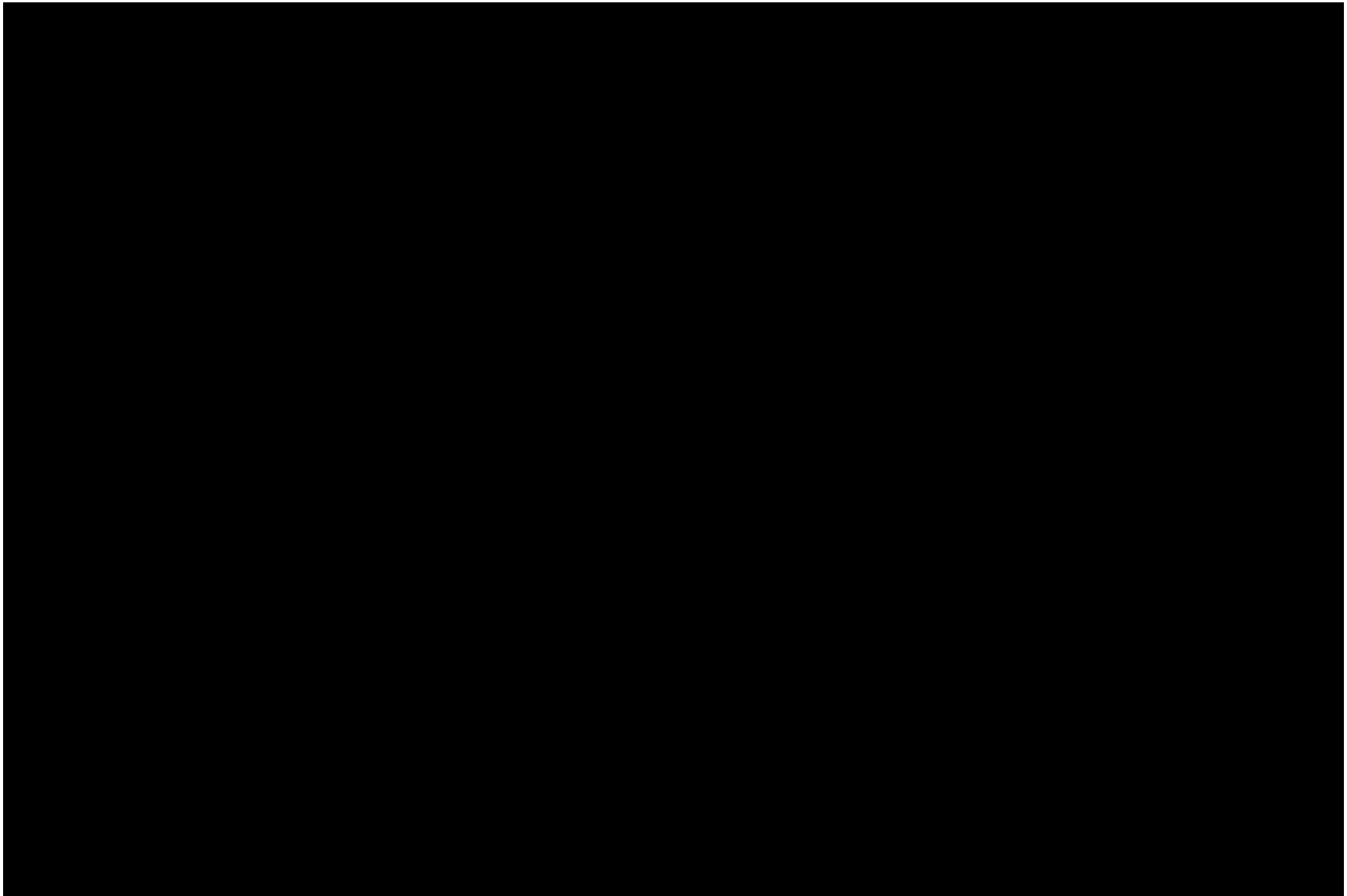
Describe the movement

- Rhythmic vs. arrhythmic
- Sustained vs. nonsustained
- Paroxysmal vs. Nonparoxysmal
- Slow vs. fast
- Amplitude
- At rest vs. Action Vs Task Specific
- Patterned vs. non-patterned
- Combination of varieties of movements
- Supressibility

Describe the movement



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Paroxysmal vs. Nonparoxysmal

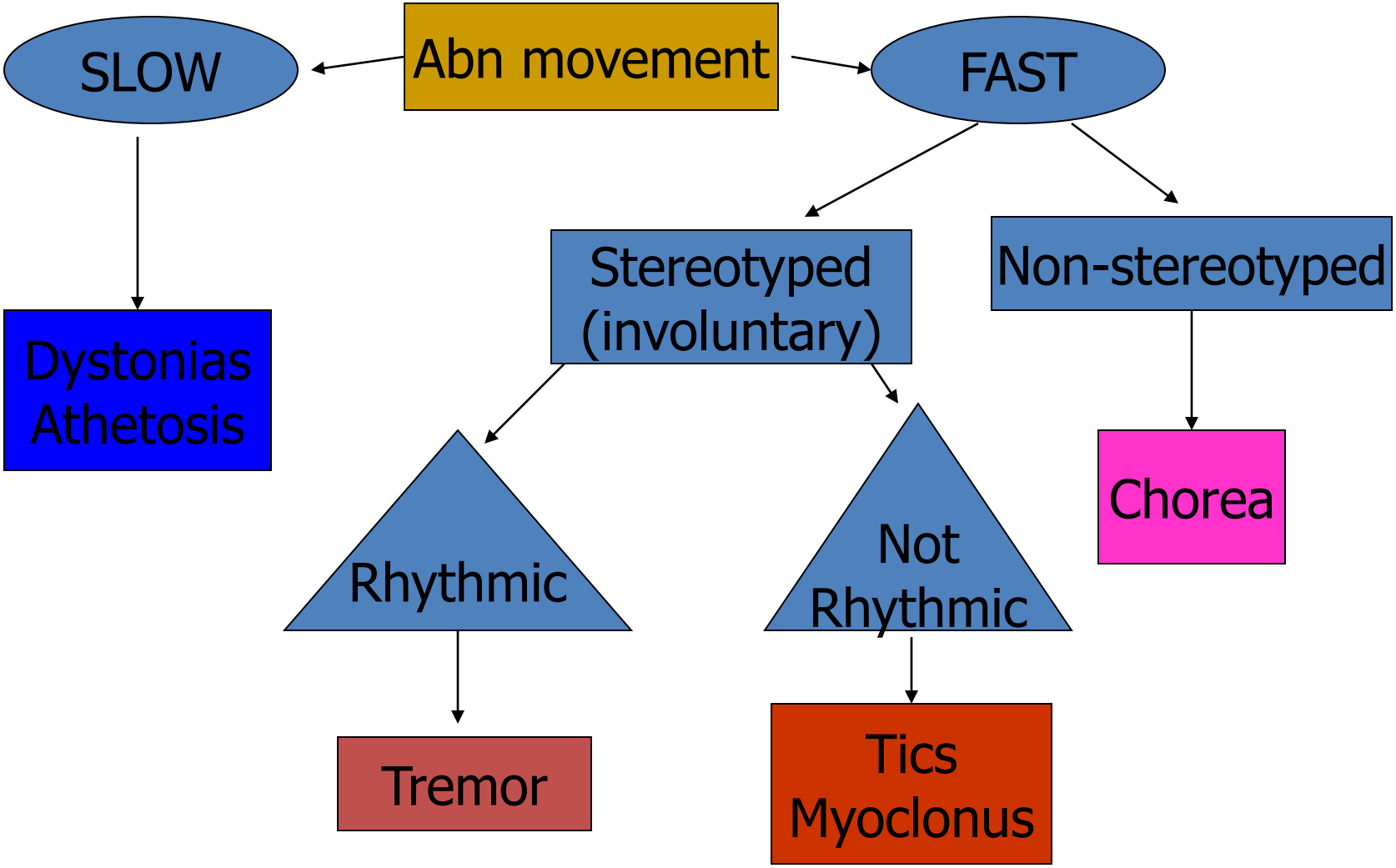
Paroxysmal

- Tics
- PKD
- PNKD
- Sterotypies
- Akathic movements
- Moving toes
- Myorhythmia

Continous

- Abdominal dyskinesias
- Athetosis
- Tremors
- Dystonic postures
- Myoclonus (rhythmic)
- Tardive sterotypy
- Myokymia
- Tic status

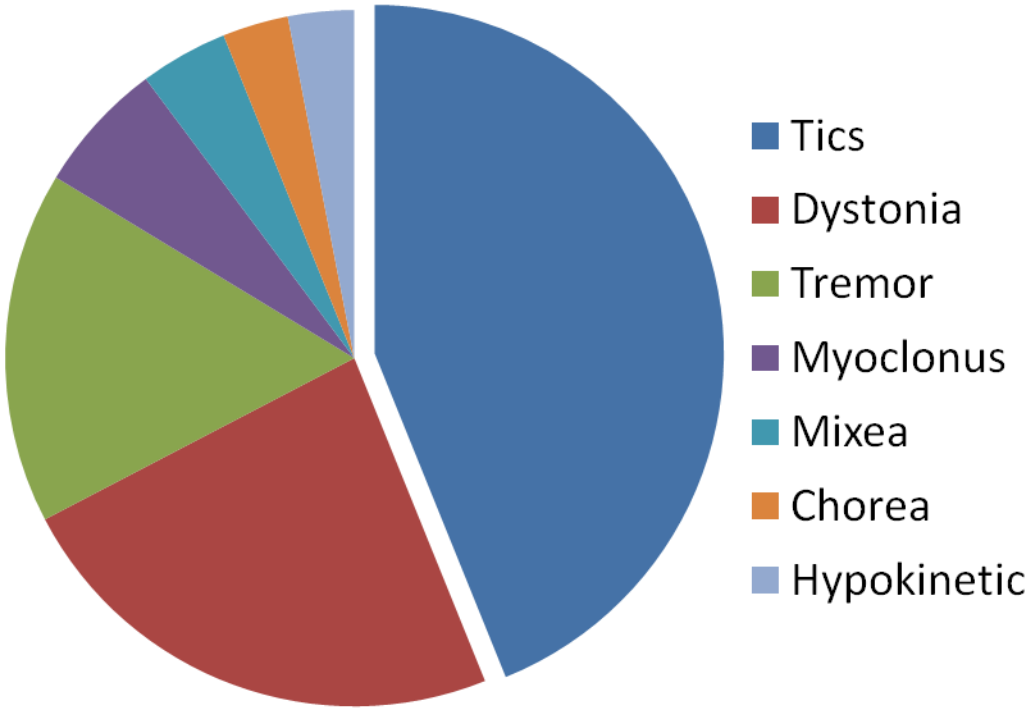
Differentiating from other MD



Fernandez alvarez, 2005

684 patient< 18 years

- **Tics - 43%**
- **Dystonia- 23%**
- **Tremor- 16%**
- **Myoclonus 6%**
- **Mixea- 4%**
- **Chorea- 3%**
- **Hypokinetic 3%**



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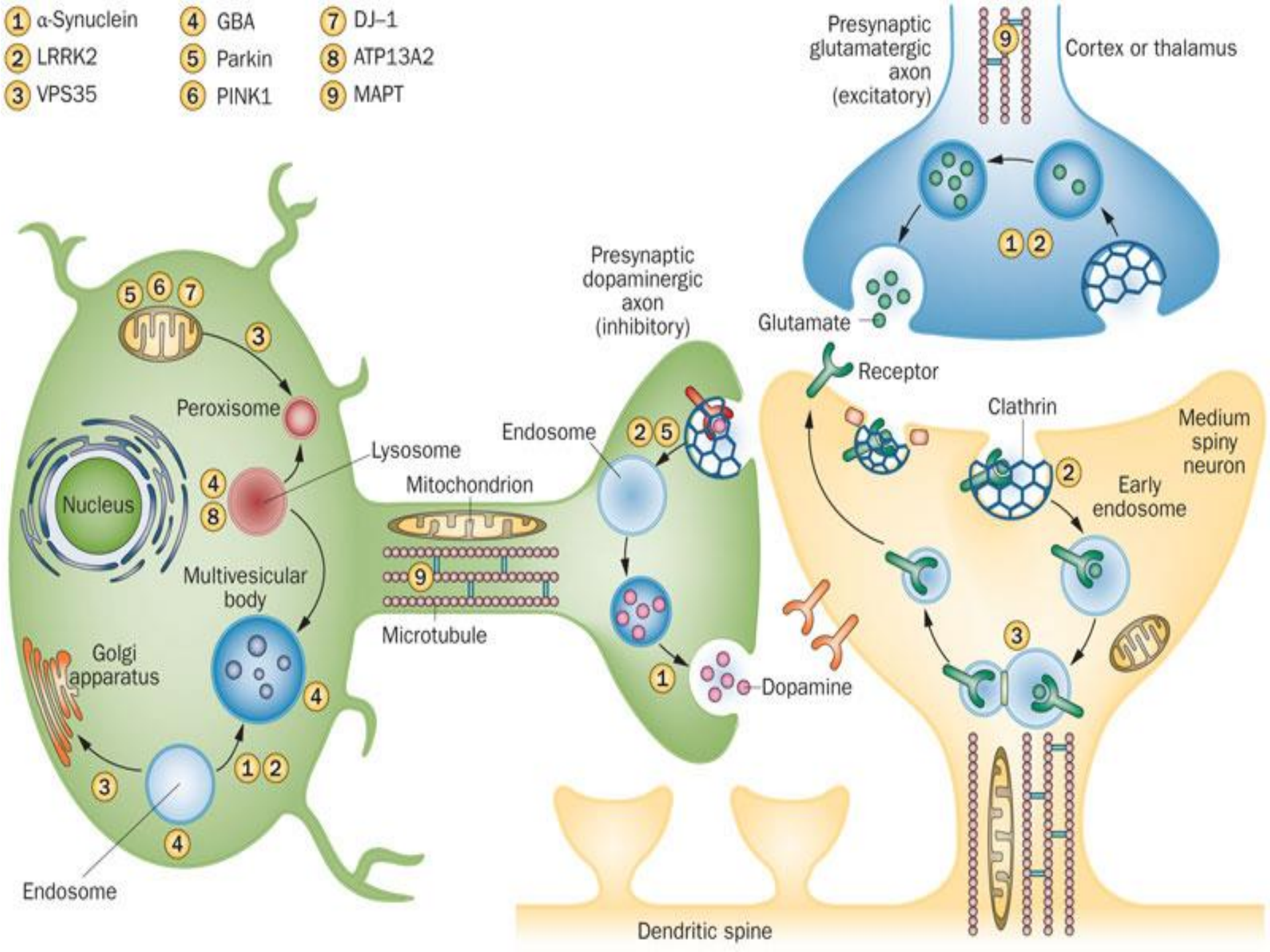
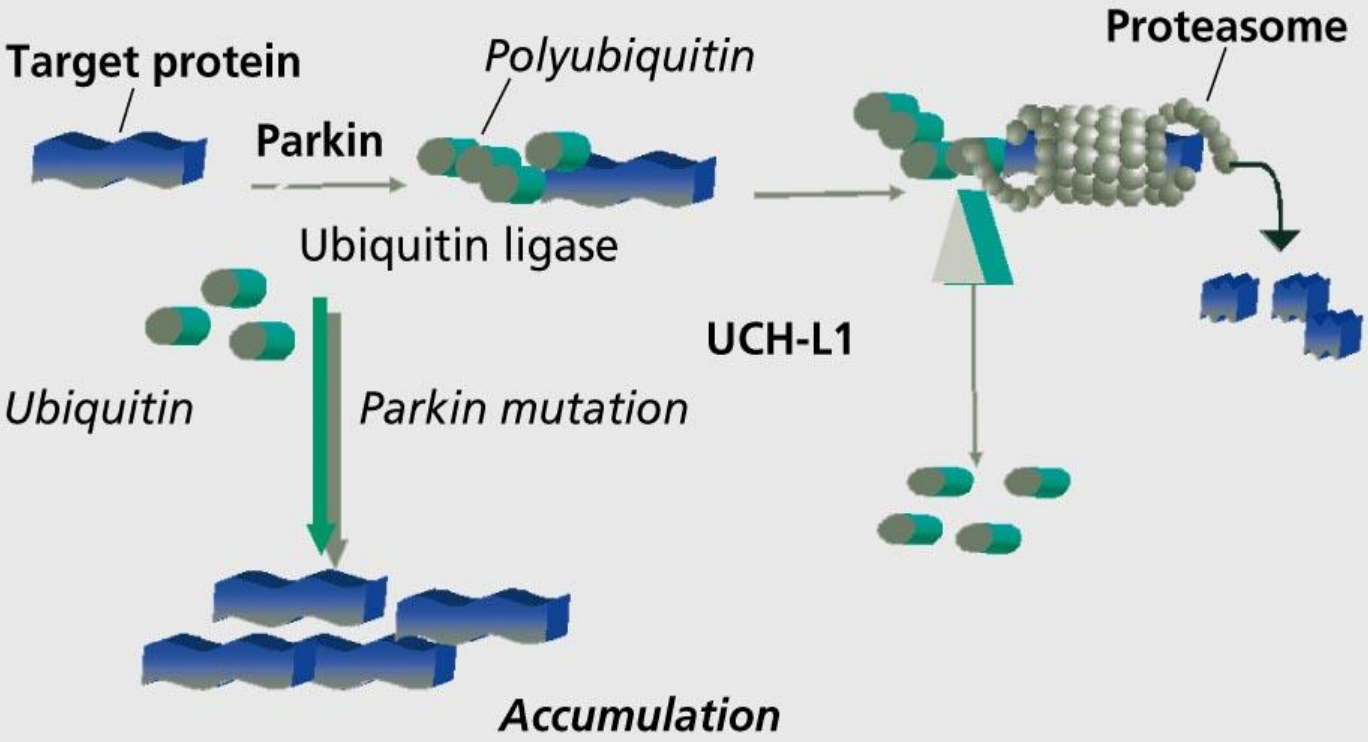
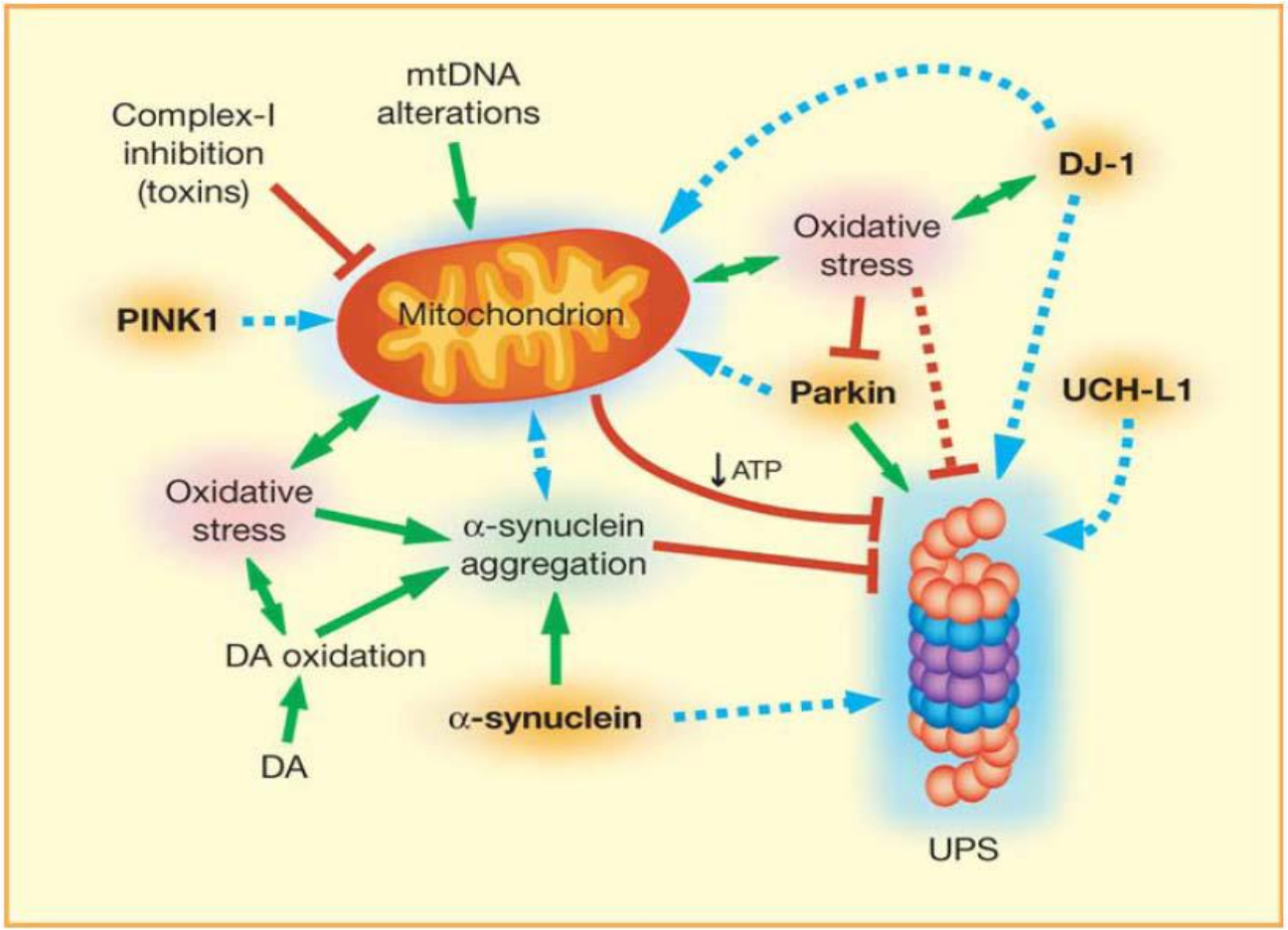
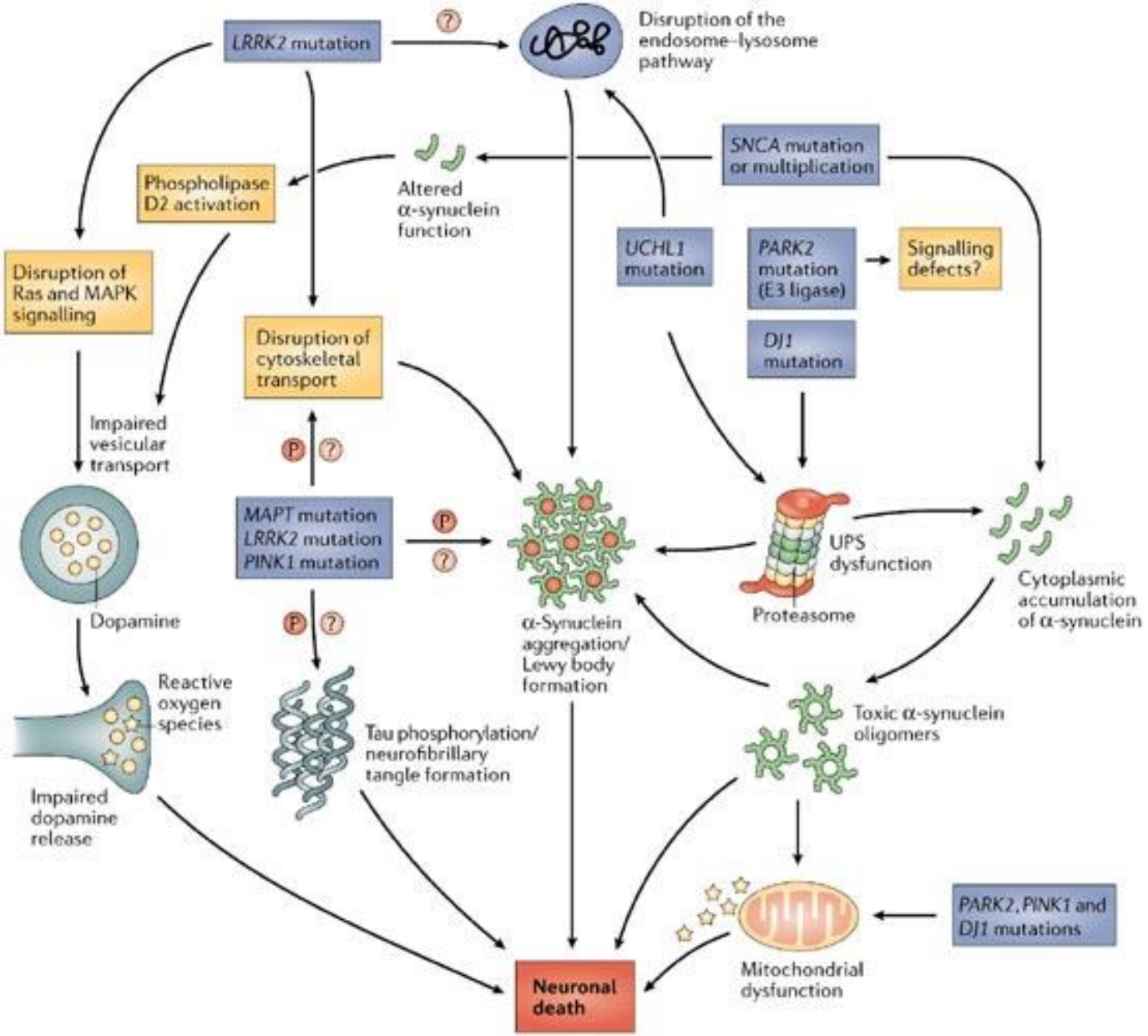

1 α-Synuclein
2 LRRK2
3 VPS35
4 GBA
5 Parkin
6 PINK1
7 DJ–1
8 ATP13A2
9 MAPT
Presynaptic glutamatergic axon (excitatory)
Cortex or thalamus
Glutamate
Receptor
Presynaptic dopaminergic axon (inhibitory)
Peroxisome
Lysosome
Endosome
Mitochondrion
Nucleus
Multivesicular body
Microtubule
Golgi apparatus
Endosome
Dopamine
Clathrin
Medium spiny neuron
Early endosome
Dendritic spine

Genetics of PD



Genetics of PD



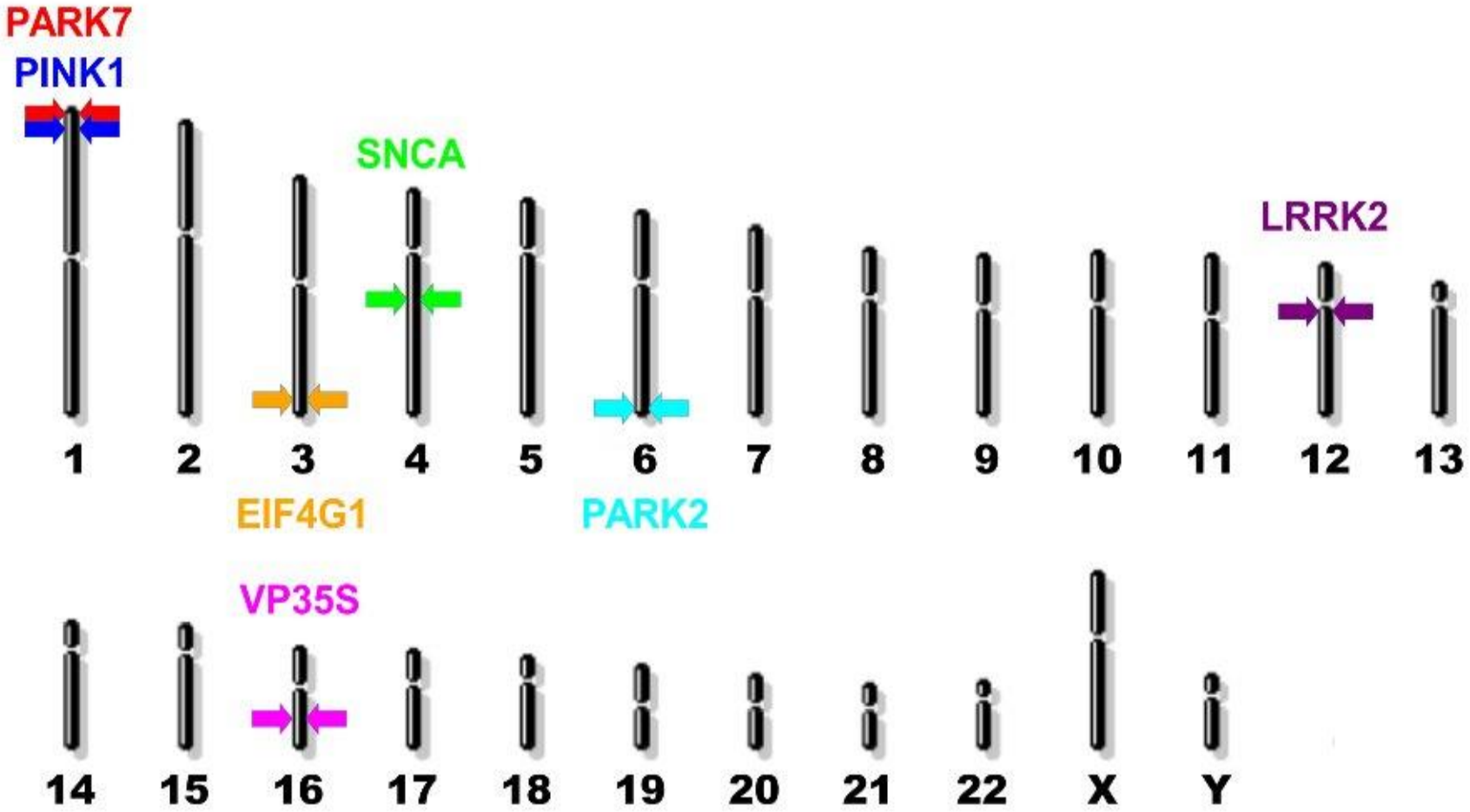


Farrer *Nature Reviews Genetics* **7**, 306–318 (April 2006) | doi:10.1038/nrg1831

nature REVIEWS GENETICS

Genetics of PD

Locations of the 7 Parkinson's disease genes in the human genome



The 1 - 22 numbered chromosomes plus the X & Y sex chromosomes

Juvenile Parkinsonism

Symbol	Gene locus	Disorder	Inheritance	Gene
PARK1	4q21-22	EOPD	AD	*SNCA*
PARK2	6q25.2–q27	EOPD	AR	*Parkin*
PARK3	2p13	Classical PD	AD	Unknown
PARK4	4q21–q23	EOPD	AD	*SNCA*
PARK5	4p13	Classical PD	AD	*UCHL1*
PARK6	1p35–p36	EOPD	AR	*PINK1*
PARK7	1p36	EOPD	AR	*DJ-1*
PARK8	12q12	Classical PD	AD	*LRRK2*

Juvenile Parkinsonism

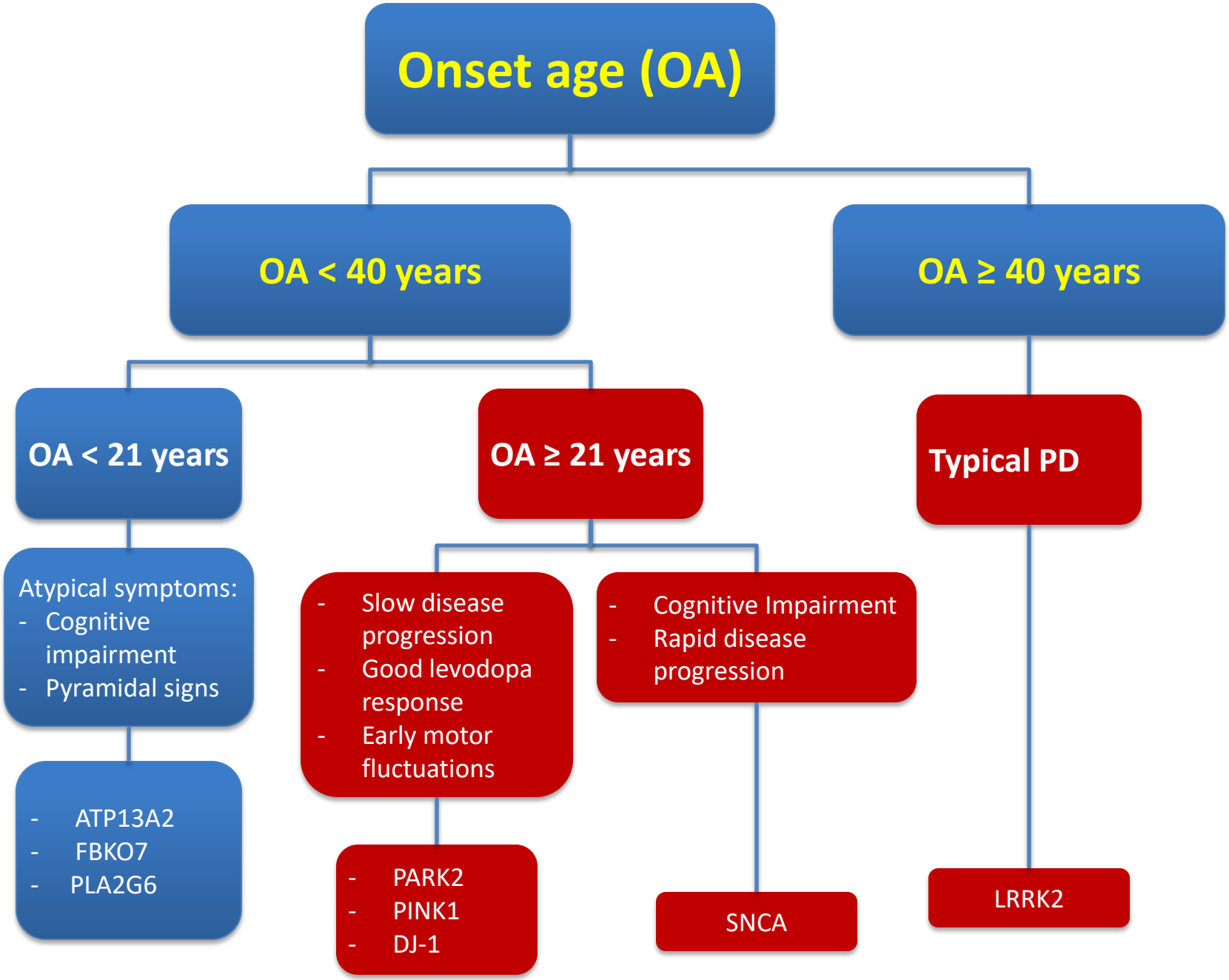
Symbol	Gene locus	Disorder	Inheritance	Gene
PARK9	1p36	Kufor-Rakeb syndrome	AR	*ATP13A2*
PARK10	1p32	Classical PD	Risk factor	Unknown
PARK11	2q36-27	Late-onset PD	AD	Unknown
PARK12	Xq21–q25	Classical PD	Risk factor	Unknown
PARK13	2p12	Classical PD	AD or risk factor	*HTRA2*
PARK14	22q13.1	EOP + Dystonia	AR	*PLA2G6*

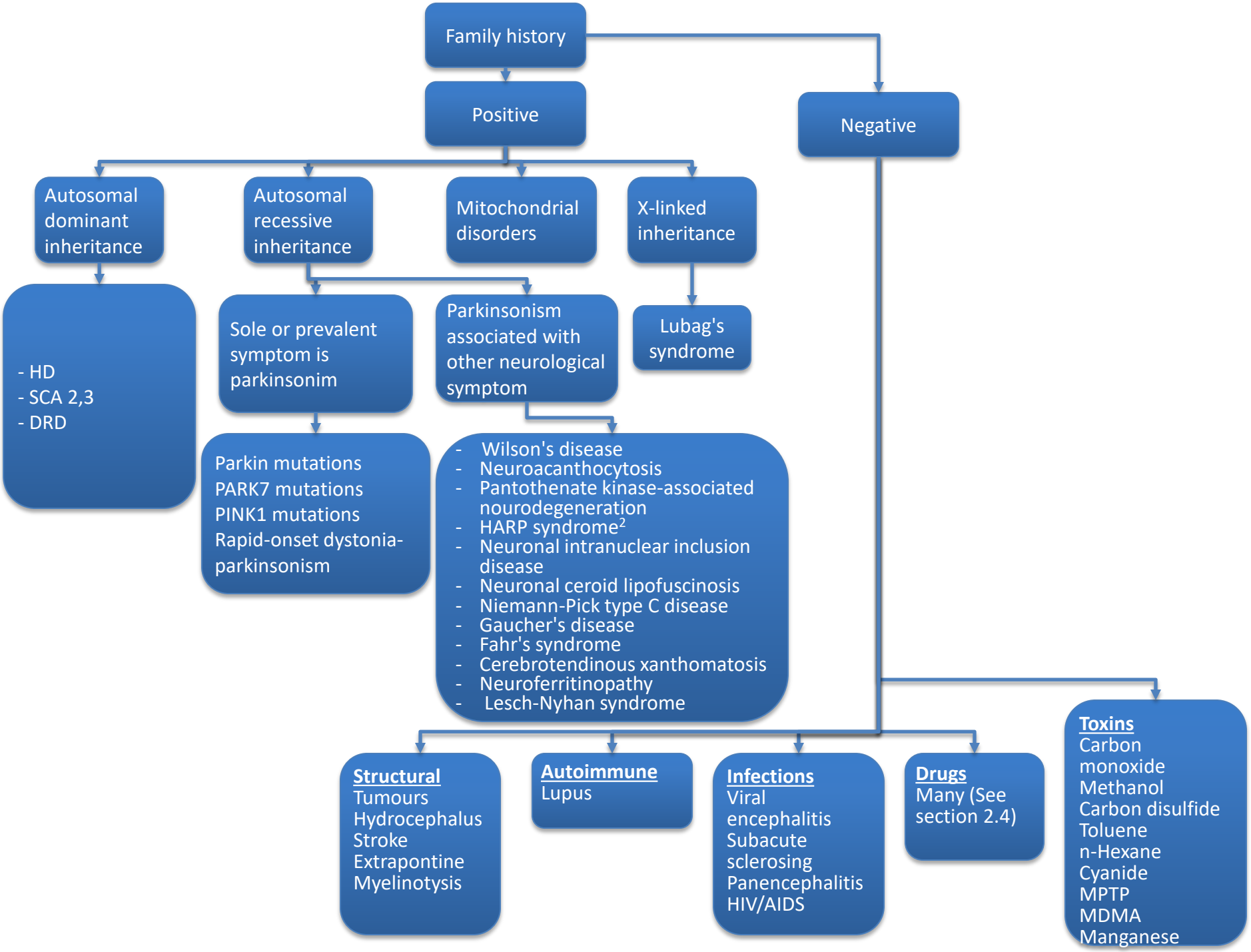
Juvenile Parkinsonism

Symbol	Gene locus	Disorder	Inheritance	Gene
PARK15	22q12–q13	EOP +Δ	AR	*FBX07*
PARK16	1q32	Classical PD	Risk factor	Unknown
PARK17	16q11.2	Classical PD	AD	*VPS35*
PARK18	3q27.1	Classical PD	AD	*EIF4G1*

Juvenile Parkinsonism

PARK	Gene	Inheritance	Phenotype
1	α-Synuclein	Dominant	Complex mix of Parkinsonism and dementia
2	Parkin	Recessive	Juvenile onset Parkinsonism
6	PINK1	Recessive	Juvenile onset Parkinsonism
7	DJ1	Recessive	Juvenile onset Parkinsonism
9	ATP13A2	Recessive	Juvenile onset Parkinsonism
14	PLA2G6	Recessive	Juvenile onset Parkinsonism dystonia
15	FBXO7	Recessive	Juvenile onset Parkinsonism


Onset age (OA)
OA < 40 years
OA ≥ 40 years
OA < 21 years
OA ≥ 21 years
Typical PD
Atypical symptoms:
- Cognitive impairment
- Pyramidal signs
- Slow disease progression
- Good levodopa response
- Early motor fluctuations
- Cognitive Impairment
- Rapid disease progression
- ATP13A2
- FBKO7
- PLA2G6
- PARK2
- PINK1
- DJ-1
SNCA
LRRK2


Family history
Positive
Negative
Autosomal dominant inheritance
Autosomal recessive inheritance
Mitochondrial disorders
X-linked inheritance
- HD
- SCA 2,3
- DRD
Sole or prevalent symptom is parkinsonim
Parkinsonism associated with other neurological symptom
Lubag's syndrome
Parkin mutations
PARK7 mutations
PINK1 mutations
Rapid-onset dystonia-parkinsonism
- Wilson's disease
- Neuroacanthocytosis
- Pantothenate kinase-associated nourodegeneration
- HARP syndrome[2]
- Neuronal intranuclear inclusion disease
- Neuronal ceroid lipofuscinosis
- Niemann-Pick type C disease
- Gaucher's disease
- Fahr's syndrome
- Cerebrotendinous xanthomatosis
- Neuroferritinopathy
- Lesch-Nyhan syndrome
Structural
Tumours
Hydrocephalus
Stroke
Extrapontine Myelinotysis
Autoimmune
Lupus
Infections
Viral encephalitis
Subacute sclerosing Panencephalitis
HIV/AIDS
Drugs
Many (See section 2.4)
Toxins
Carbon monoxide
Methanol
Carbon disulfide
Toluene
n-Hexane
Cyanide
MPTP
MDMA
Manganese

Childhood and Juvenile movement disorders

- Parkinsonism
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- Tremors
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- Mixed

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What is a tic?

A “tic” is a sudden, rapid, recurrent, non-rhythmic, stereotyped motor movement or vocalization

May appear as exaggerated fragments of ordinary motor or phonic behaviors that occur out of context

Classification of tics

Simple

few muscles

Complex

multiple groups of muscles

Simple

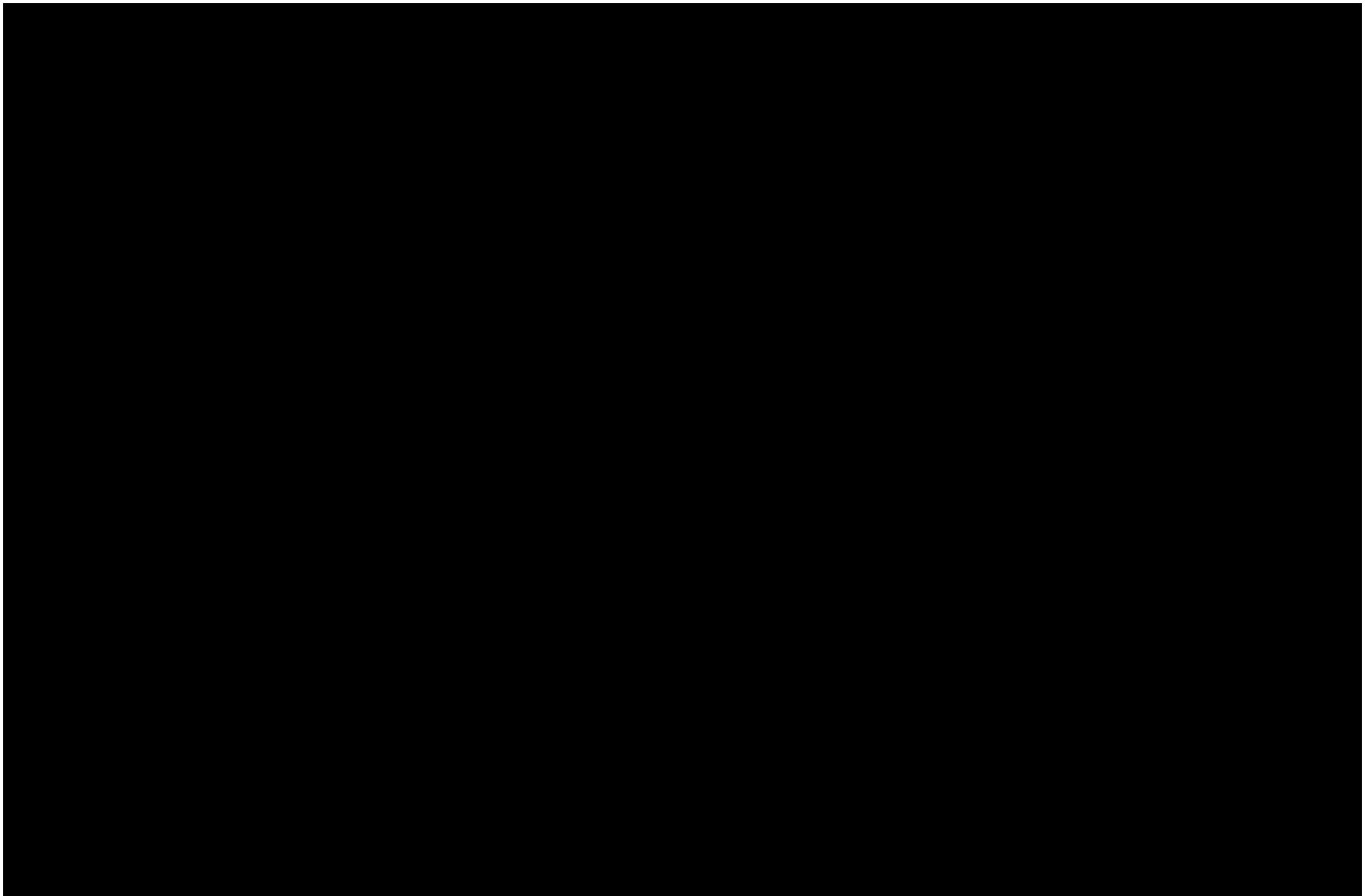
sounds

Complex

words or sentences

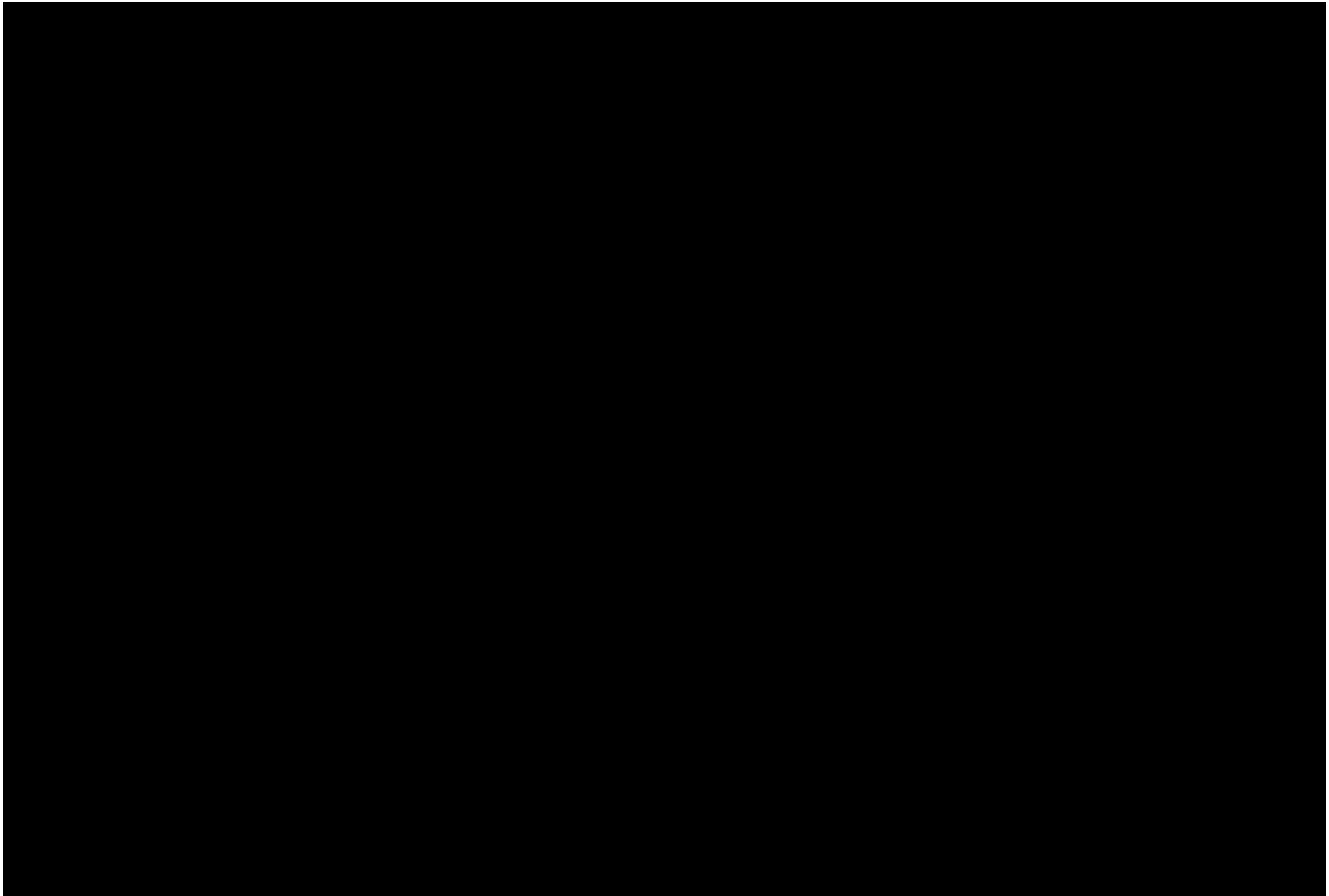
Motor Tics (Simple)

- Generally lasting less than several hundred milliseconds
- Examples include:
  - eye blinking
  - nose wrinkling
  - neck jerking
  - shoulder shrugging
  - facial grimacing
  - abdominal tensing



Motor Tics (Complex)

- Longer in duration than simple tics; usually lasting seconds or longer
- Examples include:
  - hand gestures
  - jumping, touching, pressing, or stomping
  - facial contortions
  - repeatedly smelling an object
  - squatting and/or deep knee bends
  - retracing steps and/or twirling when walking
  - assuming and holding unusual positions (including "dystonic" tics, such as holding the neck in a particular tensed position)



Tics

- Predominate in the face, upper arms and neck.

- Motor: eye blinking, shoulder shrug..
- Vocal: squeaking, cough, sniffing…
- Sensory: sensation ‘clothes not right’..

- Can be supressed; relief when expressed again

Tics

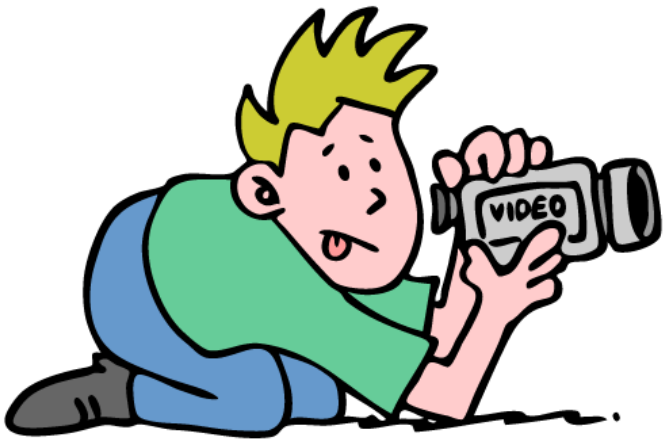
- Aggravated by stress / anxiety.
- Family history tics / OCD.
- Recurrent movements stereotyped.
- Tics are preceded by rising discomfort or urge (*sensory tic*) that is relieved by the movement (*itch and scratch*).
- Can persist in sleep.

Tics: D.D.

- Chorea
- Myoclonus
- Stereotypies
- Compulsions
- Pseudotics
- Secondary – ass Strep infection “PANDAS”

Tics: D.D.

- Tics are often less prominent in the clinical examination room.
  - Videotaping the patient.



- CAUTION: Dystonic tic:
  - The movement or posture might be slow or prolonged rather than jerky.

Transient	Chronic	Tourette's
Single/multiple motor AND/OR vocal	Single/multiple motor OR vocal	Multiple motor AND single/multiple vocal
< 1 year =/> 4 weeks	> 1 year Not tic free > 3 months	> 1 year Not tic free > 3 months

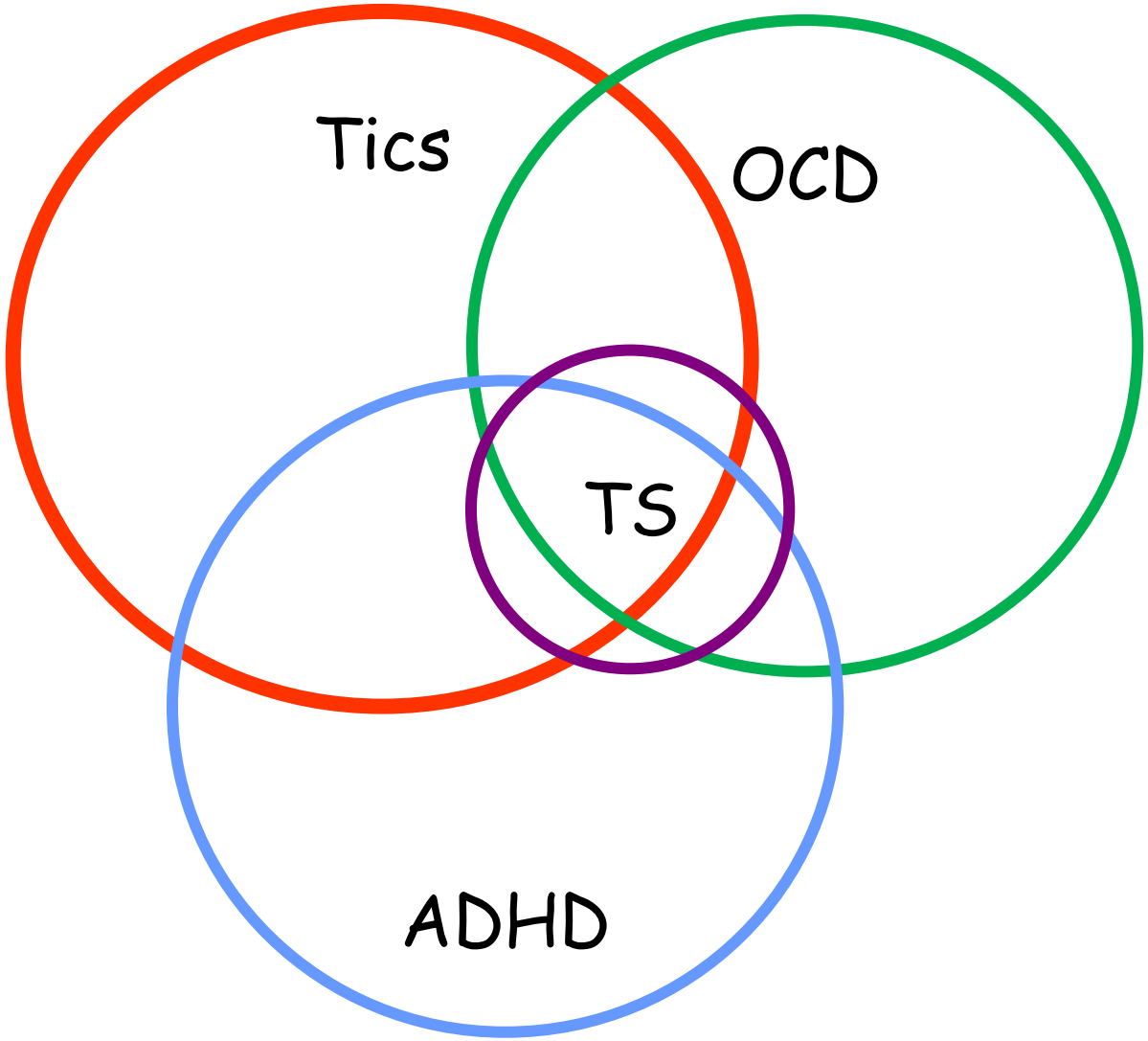
Tourettes Syndrome: Associated disorders

- Obsessions and compulsions - OCD
- ADHD

  50 – 60% of TS

  precedes tics by 2-3 years
- Sleep disorders
- Learning problems - **5X** more special ed
- Behavioural problems
- Mood disorders

Tourettes Syndrome



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Tremors: classification

Table 1 | Classification of tremors according to moment of occurrence

Moment of occurrence	Features	Example of underlying disorder
A. At rest	Best judged in a body part that is fully supported against gravity	Parkinson disease
B. With action		
Postural	Occurs in body part that assumes a posture against gravity	Physiological; enhanced physiological (stress, endocrine disorders or intoxications); essential tremor
Kinetic		
Simple	Occurs during entire movement trajectory	Essential tremor
Intention	Progressively increases towards intended target	Cerebellar ataxia
Task specific	Occurs only during specific activities	Dystonic writing tremor
Isometric	Occurs during voluntary muscle contractions against a stationary resistance	Physiological; associated with other types of tremor
C. Combinations	Various	Severe essential tremor; atypical parkinsonism; dystonic tremor; rubral (Holmes) tremor

The above classification was proposed by a Consensus Statement of the Movement Disorder Society.[17]

Tremors: classification

REST TREMORS	ACTION TREMORS		
• Parkinsonian • ET variants • Midbrain lesions • Myorhythmia	**POSTURAL**	**KINETIC**	**MISCELLANEOUS**
	•Physiologic • Enhanced physiologic (stress, drugs, endocrine) • ET • Orthostatic • PD (reemergent) • Dystonic • Cerebellar • Neuropathic	• Cerebellar lesions as in MS, stroke, wilson disease • Midbrain • Task specific	• Idiopathic • Psychogenic • Other involuntary movements like Myoclonus, Fasciculations, Asterixis, Clonus

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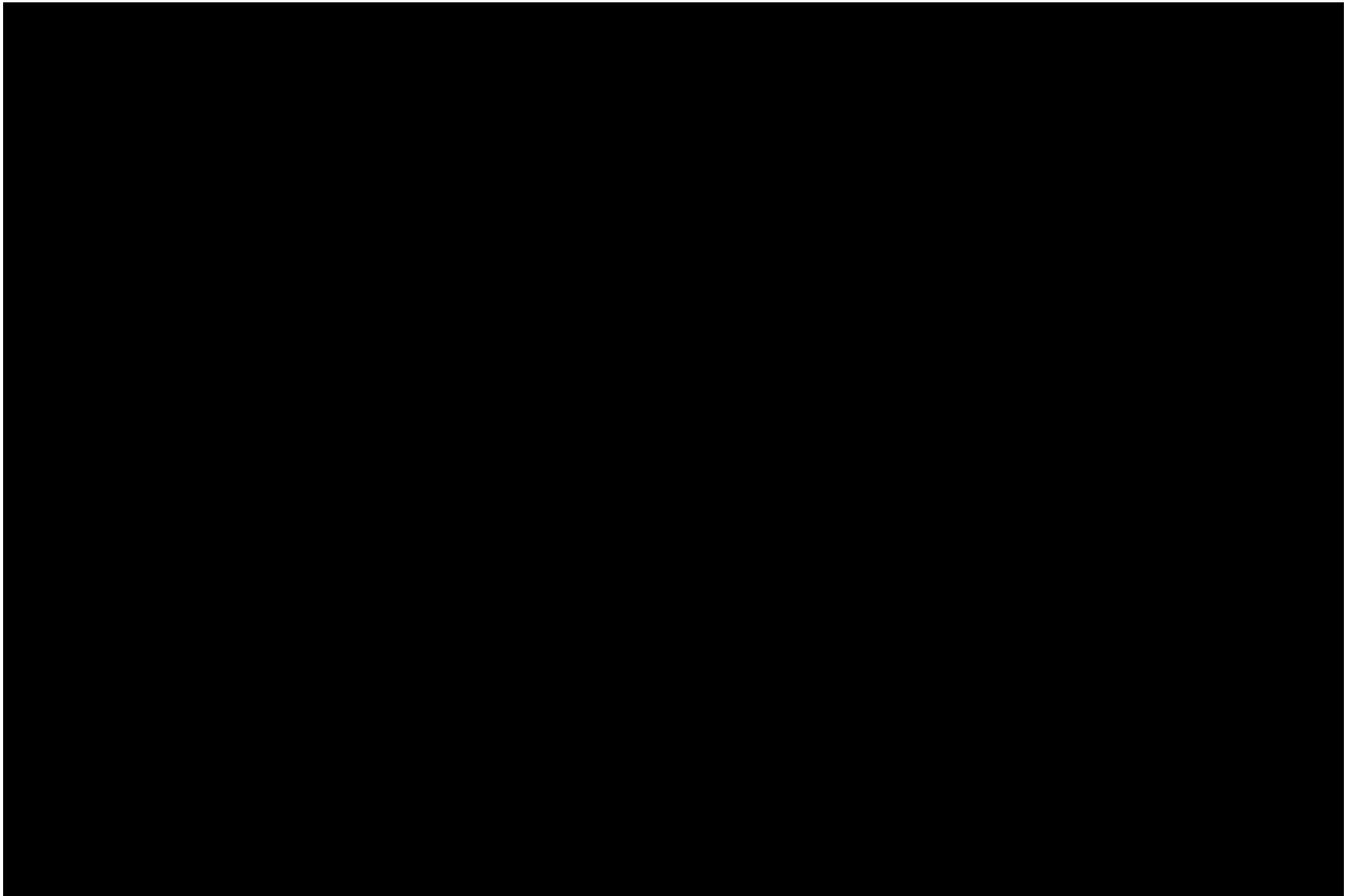
Choreo athetosis

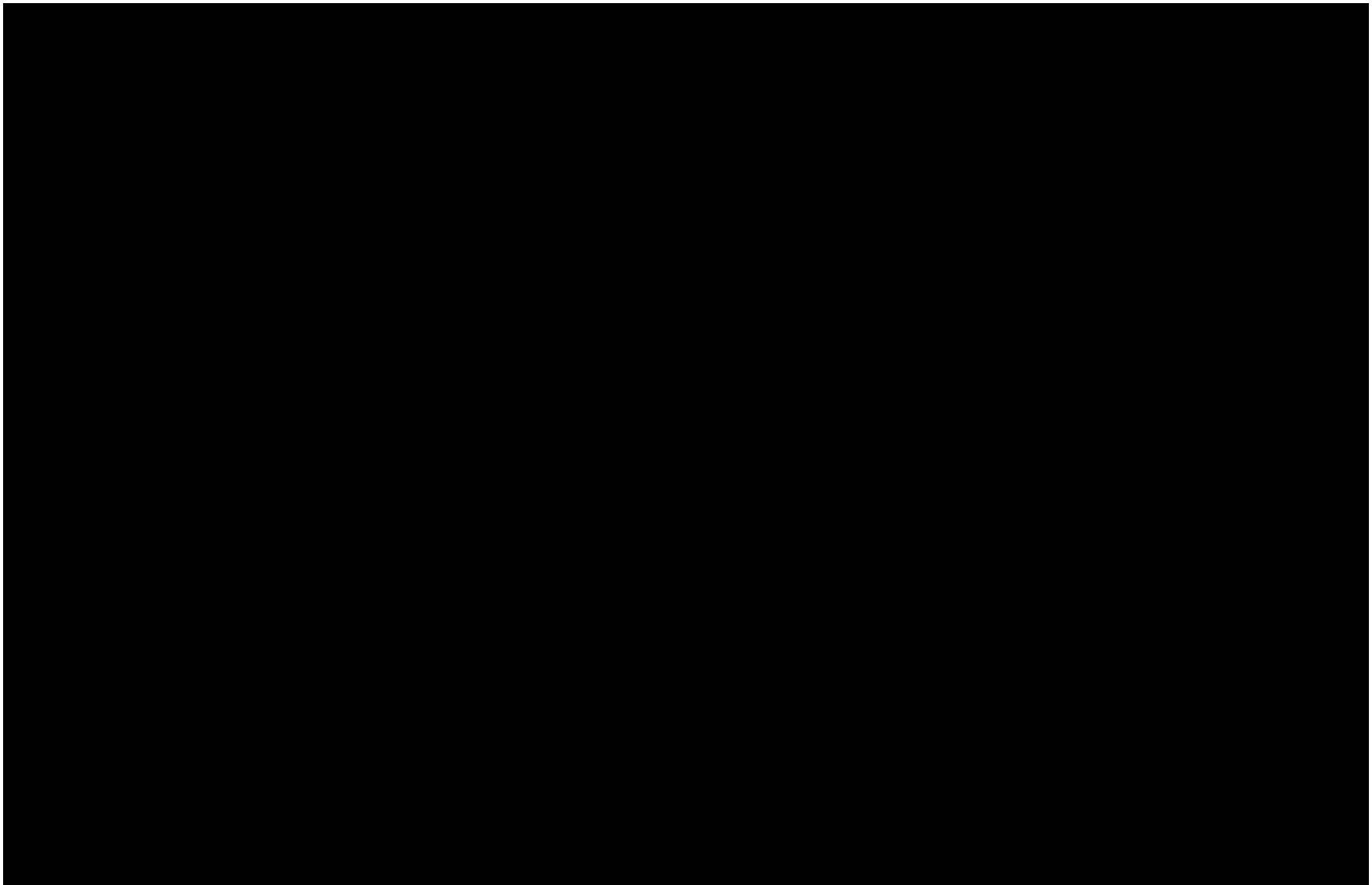


Chorea

- Infectious:
  - Rheumatic fever / Sydenham chorea
  - Herpes encephalitis
  - HIV
  - Cysticercosis
  - Toxoplasmosis
  - Diphtheria
  - Scarlet fever
- Systemic diseases:
  - SLE
- Vascular:
  - Cyanotic heart disease
- Intoxication:
  - CO
  - Methyl alcohol
- Primary genetic:
  - Benign hereditary
  - Huntington`s disease
  - Ataxia telangiectasia
- Metabolic:
  - Wilson`s disease
  - Galactosaemia

Chorea

- Metabolic or toxic encephalopathies-
  - Hypo/ hypernatremia
  - Hypocalcemia
  - Hyperthyroidism
  - Hypoparathyroidism
  - Hepatic/ Renal failure
  - Carbon monoxide, Manganese, mercury, OP poisoning
- Drug induced chorea-
  - Dopamine receptor blocking agents-
    - Phenothiazines
  - Antiparkinsonian drugs-
    - L-dopa
    - Dopamine agonists
    - Anticholinergics
  - Antiepileptic drugs-
    - Phenytoin
    - Carbamazepine



Sydenham Chorea

- Described in 1686
- Major feature of Rheumatic Fever
- In older than 10 year group: > in girls
- Progressive – starts with behaviour problems, clumsiness, difficulty writing, restlessness then after weeks chorea becomes evident
- Present weeks to months; usually good outcome

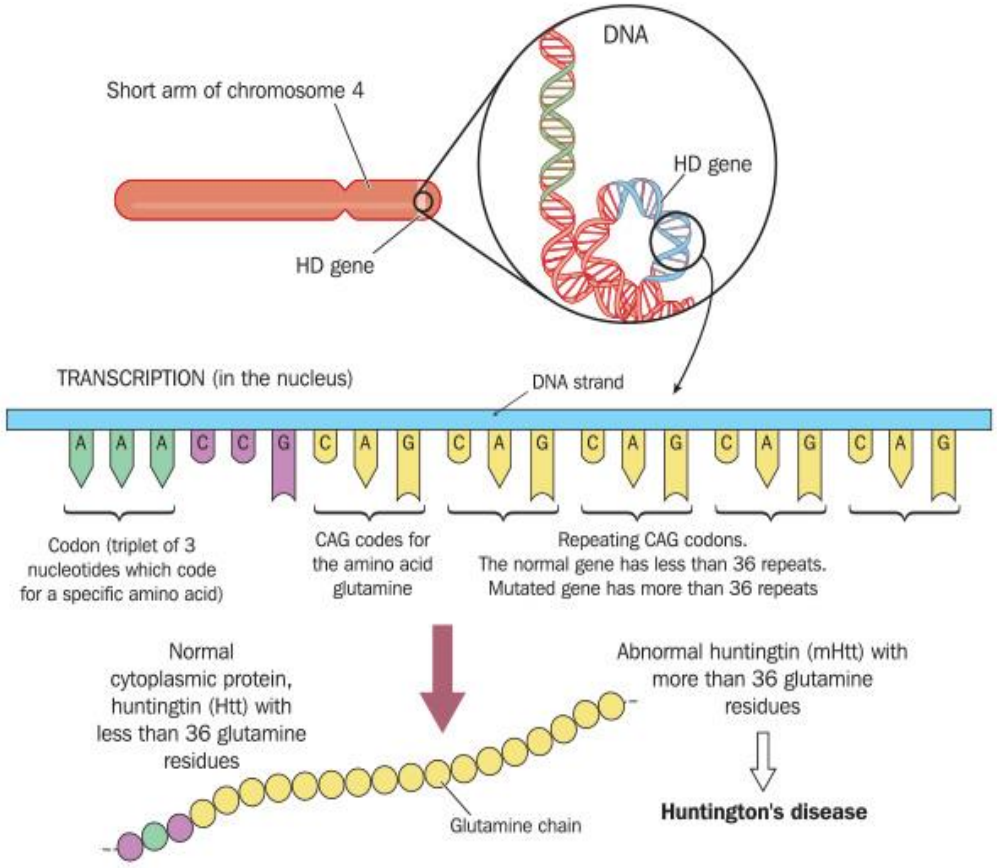
Huntington's disease

- From childhood to the 80s.
- The important point is that HD should be considered in all cases of chorea.
- AD (But anticipation)

✓ A child may present before the parent is symptomatic.

✓ A parent could have died before becoming symptomatic, or may have been misdiagnosed.

Huntington's disease



CAG

10-26 Normal

27-35 Intermediate

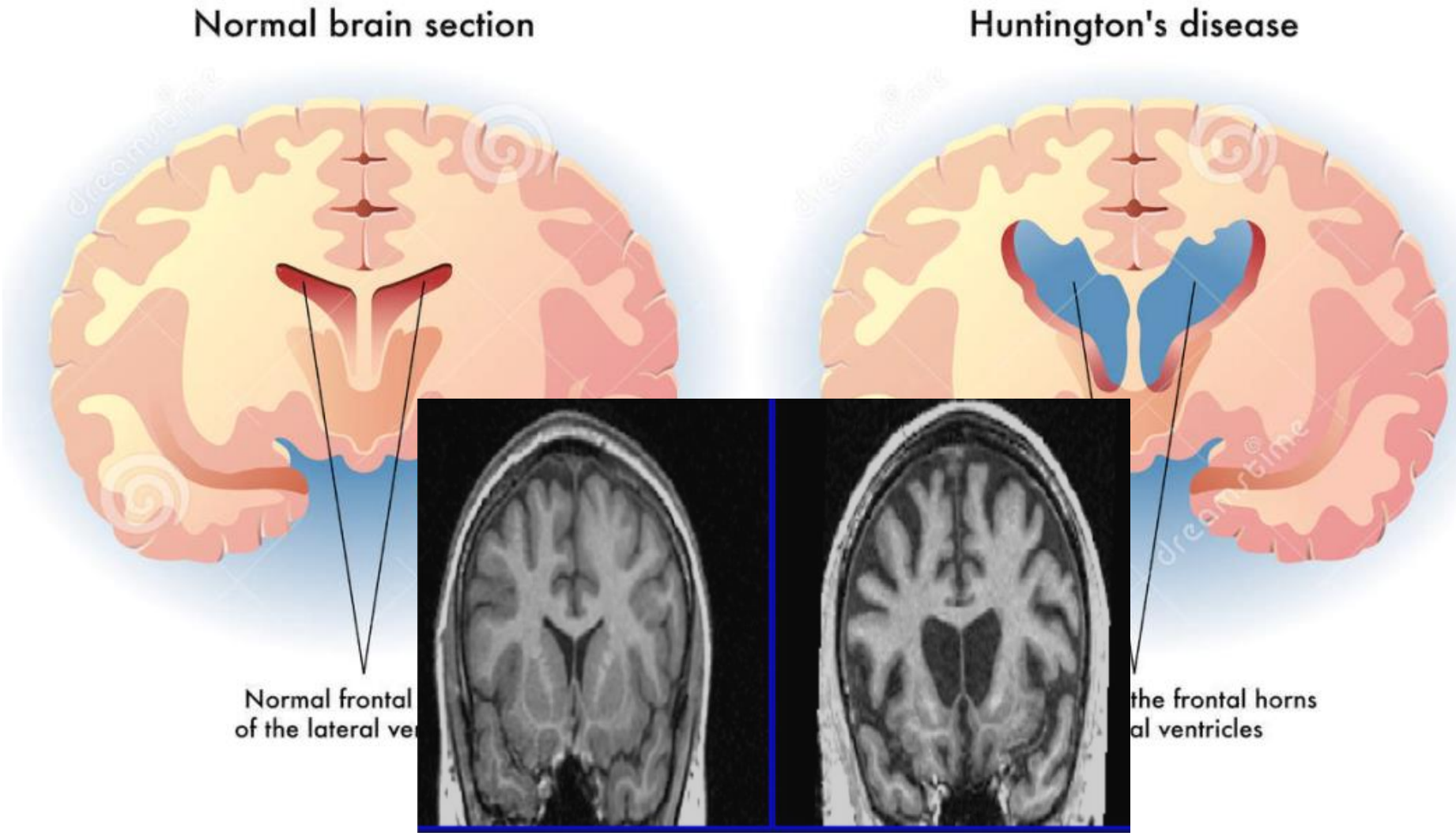
36-39 Reduced penetrance

40+ Full penetrance HD

Huntington's disease

Neurological	Psychiatric	Cognition	Non-neurological
Chorea	Depression	Speech difficulty	Muscle and testicular atrophy
Dystonia	Mania	Executive dysfunction	Weight loss
Rigidity	Psychosis	Short term memory loss	Osteoporosis
Gait abnormality	Anxiety	Poor attention	Impaired glucose tolerance test
Eye movement abnormality	Suicidal tendency	Poor calculation	Heart failure

Huntington’s disease



Huntington's disease

GEN News Highlights

More »

April 4, 2017

FDA Approves Teva's AUSTEDO for Treating Huntington's Disease

The FDA approved Teva Pharmaceutical's AUSTEDO™ (deutetrabenazine; SD-809) for treating chorea associated with Huntington's disease (HD). The drug is an oral, small-molecule inhibitor of vesicular monoamine 2 transporter (VMAT2).

FDA approval was based on data from a 90-patient, placebo-controlled Phase III FIRST-HD trial, which showed that patients treated using AUSTEDO achieved a 4.4 unit improvement from baseline in their Total Maximal Chorea Score, compared with an approximately 1.9 unit change in the placebo group

GEN Quizzes

GEN Quiz: Evaluate Your Knowledge on the NIH Budget, Spinach, and CRISPR

- GEN Quiz: Evaluate Your Knowledge on Trump, Marijuana, and Yogurt
- GEN Quiz: Evaluate Your Knowledge on Opioids, Malaria Vaccines, and CRISPR Patents
- GEN Quiz: Evaluate Your Knowledge on Grapes, Mini-Brains, and Stem Cells

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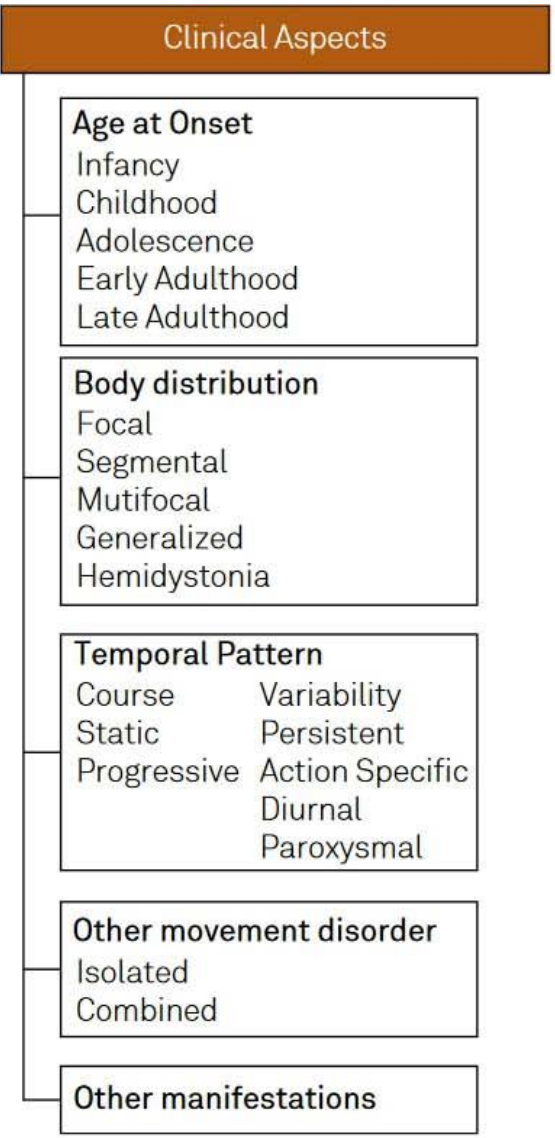
Classification of dystonia



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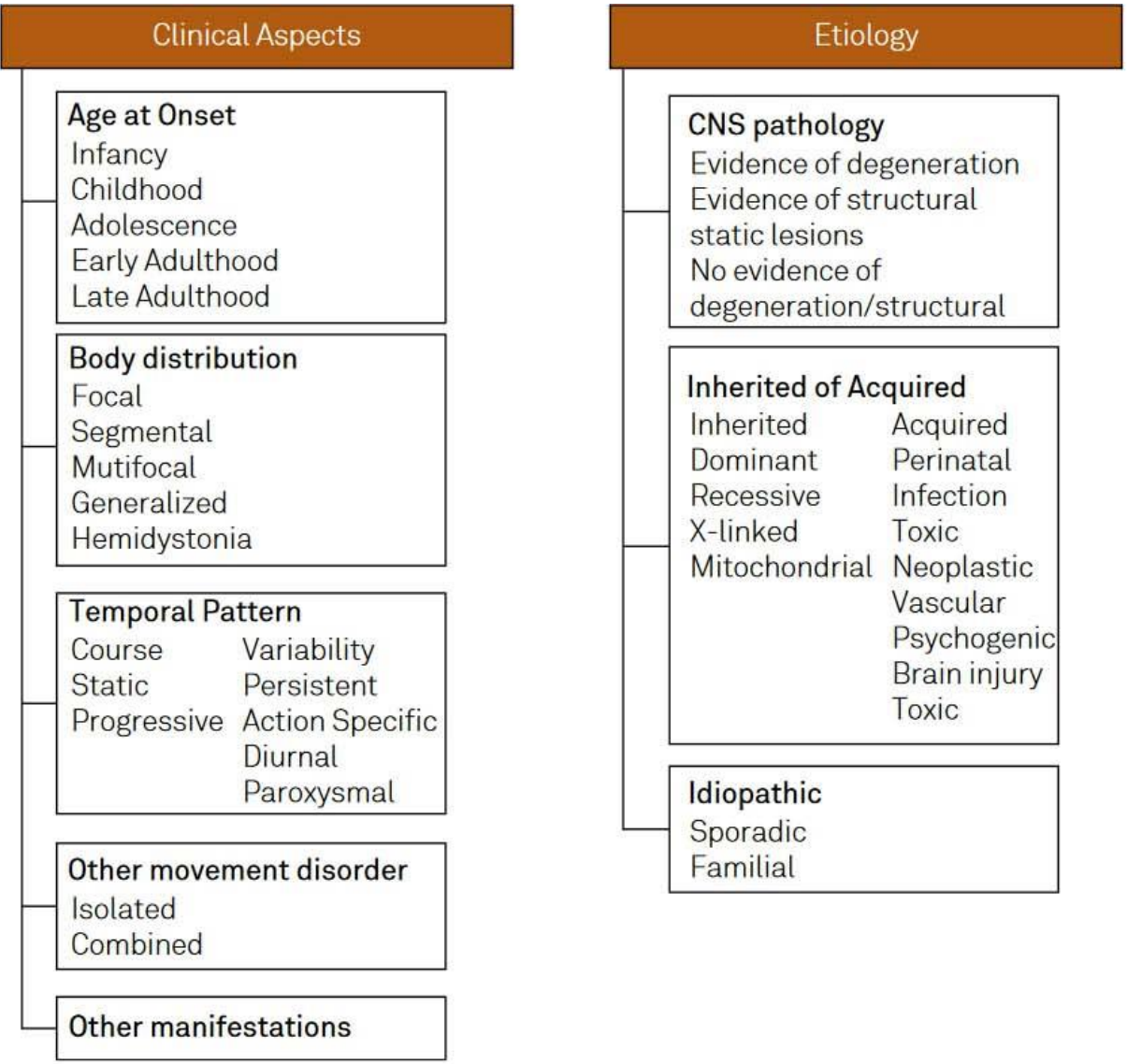
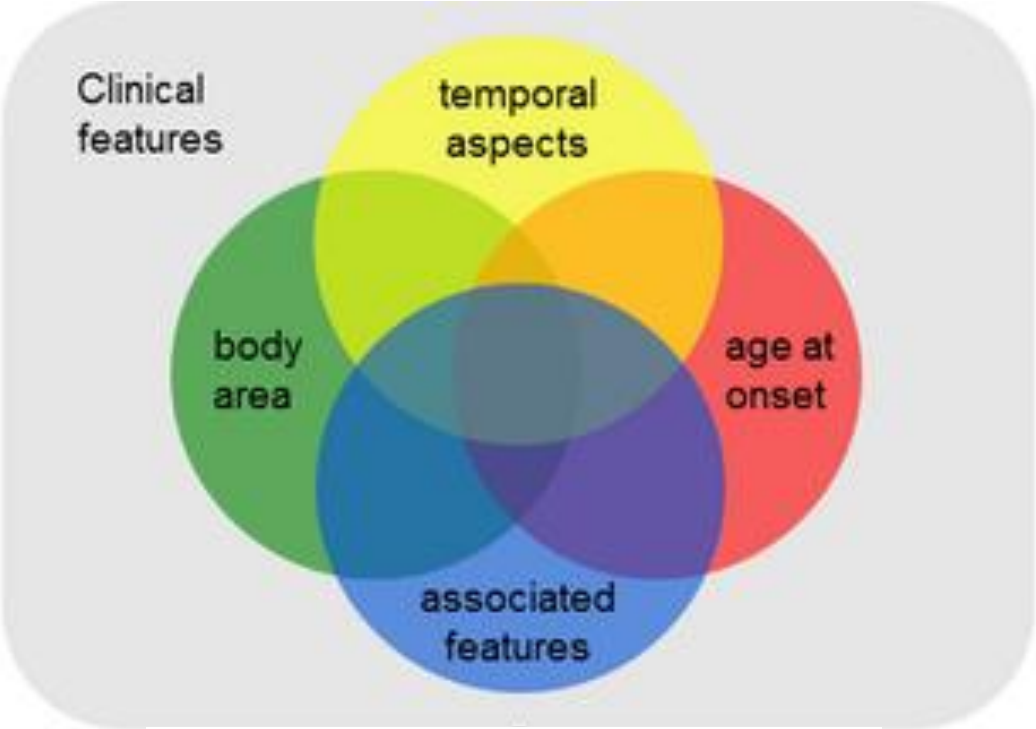


- **Focal:**
  Blepharospasm.
  Cervical dystonia.
  Hemifacial spasm.
- **Segmental.**
- **Multifocal.**
- **Generalized.**
- **Hemidystonia.**



- **Early < 26.**
- **Late>26 years**.

Isolated dystonia (1ry dystonia)

Combined dystonia (Dystonia-plus, Degenerative, 2ry)

Clinical assessment of dystonia

- **D**escribe the movement
- **D**ifferentiate from other MD
- **D**ystonia or dystonia plus
- **D**istribution
- **D**ecreased by , Increased by
- **D**iurnal variation
- **D**uration
- **D**istinguished phenomenon
  - Sensory tricks
  - Overflow
  - mirroring

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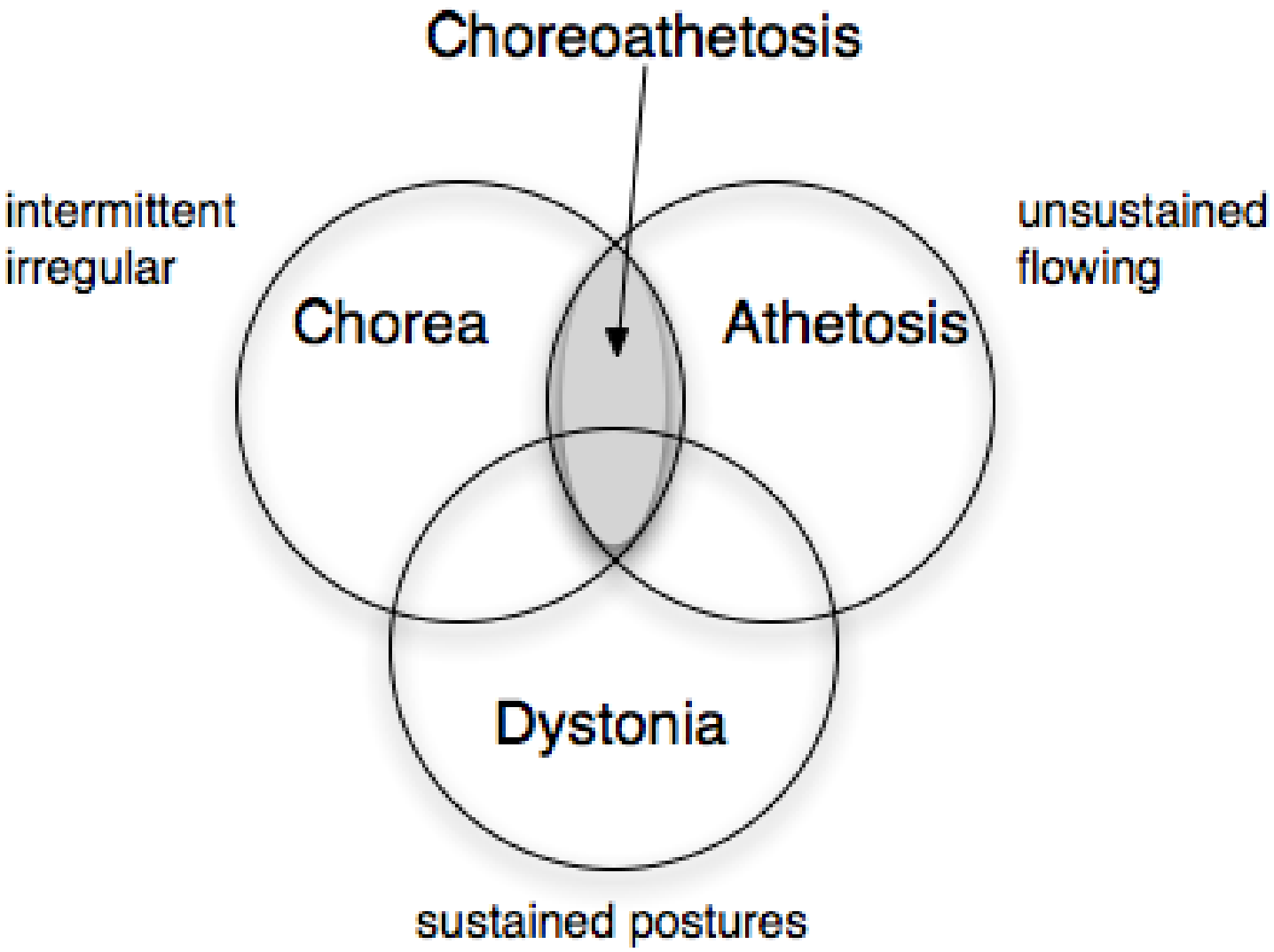
Hyperkinetic Dystonia



Clinical assessment of dystonia

- **Describe the movement**
- **Differentiate from other MD**
- Dystonia or dystonia plus
- Distribution
- Decreased by , Increased by
- Diurnal variation
- Duration
- Distinguished phenomenon
  - Sensory tricks
  - Overflow
  - mirroring

Dr Amr Hassan 2017

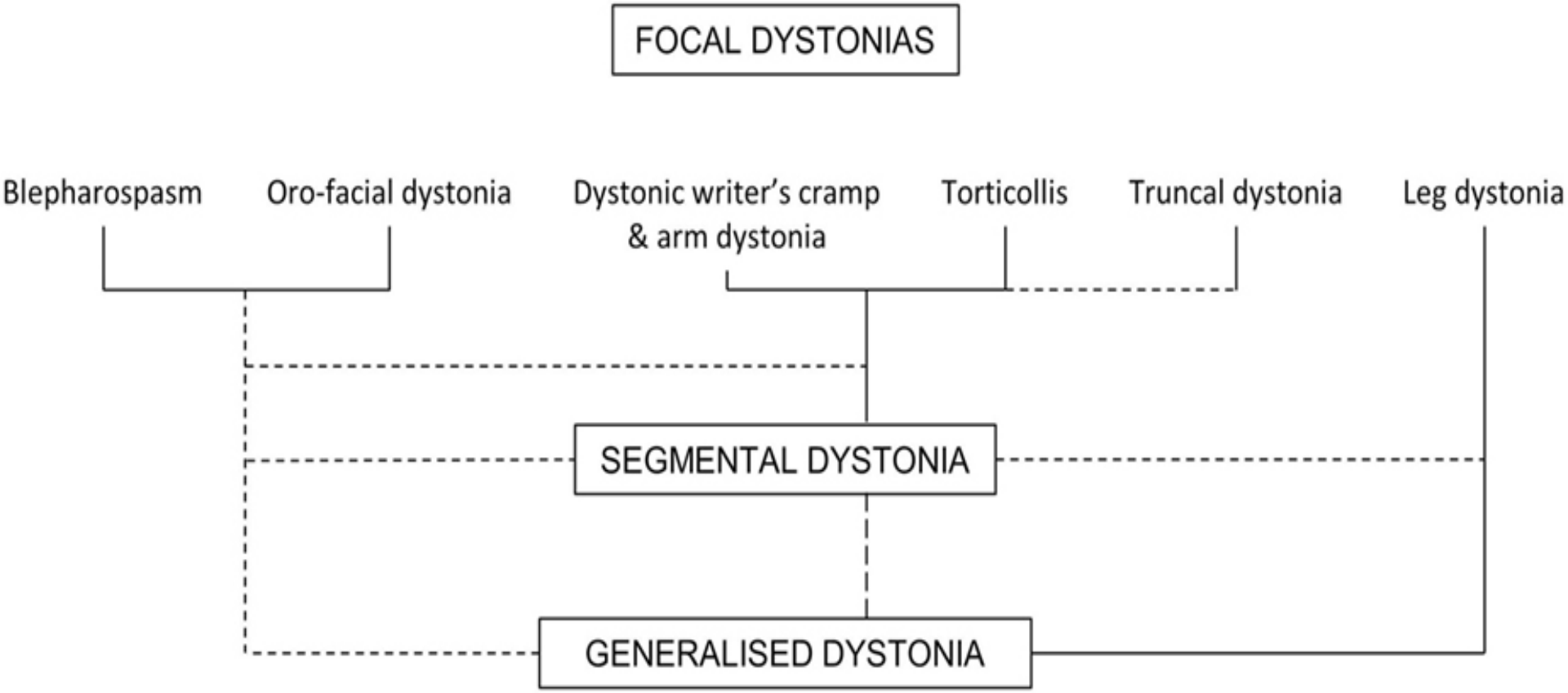
Isolated: dystonia is the only motor feature	Adult-onset task-specific	• Writer's cramp • Musician's dystonia • Runner's dystonia
	Adult-onset non-task-specific limb dystonia	• Idiopathic

Isolated: dystonia is the only motor feature	Adult-onset task-specific	• Writer's cramp • Musician's dystonia • Runner's dystonia
	Adult-onset non-task-specific limb dystonia	• Idiopathic
Combined: dystonia is combined with other movement disorders	Adult-onset non-task-specific limb dystonia	• Parkinson disease • Atypical parkinsonian disorder (i.e., corticobasal degeneration) • Posttraumatic or complex regional pain syndrome • Psychogenic
	Dystonia-plus syndromes	• Dopa-responsive dystonia • Rapid-onset dystonia parkinsonism • Myoclonus-dystonia syndrome
	Paroxysmal dyskinesia and dystonia	• Paroxysmal kinesigenic dystonia • Paroxysmal non-kinesigenic dystonia • Paroxysmal exercise-induced dystonia
	Heredodegenerative dystonia	• Wilson's disease • Huntington's disease • Neuroferritinopathy
	Structural lesions	• Stroke • Tumor

Mixed movement disorders

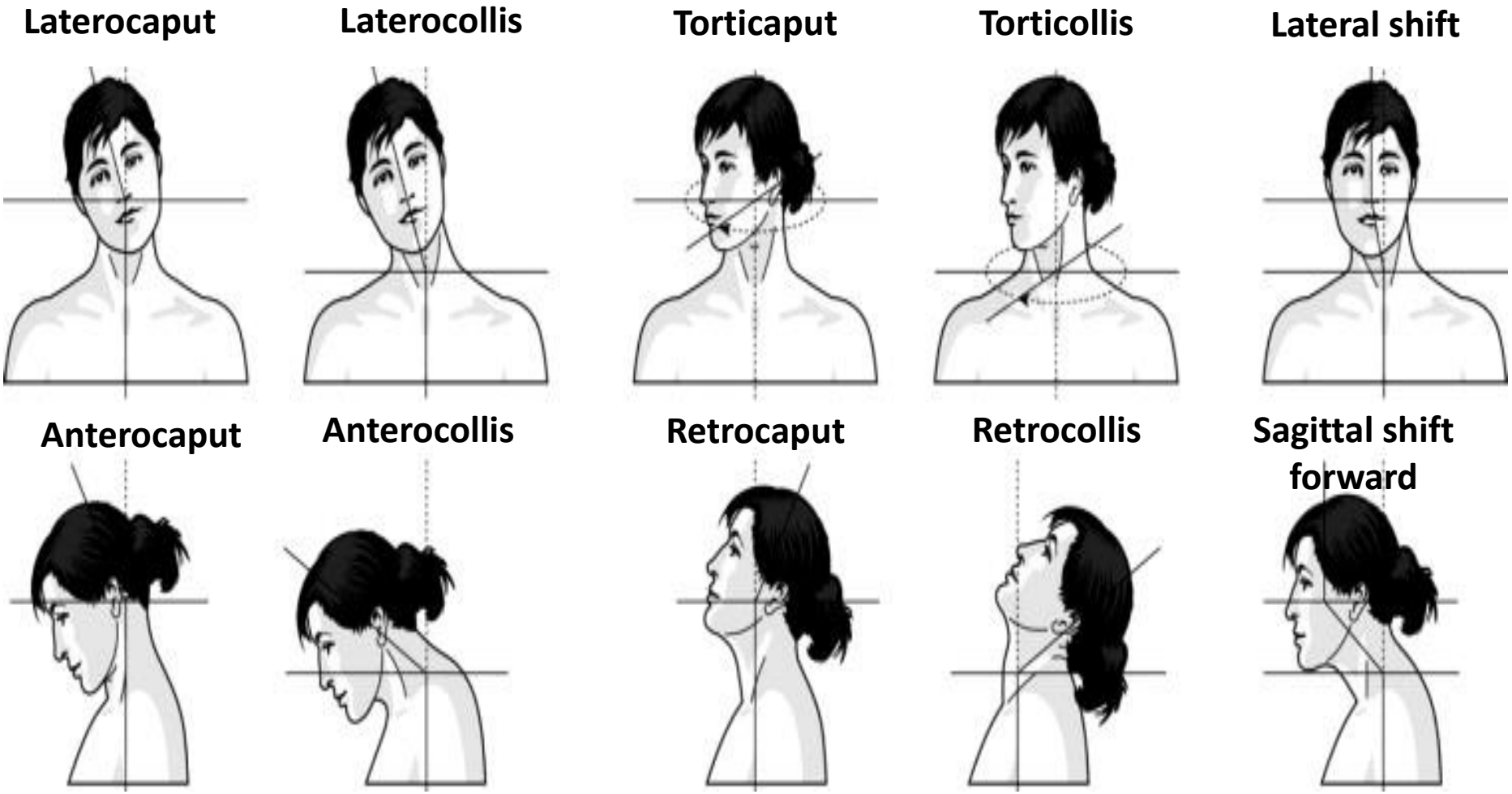
Combinations	Possible etiology
Tremor and akinesia	Parkinson disease or atypical parkinsonism
Parkinsonism, ataxia, autonomic dysfunction, spasticity, myoclonus	Multiple system atrophy
Vertical supranuclear gaze palsy and falls, symmetrical parkinsonism	Progressive supranuclear palsy
Akinesia, rigidity, myoclonus, dystonia and apraxia, asymmetrical clinical phenotype	Corticobasal degeneration
Chorea, dystonia and bradykinesia	Huntington disease
Dystonia plus tremor	Primary dystonia
Tremor (rest and postural), dystonia, akinetic–rigid syndrome	Wilson disease
Ataxia and myoclonus (Ramsay Hunt syndrome, 'progressive myoclonic ataxia')	Mitochondrial disease; celiac disease; Unverricht–Lundborg disease

Distribution of dystonia



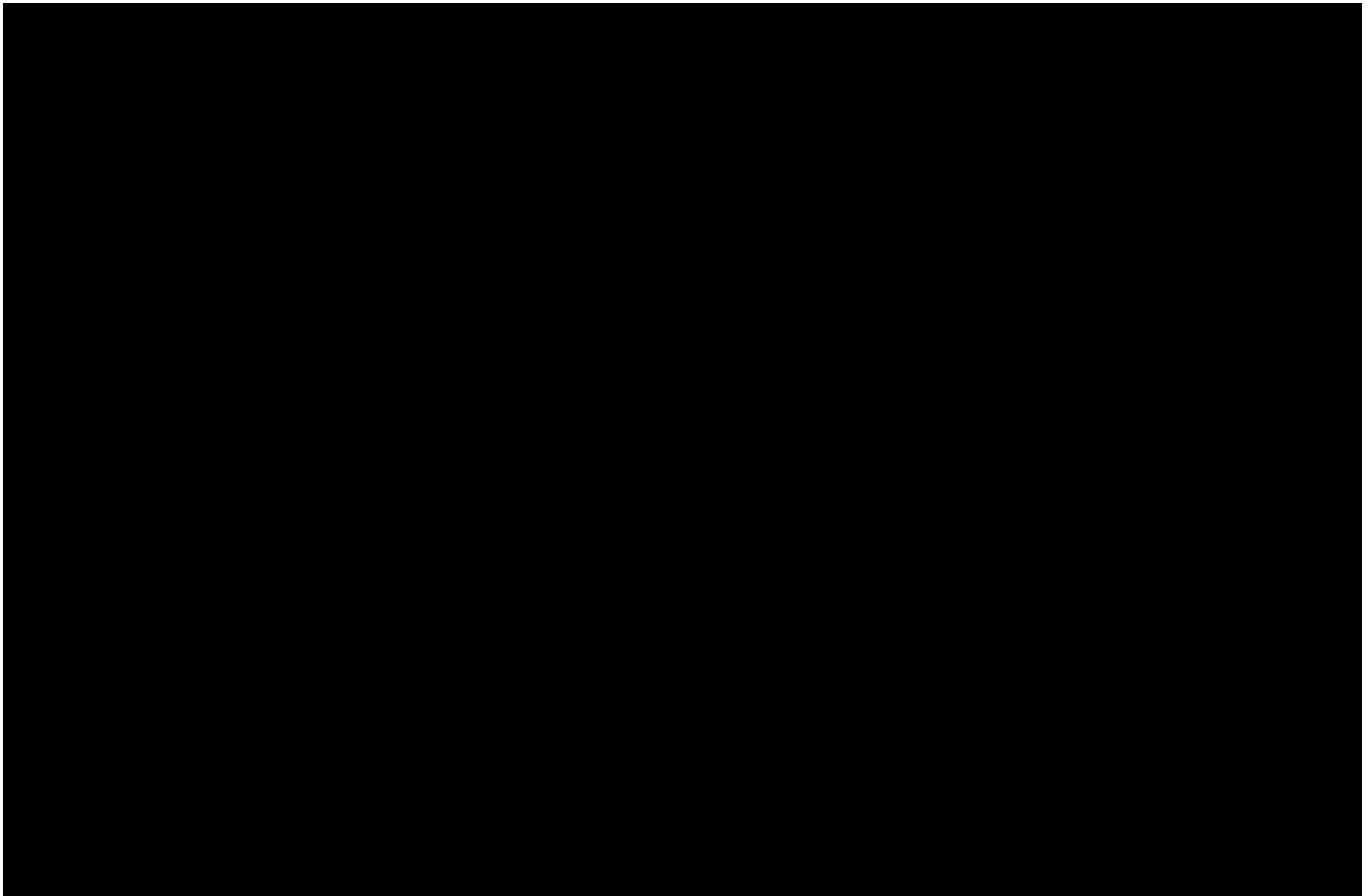
Alberto Albanese, 2017

Cervical dystonia

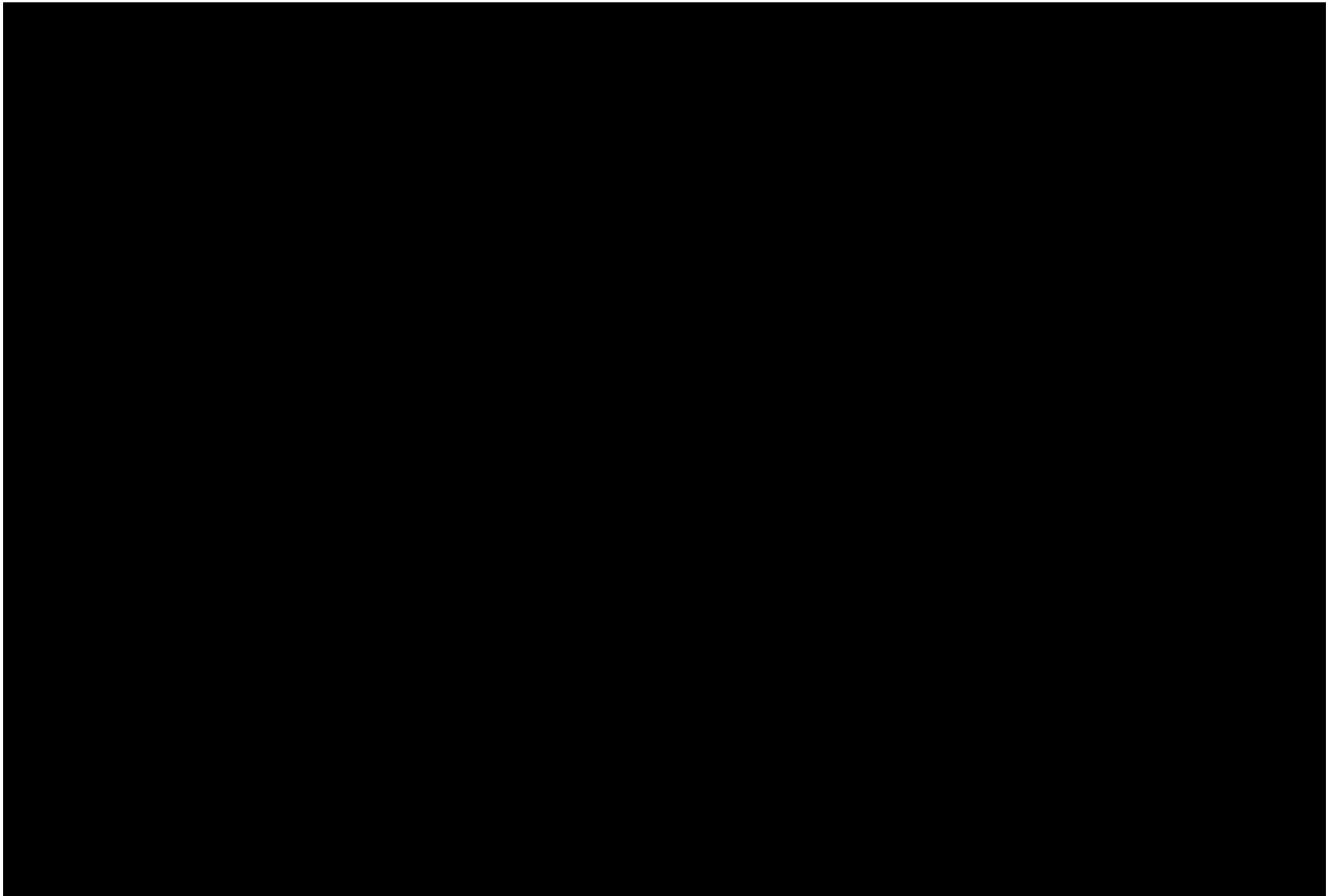


Writer cramp

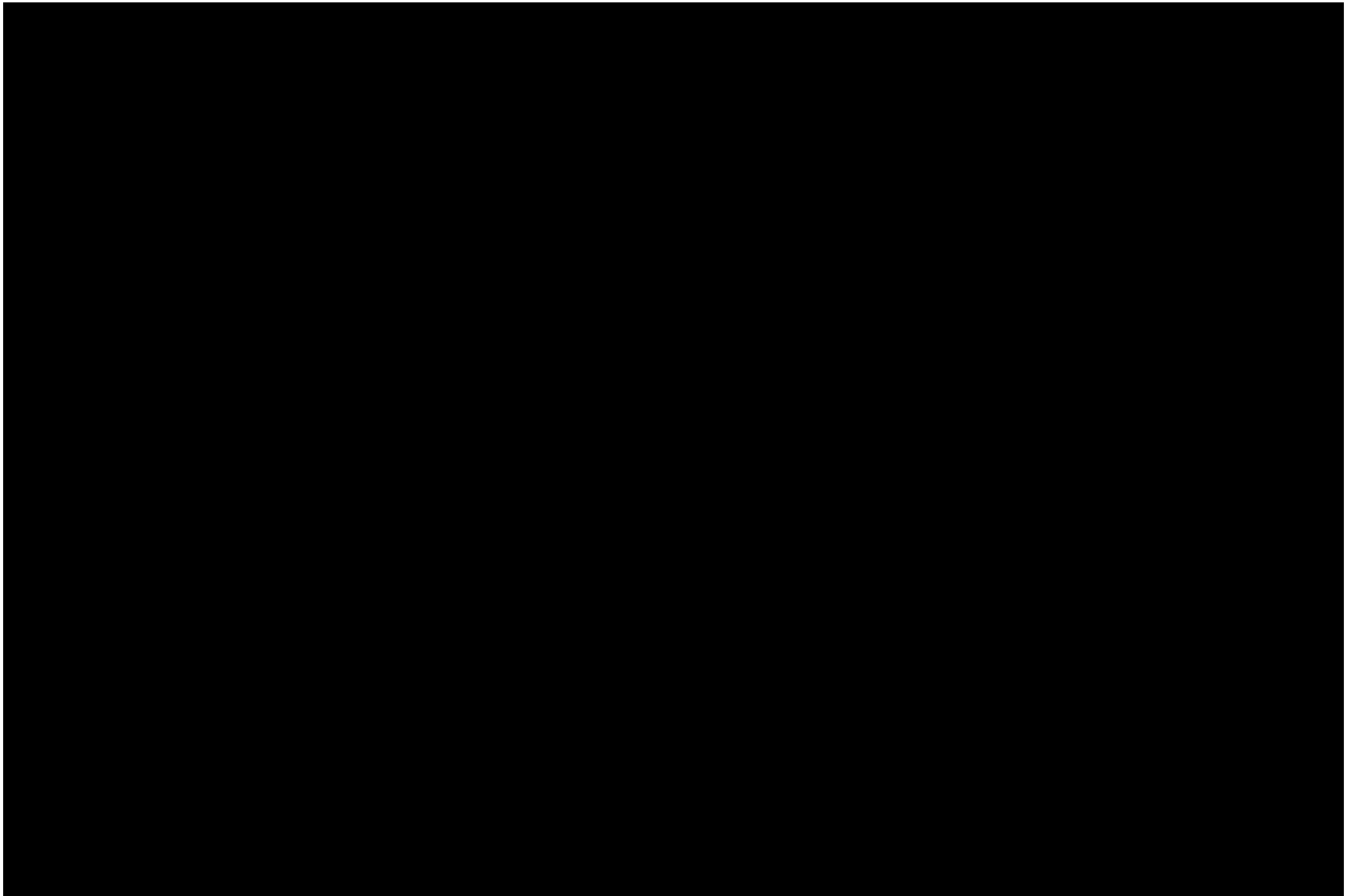
Segmental dystonia



Trunkal dystonia



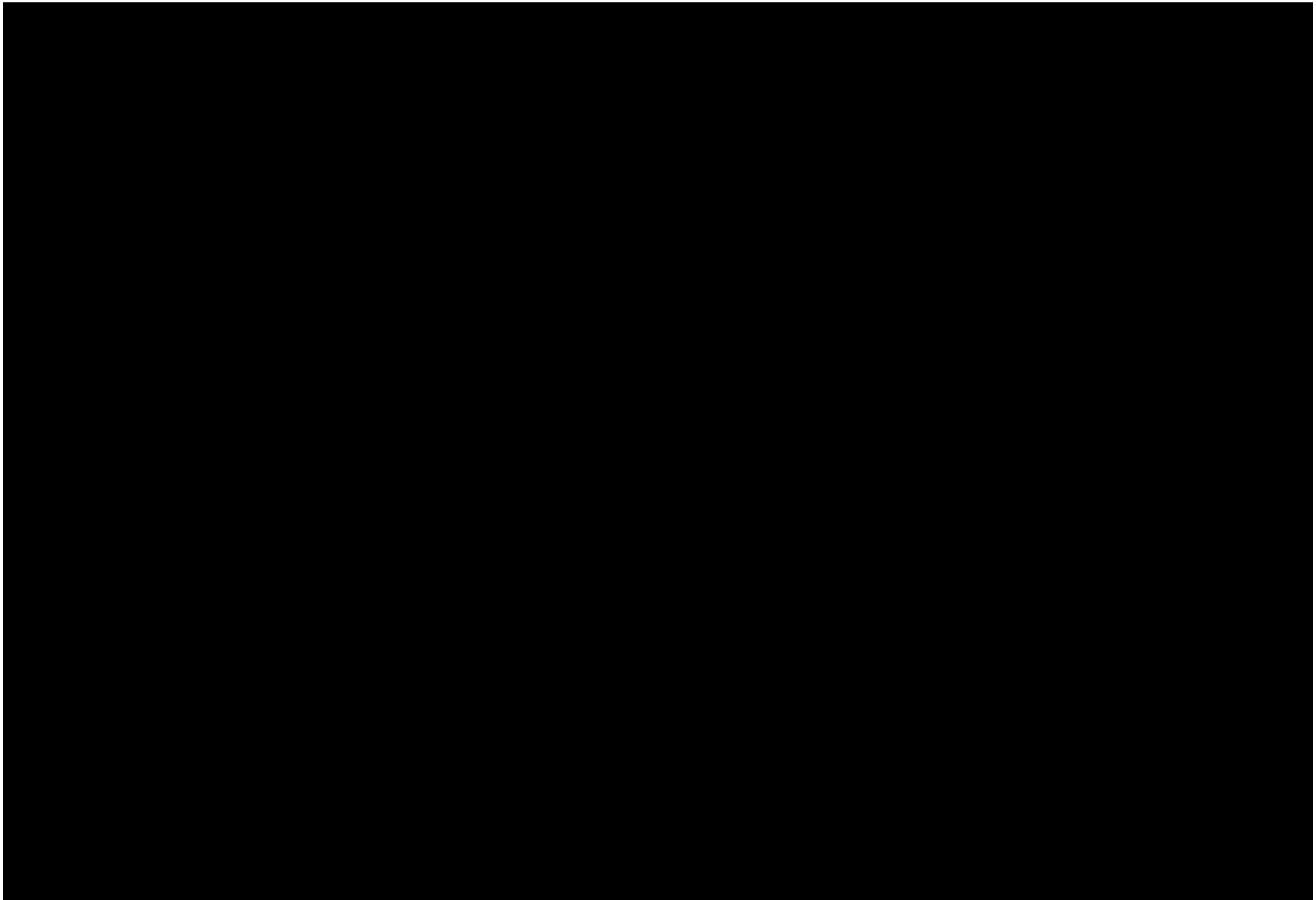
Athetoid CP



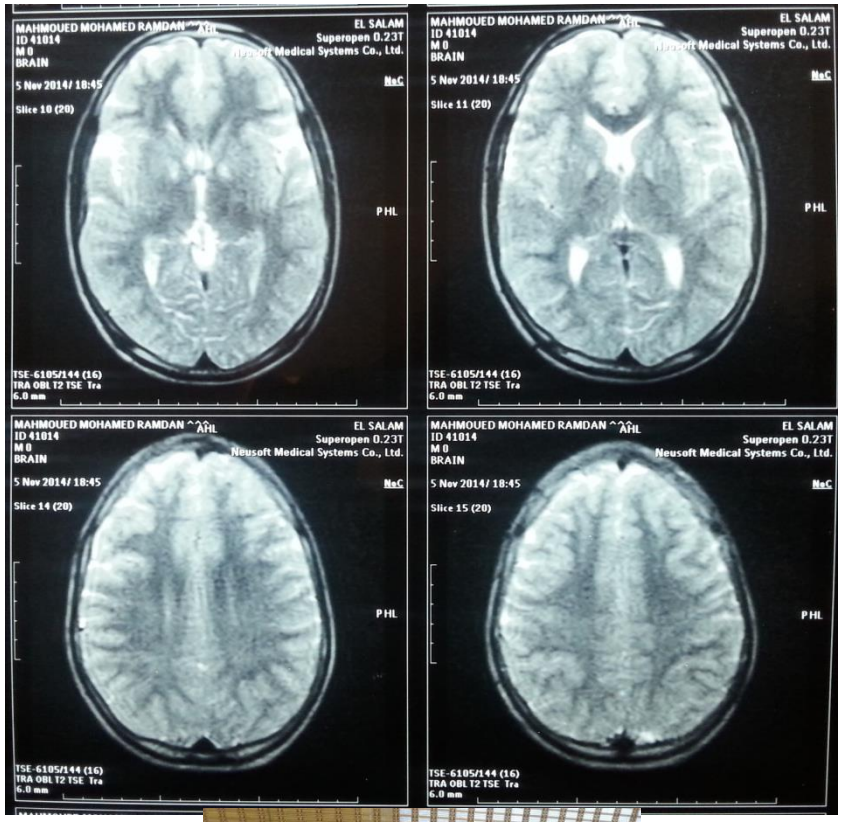
Dyskinetic CP

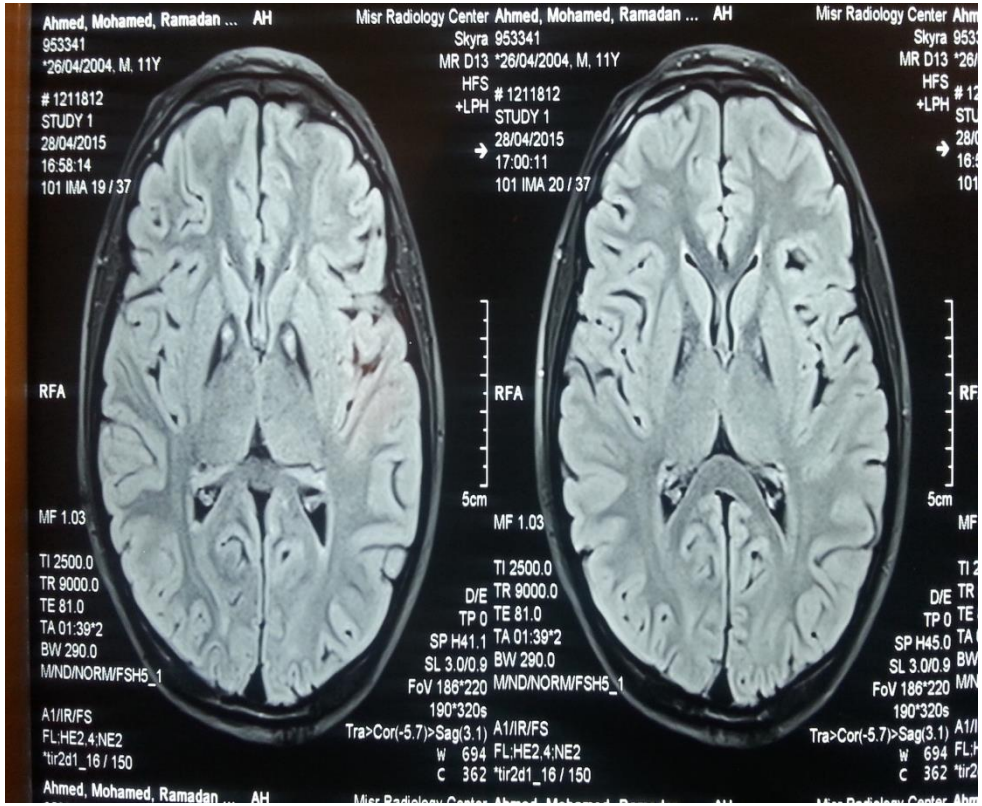
- 2 groups : Choreo-athetotic and dystonic
- Often severe hypoxia in term baby; previously kernicterus
- History of insult + UMN signs
- Incidence of MR 30%

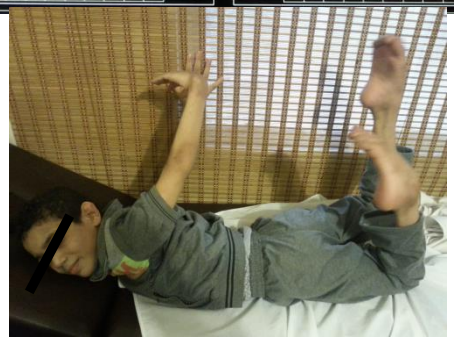
Generalized dystonia

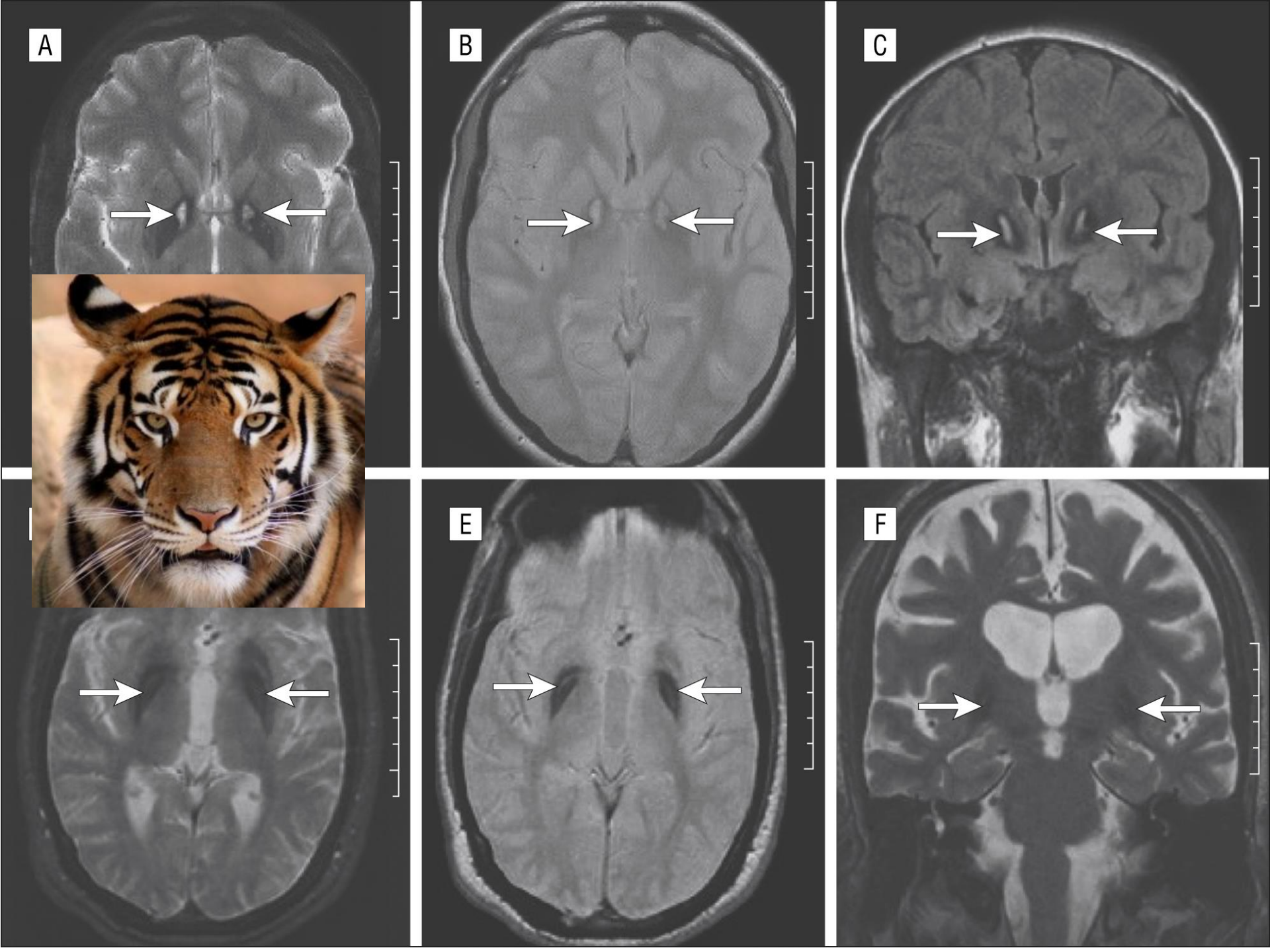


Hallervorden–Spatz syndrome



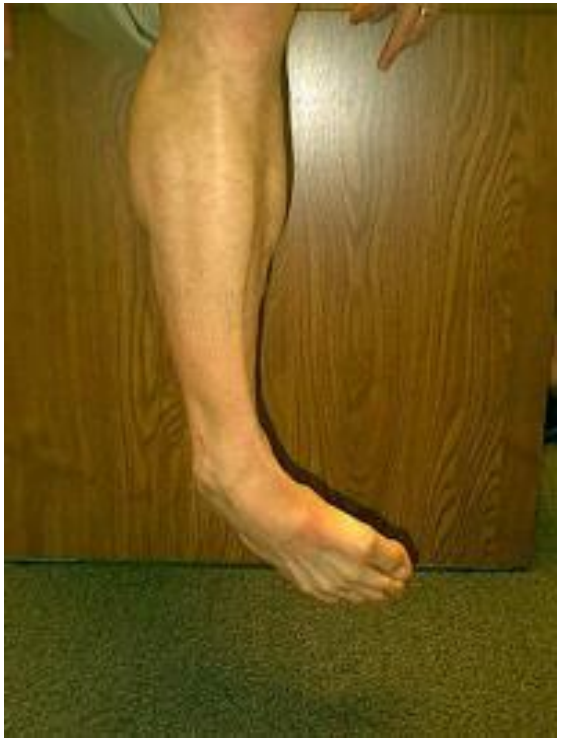





A
B
C
E
F

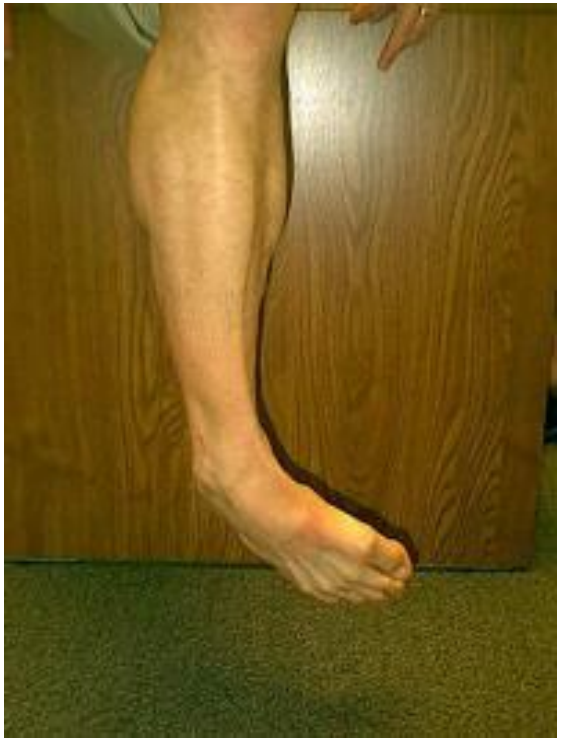
Dopa-responsive dystonia

- AD
- Mutation of the enzyme GTP cyclohydrolase, which is the rate-limiting step in the production of tetrahydrobiopterin, a cofactor in the metabolism of dopamine.
- Limb dystonia that typically affects walking.



Dopa-responsive dystonia

- Diurnal fluctuation.
- Spastic gait, parkinsonism, or cerebral palsy.
- Focal dystonia or parkinsonism in adults.
- Patients respond to low dosages: 300 mg per day.



Paroxysmal Dystonia

Disorder	Age of Onset	Reported Triggers	Duration of Episode	Treatment	Causative Gene	Allelic Disorders
Paroxysmal kinesogenic dyskinesia	Infancy to fourth decade	Sudden movement	Short: seconds to minutes	Carbamazepine, phenytoin	*PRRT2*	Infantile convulsions choreoathetosis, familial Benign paroxysmal torticollis of infancy Familial migraine
Paroxysmal nonkinesogenic dyskinesia	Infancy to fourth decade	Caffeine, alcohol, stress/anxiety, sleep deprivation	Longer: minutes to hours	Benzodiazepines	*MR1*	None known
Paroxysmal exercise-induced dyskinesia	Infancy to adulthood	Exercise, stress, fasting	Longer: minutes to hours	Ketogenic diet	*SLC2A1*	Glucose transporter deficiency phenotypes like absence epilepsy, myoclonic-atonic epilepsy, generalized epilepsy, early infantile epileptic encephalopathy

Overflow

- Commonly found in dystonia.
- Unintentional muscle contraction which accompanies, but is anatomically distinct from the primary dystonic movement.
- It commonly occurs at the peak of dystonic movements.

Mirror dystonia

- Mirror dystonia is a unilateral posture or movement that is the same or similar in character to a dystonic feature that can be elicited, usually in the more severely affected side, when contralateral movements or actions are performed.

Childhood and Juvenile movement disorders

- Parkinsonism
- Tics
- Tremors
- Chorea
- Dystonias
- Ataxia
- Myoclonus
- Mixed

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Ataxia: causes

Acute

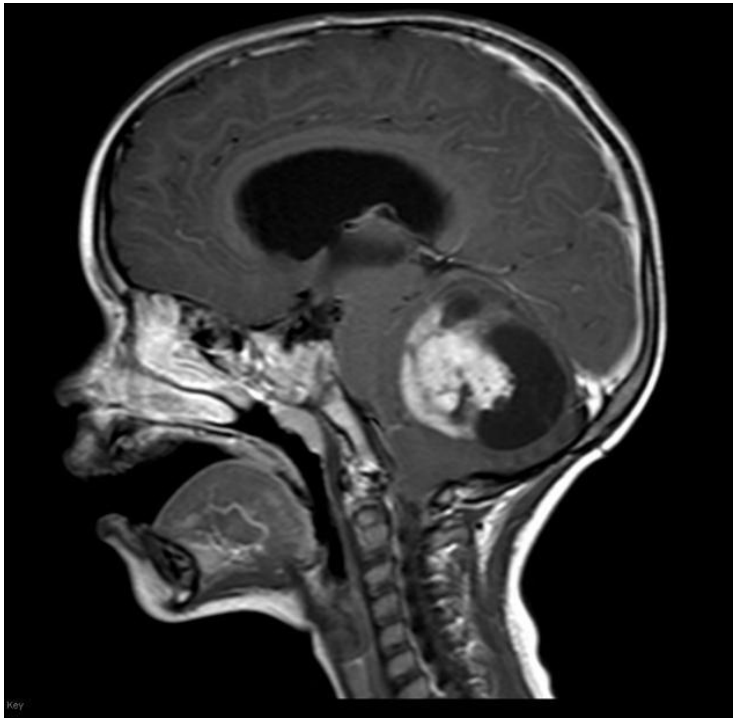
- **Infections**
  - Cerebellar abscess
  - Viral cerebellitis
  - Bacterial
- **Metabolic:**
  - Organic acidurias
  - Leigh's encephalopaties
  - Hypoglycaemia
  - Hyperammonaemia
- **Toxins**
  - Alcohol
  - Phenytoin
  - Phenobarbitone,
  - Lead
  - Glue
  - Vit A
- **Posterior fossa tumour**
- **Vascular**
  - Haemorrhage
  - Embolism
  - AVM
- **Pseudo-ataxia**

Chronic non progressive

- **Perinatal insults**
  - Birth asphyxia
  - Metabolic
  - Intra ventricular haemorrhage
  - Meningitis
- **Congenital malformations**
  - Primary cerebellar hypoplasia
  - Hydrocephalus
- **Foetal alcohol syndrome**
- **Joubert syndrome**
- **Postnatal acquired**
  - Hypoxia
  - Hypoglycaemia
  - Chronic phenytoin
  - Thiamine deficiency
  - Trauma

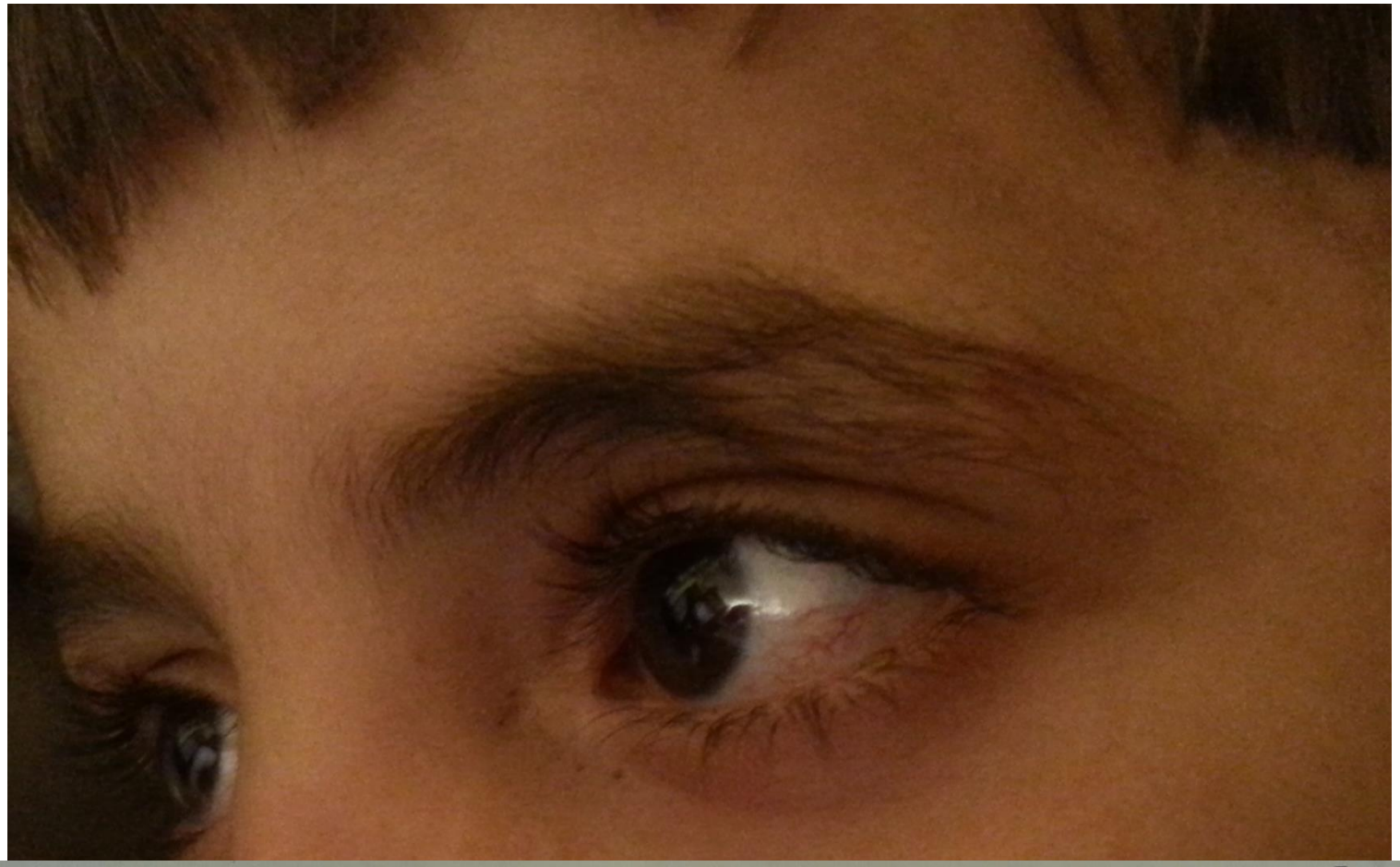
Ataxia: causes

- Chronic or Progressive Ataxia-
  - Brain tumors
  - Congenital malformations-
    - Cerebellar aplasias
    - Dandy- Walker malformation
    - Chiari malformation
  - Hereditary ataxias



Condition	Inheritance	Gene(s)	Age of Presentation	Movement Symptomatology
Friedreich ataxia	Autosomal recessive	*FXN*	Childhood: 2–15 years	Ataxia

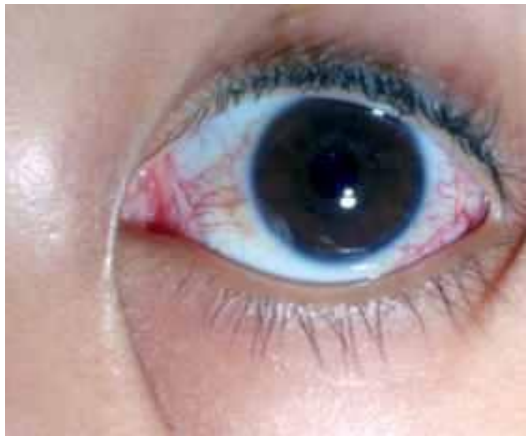
Ataxia telangiectasia



Test	Result	Unit	Reference Range
Alpha Feto protein	138.0	ng/mL	(Up to 10.0

Ataxia telangiectasia

- Slowly progressive cerebellar ataxia
- Telangiectasis of skin and congunctivae
- Frequent pulmonary infections
- Chorea-athetosis
- Malignancies – lymphoreticular
- Sensitivity to ionizing radiation
- Ocularmotor apraxia
- Elevated alpha feto protein



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Myoclonus like disorders

Phenotype	Most Common Etiologies
Myokymia	Postparalytic facial palsy
	Peripheral nerve hyperexcitability (eg, metabolic, autoimmune, or paraneoplastic disorders)
Fasciculations	Benign fasciculations
	Cramp-fasciculation syndrome
	Motor neuron disease
Tics	Tourette syndrome
	Secondary tourettism
	Dystonic tics
Chorea (''chorea minor'')	Sydenham disease
	Benign hereditary chorea
Ballism (severe chorea)	Subthalamic outflow strokes
	Nonketotic diabetic ketoacidosis
Tremor (''jerky tremor'')	Enhanced physiologic tremor
	Dystonic tremor

Non progressive myoclonus

Epileptic

- Benign rolandic epilepsy[a]
- Juvenile myclonic epilepsy[a]
- Angelman syndrome

Secondary

- Posthypoxic myoclonus (Lance-Adams syndrome)
- Iatrogenic (valproate, lamotrigine, meperidine, amantadine, levodopa)
- Metabolic (hypematremia, hypercalcemia, hyperthyroidism, hypomagnesemia, nonketotic hyperglycemia, biotin deficiency, metabolic alkalosis)

With dystonia

- Myodonus-dystonia (DYT11, DYT15)

With ataxia

- Heroin toxicity (acute)
- Ataxia-telangiectasia
- Myoclonic epilepsy with ragged red fibers[a] (MERRF)
- Mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes (MELAS)
- Opsoclonus-mrclonus ataxia

Progressive myoclonus

With ataxia

- Autosomal dominant spinocerebellar ataxias with myoctonus (SCA2, SCA3, SCA14, SCA19)
- Dentatorubral-pallidoluysian atrophy
- Friedreich ataxia
- Ataxia-telangiectasia
- Orthostatic myoclonus

Severe/rapidly progressive

- Creutzfeldt-Jakob disease
- Progressive myodonic encephalopathies
- Subacute sclerosing panencephalitis
- Infectious encephalitis (herpes simplex virus, arbovirirs, human T-cell tymphotropic virus 1, HIV)
- Postinfectious encephalitis
- Hashimoto encephalopathy
- Celiac disease
- N-methyl-o-aspartate (NMDA) receptor antibody encephalitis
- latrogienic (bismuth encephalopathy)

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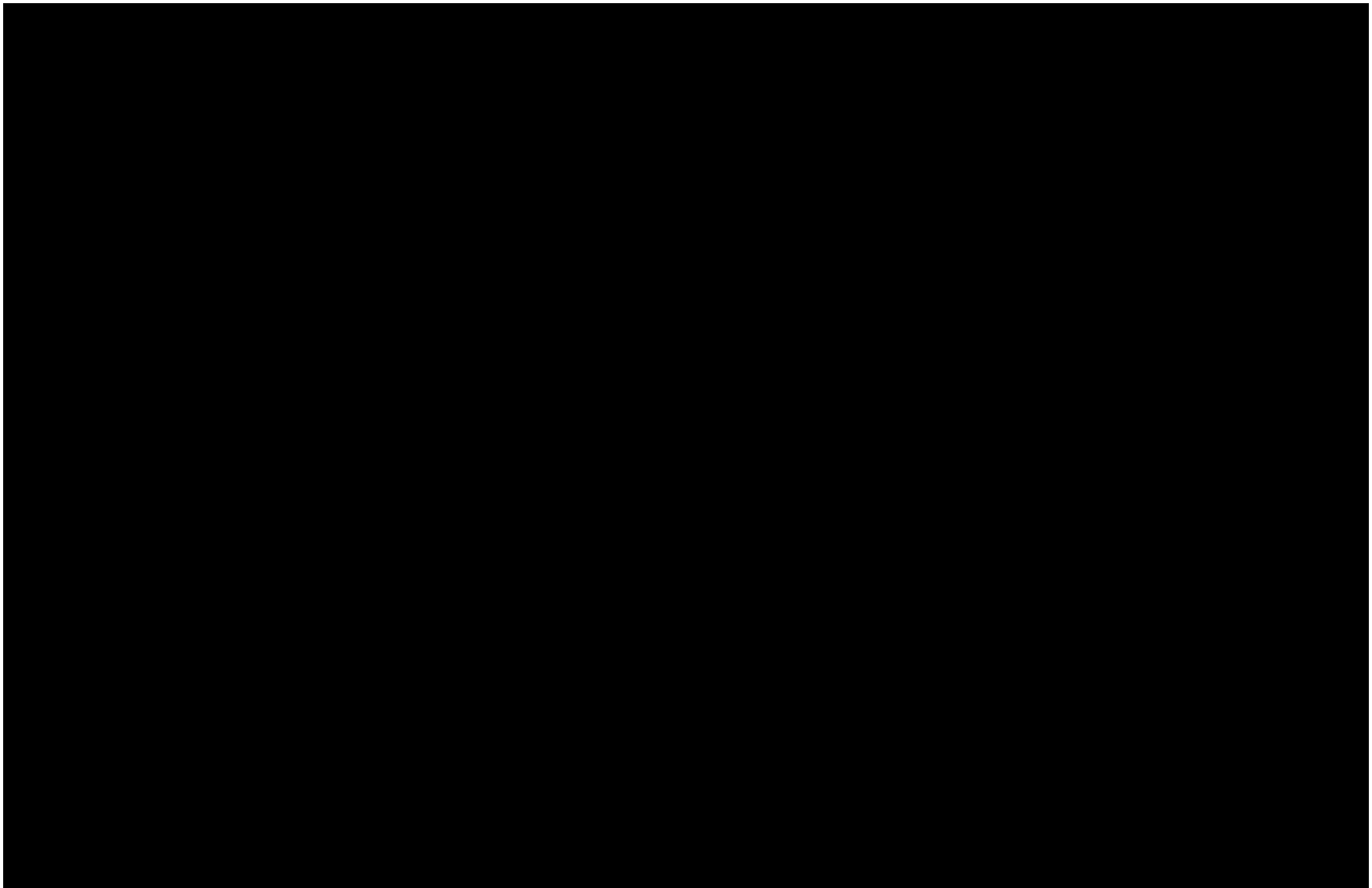
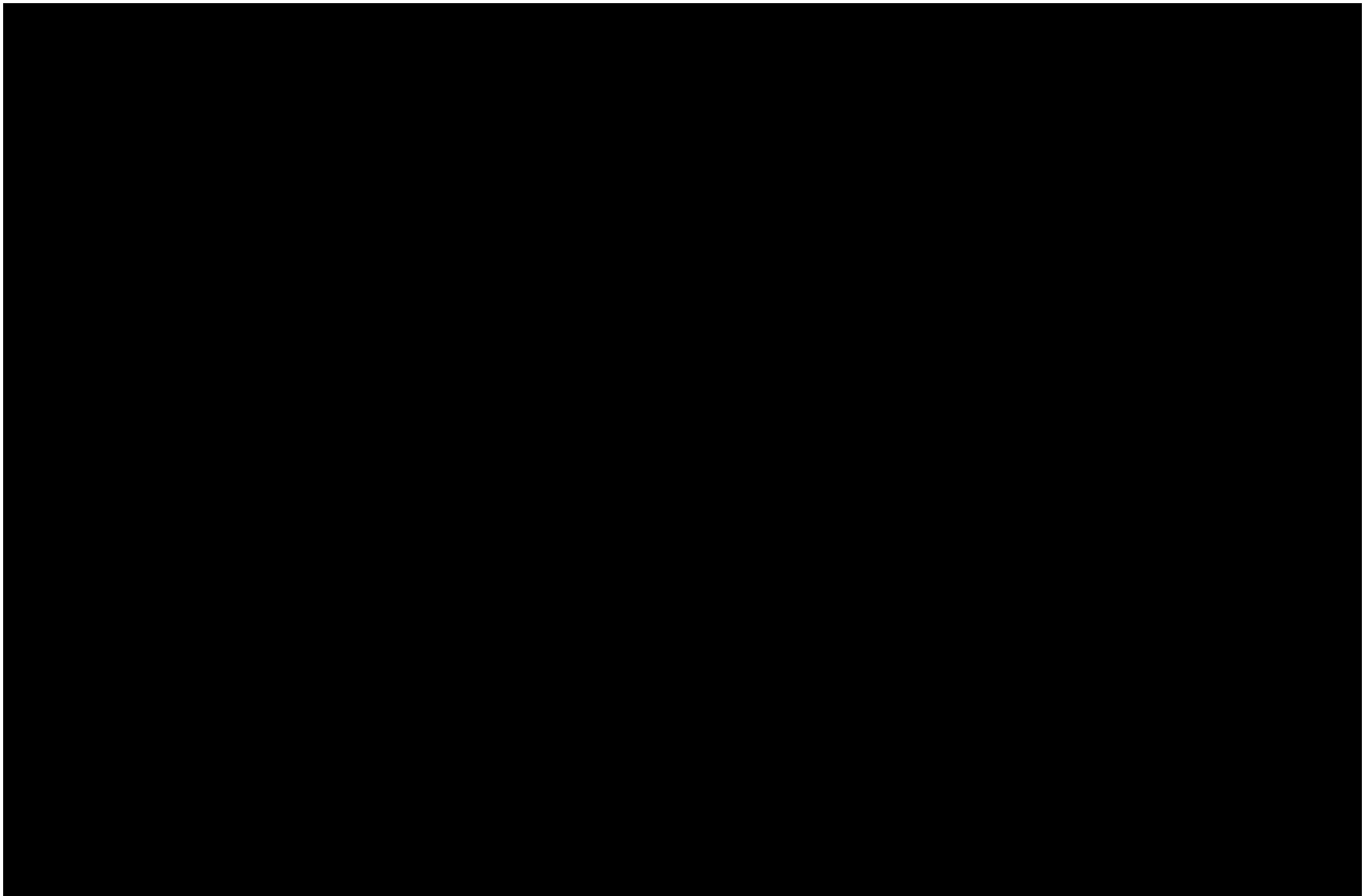
Myoclonus



Benign Neonatal Sleep Myoclonus



Benign Neonatal Sleep Myoclonus

- Rapid, random, bilateral/asynchronous
- jerking, may be forceful and rhythmic
- Seconds-minutes or even hours in sleep
- All stages of sleep (Quiet sleep/NREM)
- Differential: Seizures and Jitteriness
- Disappear when infant is woken up
- Not seen during alert wakefulness
- Does not stop on passive flexion (jitter stops)
- EEG: Normal baseline and during events
- Mostly disappear by late infancy

Juvenile movement disorders

- Parkinsonism
- Tics
- Tremors
- Chorea
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- Ataxia
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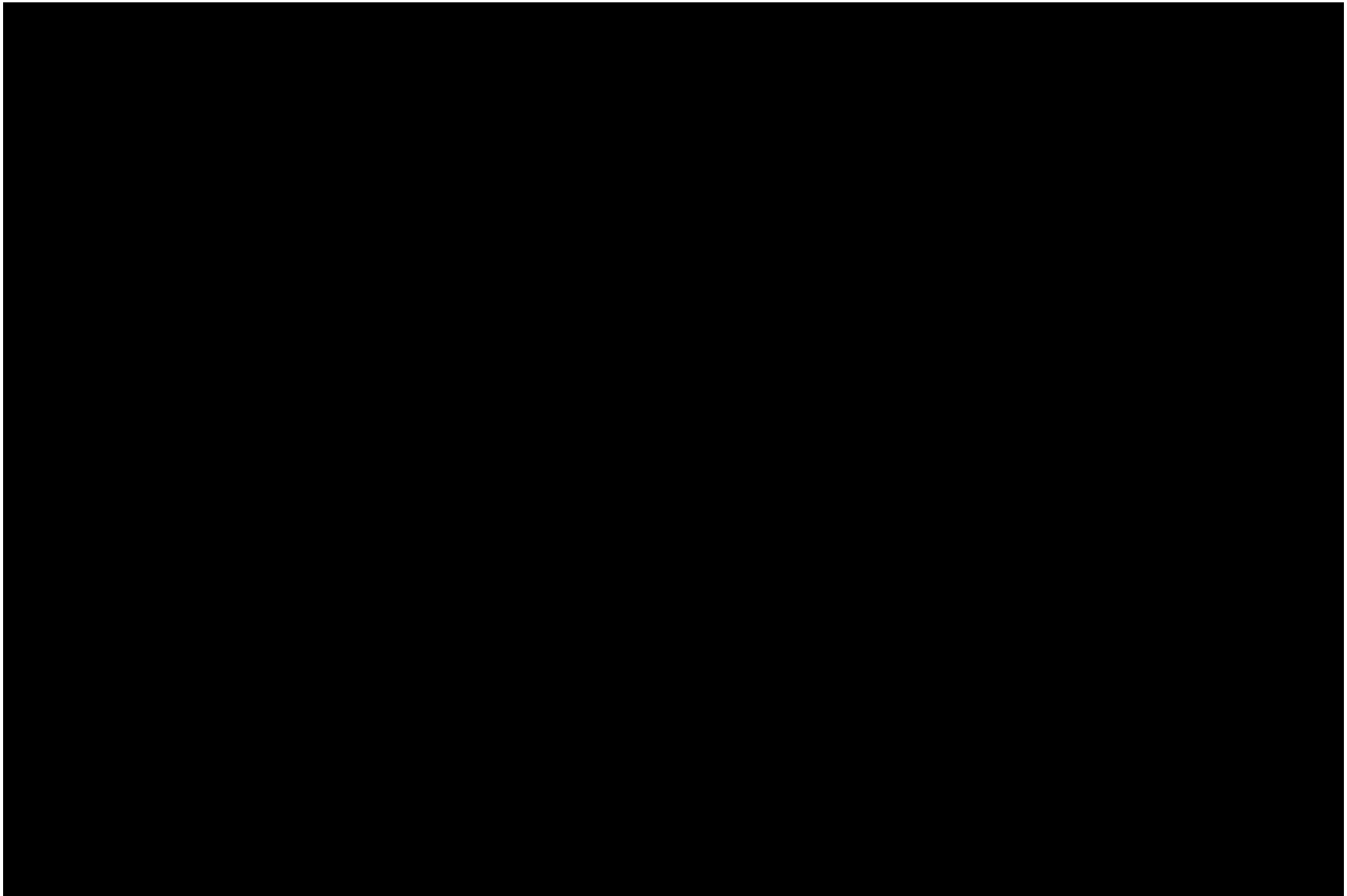
- Mixed

Tics → Tourette syndrome



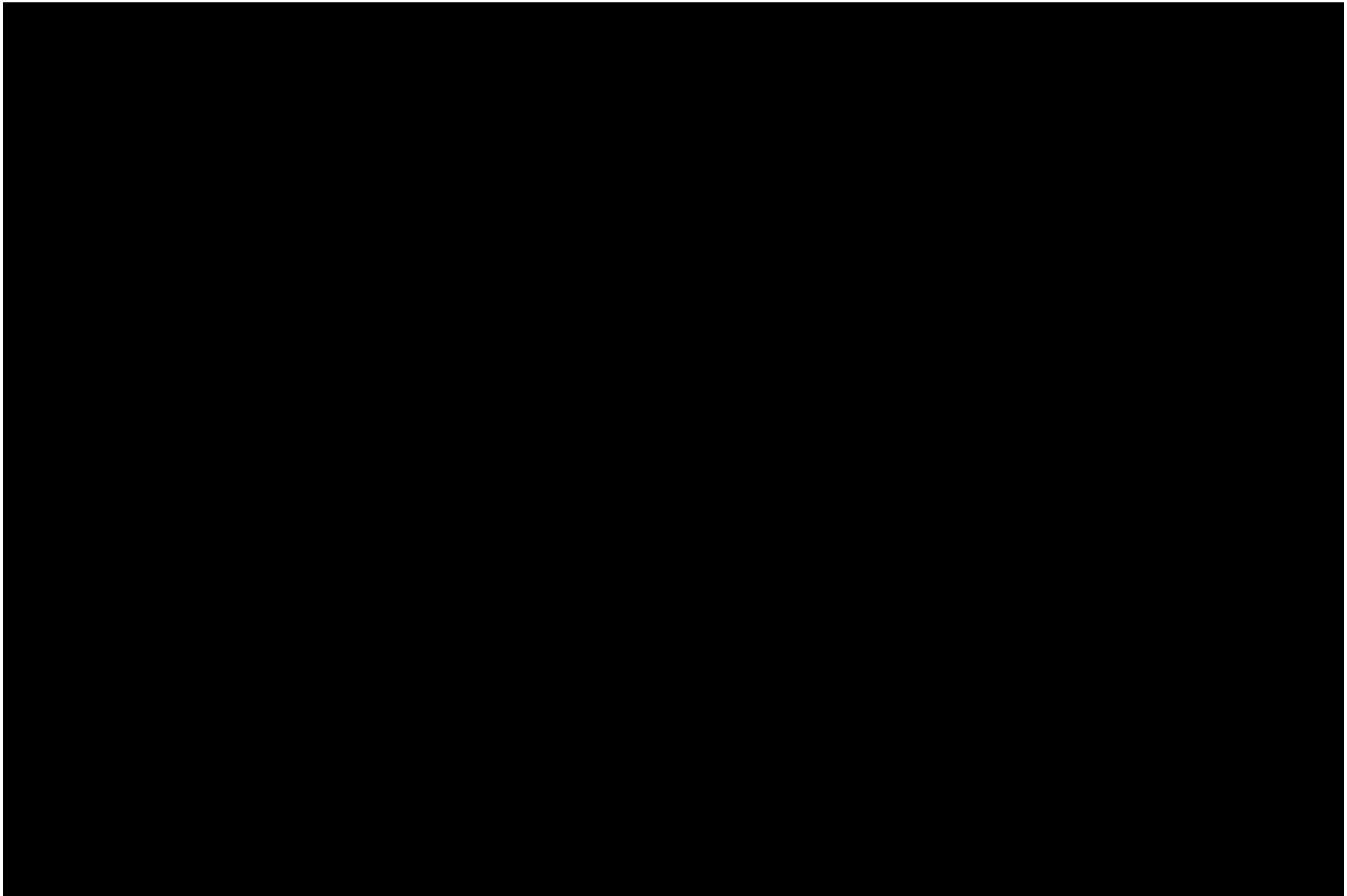
Tics Vs Myoclonus

	Myoclonus	Tics
Onset	Any	School age
Pattern	Patterned, predictable, identical	Variable, wax and wane
Movements	Jerky, shock like, sudden	Blink, grimace, shrug
Rhythm	Maybe Rhythmic	Rapid, sudden , random
Duration	Brief, intermittent	Brief, intermittent
Premonitory	No	Yes
Trigger	No, action, stimulus sensitive	Excitement, stress
Suppression	No	Brief (causes inner tension).
Family History	May be positive	Frequently positive
Treatment	AED	Neuroleptics

Mixed movement disorders

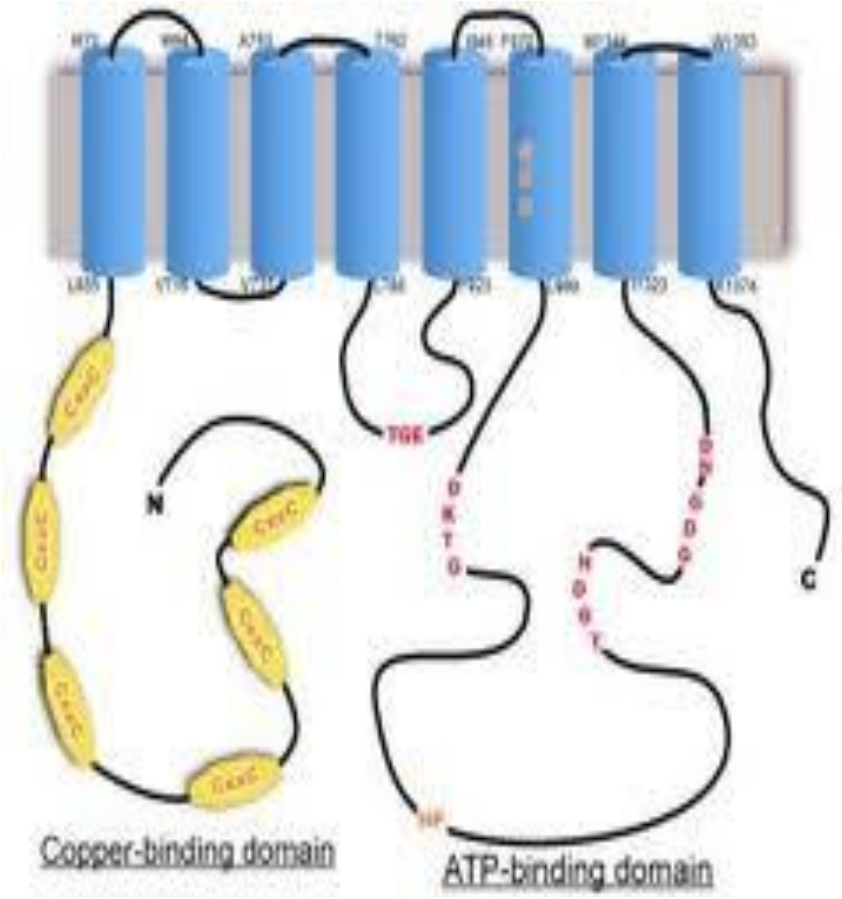
Chorea, dystonia and bradykinesia	Huntington disease
Dystonia plus tremor	Primary dystonia
Tremor (rest and postural), dystonia, akinetic–rigid syndrome	Wilson disease
Ataxia and myoclonus (Ramsay Hunt syndrome, 'progressive myoclonic ataxia')	Mitochondrial disease; celiac disease; Unverricht–Lundborg disease

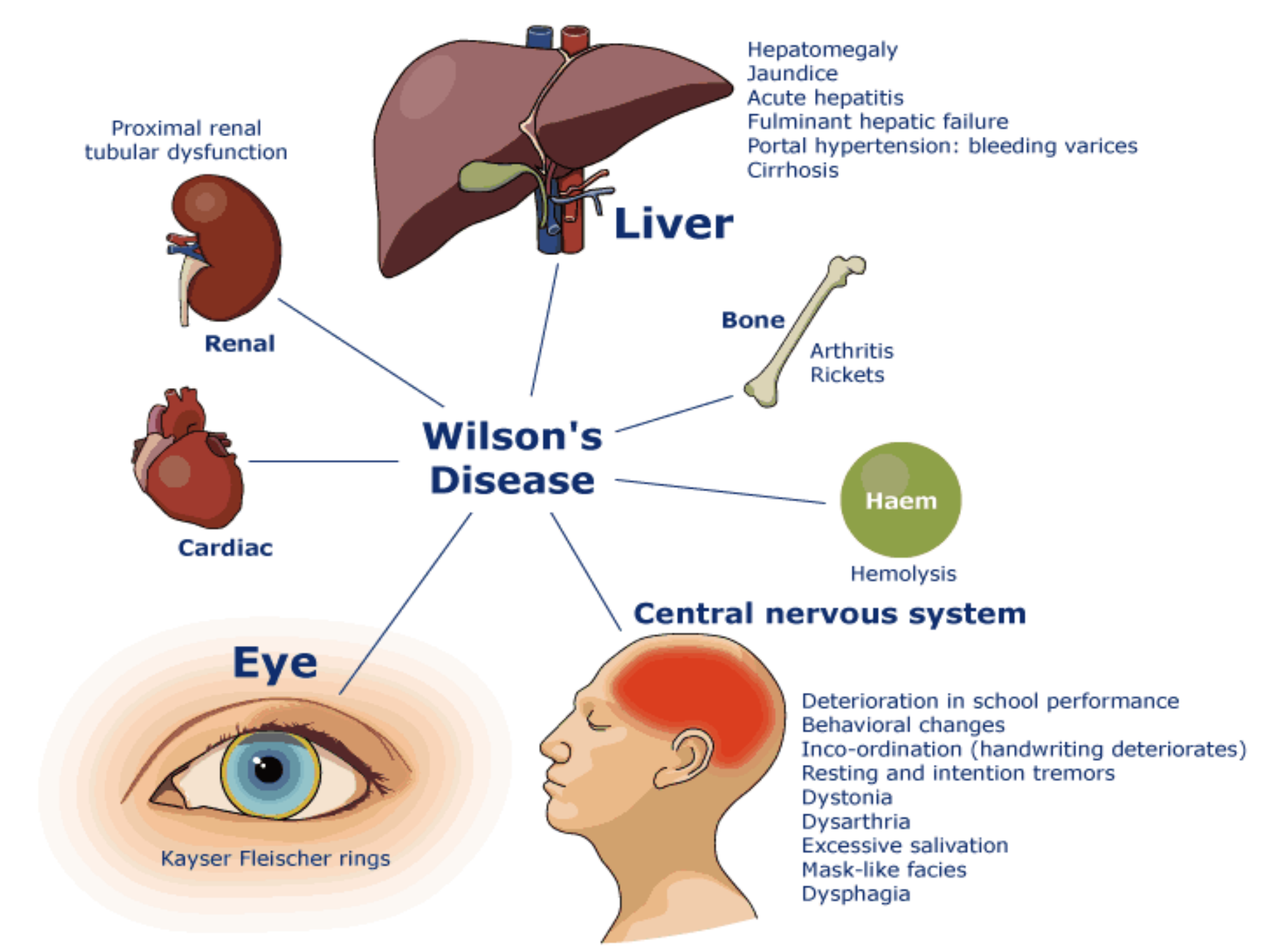
Wilson Disease



Wilson disease

- AR, chromosome 13.
- Mutations to the gene coding for ATPase copper transporting beta polypeptide (*ATP7B*), which is located on.
- *ATP7B* is a relatively large gene at around 80 kb, and it contains 21 exons.




Hepatomegaly
Jaundice
Acute hepatitis
Fulminant hepatic failure
Portal hypertension: bleeding varices
Cirrhosis
Liver
Proximal renal tubular dysfunction
Renal
Bone
Arthritis
Rickets
Wilson's Disease
Cardiac
Haem
Hemolysis
Central nervous system
Eye
Kayser Fleischer rings
Deterioration in school performance
Behavioral changes
Inco-ordination (handwriting deteriorates)
Resting and intention tremors
Dystonia
Dysarthria
Excessive salivation
Mask-like facies
Dysphagia

TEST	COMMENTS
Urinary Copper	24 hour copper excretion >100µg in 65% of WD patients
Urinary copper penicillamine challenge with two dosages of 500mg 12 hours apart and measure urine copper	24 hour copper excretion > 1600 µg in patients with active liver disease
Serum Copper	Serum copper may be low in asymptomatic cases (because caeruloplasmin is low) or high in cases with active liver disease (because free copper is raised)
Serum "free" copper Calculated on the basis that caeruloplasmin contains 0.3% copper	Free Copper >25µg/dl
Serum Caeruloplasmin	< 20 mg/dl (in 95% of WD patients)
KF rings	Identification in most patients requires an experienced observer
Liver Copper	>250 µg/gm of dry weight liver
Coombs negative haemolytic anaemia	
Biochemical indices	Abnormal liver function tests
MRI scan	Abnormal
Molecular diagnosis	Over 200 mutations are known

Wilson disease

Table 5. Scoring system developed at the 8th International Meeting on Wilson's disease, Leipzig 2001 [44].

Typical clinical symptoms and signs	
KF rings	
Present	2
Absent	0
Neurologic symptoms**	
Severe	2
Mild	1
Absent	0
Serum ceruloplasmin	
Normal (>0.2 g/L)	0
0.1-0.2 g/L	1
<0.1 g/L	2
Coombs-negative hemolytic anemia	
Present	1
Absent	0

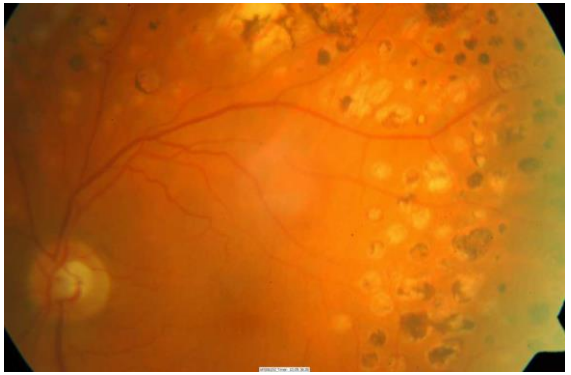
Other tests	
Liver copper (in the absence of cholestasis)	
>5x ULN (>4 μmol/g)	2
0.8-4 μmol/g	1
Normal (<0.8 μmol/g)	-1
Rhodanine-positive granules*	1
Urinary copper (in the absence of acute hepatitis)	
Normal	0
1-2x ULN	1
>2x ULN	2
Normal, but >5x ULN after D-penicillamine	2
Mutation analysis	
On both chromosomes detected	4
On 1 chromosome detected	1
No mutations detected	0

TOTAL SCORE	Evaluation:
4 or more	Diagnosis established
3	Diagnosis possible, more tests needed
2 or less	Diagnosis very unlikely

*If no quantitative liver copper available, **or typical abnormalities at brain magnetic resonance imaging. KF, Kayser–Fleischer; ULN, upper limit of normal.

Mitochondrial disorders

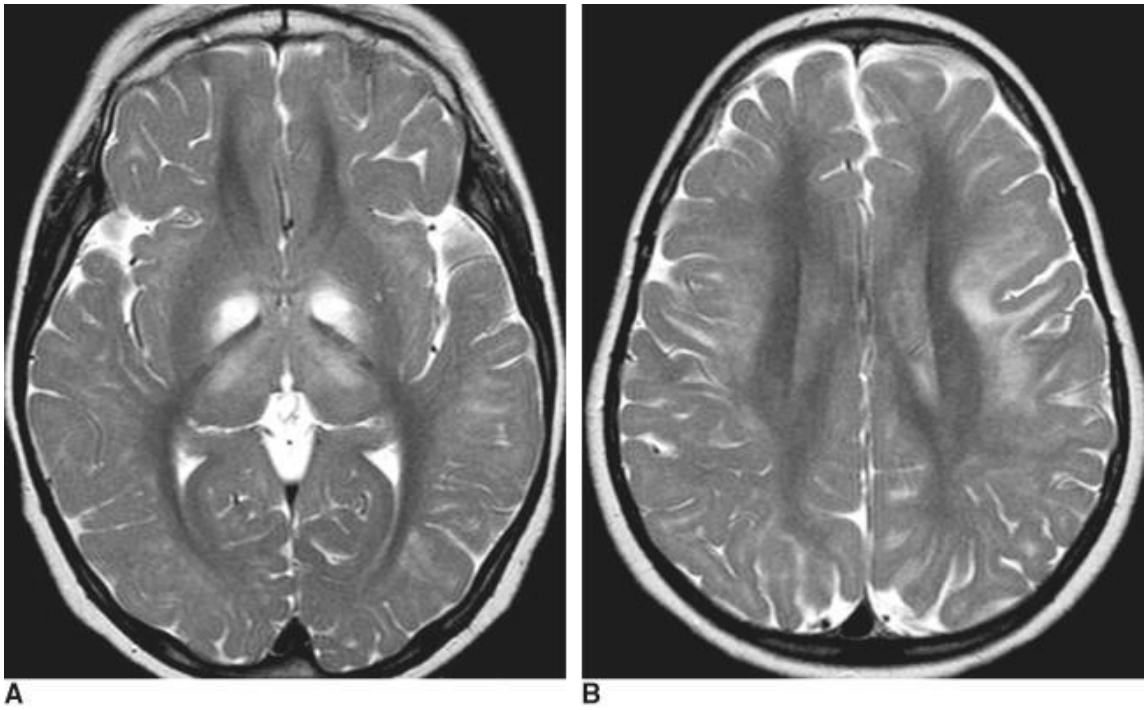
Symptoms/Clinical Features:



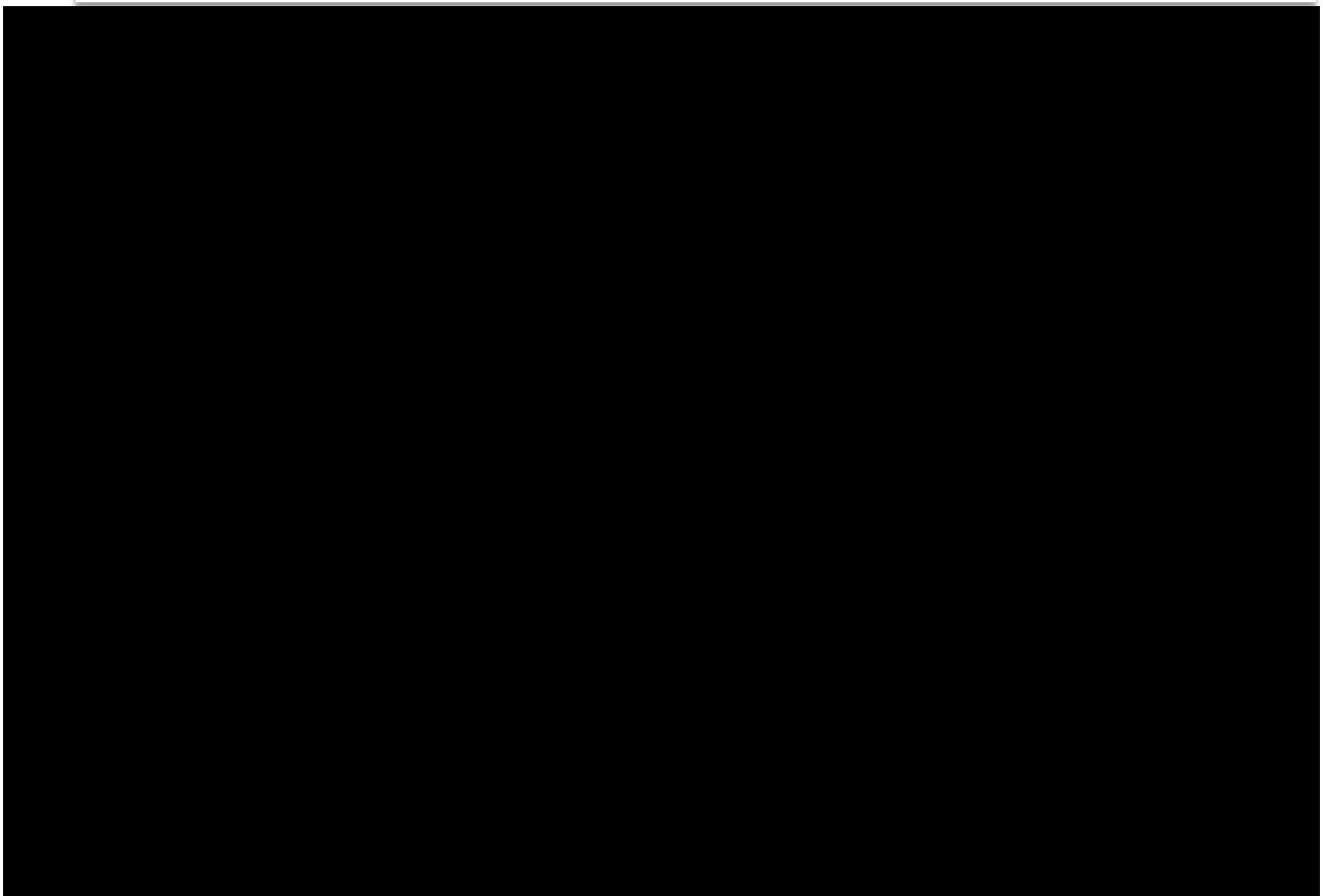
- Mitochondrial Myopathy (proximal weakness
- CPEO
- retinal degeneration (pigmentary retinopathy)
- Cardiac conduction defects (heart block)
- Ataxia/cerebellar syndrome
- Other symptoms include small stature, deafness, dementia, delayed puberty, and endocrine dysfunction

Mitochondrial disorders

- Laboratory: Increased CSF protein and lactate
- MRI- bilateral subcortical white matter T2 hyperintensities involving basal ganglia, thalamus, and brainstem
- Pathology: ragged red fibers

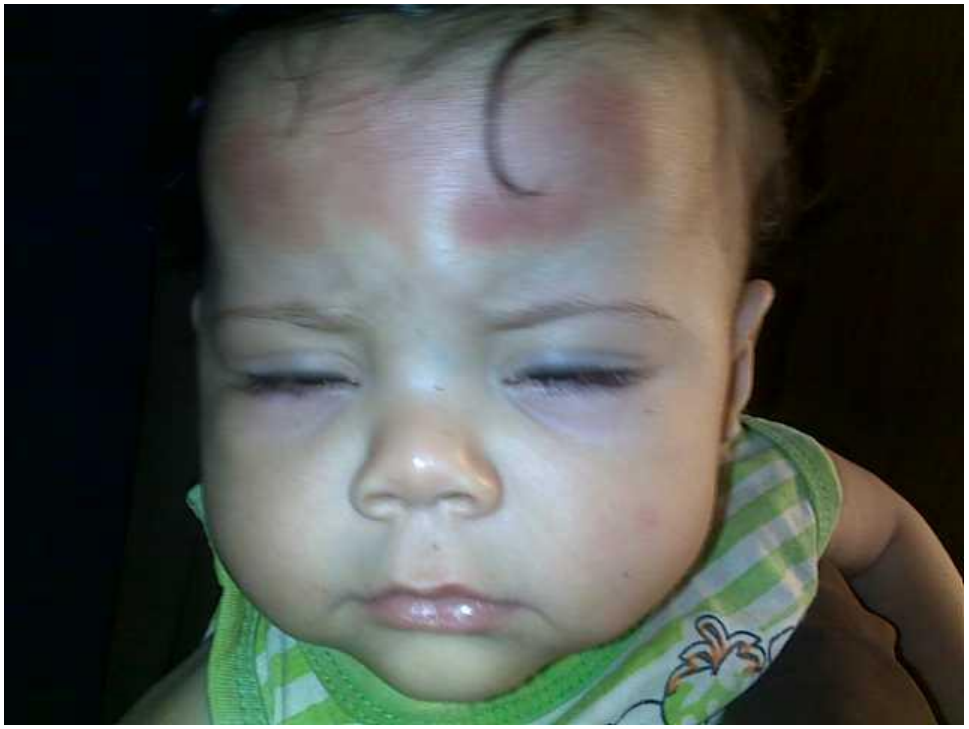


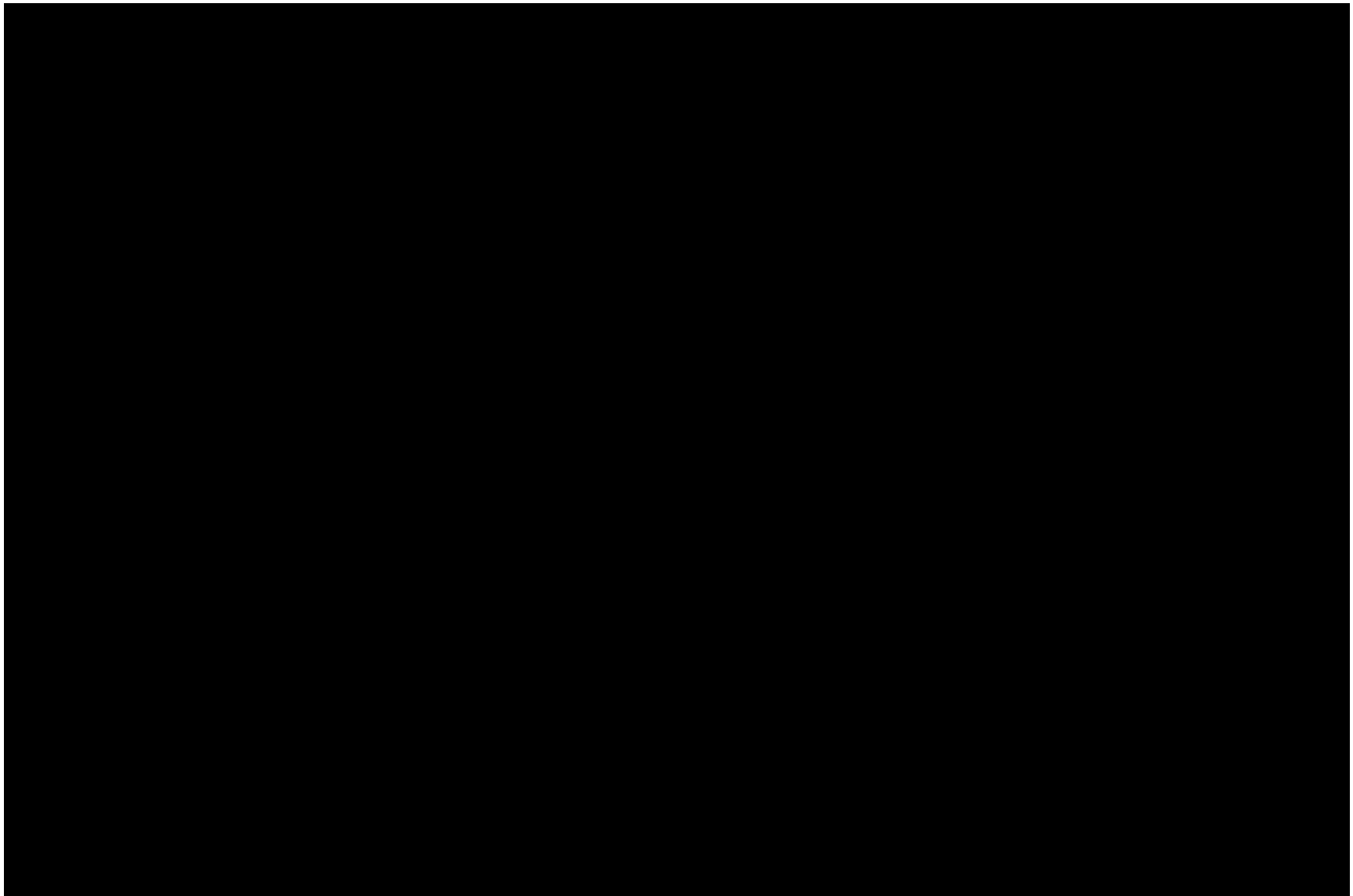
Rhythmic Movement Disorder



Rhythmic Movement Disorder

- Body rocking
- Head rolling
- Other less common muscle movements include:
- Body rolling
- Leg rolling
- Leg banging
- A combination of the aforementioned symptoms
- Head banging





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THANK YOU