常見精神科及神經內科疾病處方判讀及處置

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藥事照護

| 發現了
什麼藥物
相關問題 | 如何解決
問題 | 預防了
什麼藥物或疾
病相關問題 | 要追蹤
什麼 |

巴金森氏病

常見老人運動障礙疾病

Movement disorder

Hypokinetic disorder

運動減退

- Parkinson's disease
- Secondary parkinsonism
- Progressive supranuclear palsy (PSP) 進行性核上眼神經麻痺症
- Multisystem atrophy (MSA) 多發性系統退化症

Hyperkinetic disorder

運動機能亢進

- Tremor (eg,essential tremor, dystonic tremor肌張力異常性顫抖 , drug-induced tremor, physiological)
- Tic disorder 抽動性疾患 (eg,tourette's syndrome(TS))
- Chorea 舞蹈症 (eg,huntington's disease)亨丁頓舞蹈症
- Myoclonus 肌躍症
- Dystonia 肌張力不全
- Ataxia 運動失調症

Tremors

Clinical Classification of Tremors

- Enhanced physiologic tremors

- Essential tremor

- Tremors as part of specific neurologic diseases

Textbook of Primary Care Medicine, 3rd ed. /Chapter 163 - Movement Disorders

Physiologic tremors

Clinical Classification of Tremors - physiologic tremors

■Enhanced physiologic tremors

—Metabolic causes

—Toxic causes

—Drug and alcohol withdrawal states

Causes of Enhanced Physiologic Tremor

■ Related to drugs and alcohol

- Alcohol withdrawal

- Beta adrenergic drugs (Terbutaline)

- Valproate

- Lithium

- Methylxanthines (caffeine theophylline)

- Tricyclic antidepressants

- Hormonal drugs (thyroid supplements and adrenocorticosteroids)

- Metrizamide used as contrast agent

- Amiodarone

- Cyclosporine

Essential tremor

■ Essential tremor (ET) is the most common neurologic cause of postural or action tremor, with an estimated prevalence worldwide of up to 5 percent of the population.

■ The incidence of ET **increases with age,** although it often affects young individuals, especially when it is familial.

Overview of tremor --*UpToDate®*

Clinical Classification of Tremors - Essential Tremor

■ A community-based study from Canada showed

– prevalence of **14**% for essential tremor (ET) in persons over the age of **65 years** compared with a rate of **3**% for Parkinson's disease.

■ The etiology of ET is unknown.

■ Brain imaging and pathologic studies are normal, but positron emission tomography (PET) studies reveal hypermetabolism in the cerebellum, red nuclei, and thalamic and inferior olivary nuclei.

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Clinical Classification of Tremors - Essential Tremor

- The <u>diagnosis of ET is clinical</u>, and neuroimaging is not indicated.

- ET as a risk factor for Parkinson's disease remains <u>unproven</u> although they often <u>coexist</u>.

- Over 25 randomized, placebo-controlled studies have established **propranolol** as the most effective treatment to decrease the amplitude of the tremor of the <u>hands</u> and <u>tongue</u> in about 50% to 60% of the patients.

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Criteria for diagnosis of essential tremor

Core criteria	Secondary criteria
Bilateral action tremor of the hands and forearms (but not rest tremor)	Long duration (>3 years)
Absence of other neurologic signs, with the exception of cogwheel phenomenon	Positive family history
May have isolated head tremor with no signs of dystonia	Beneficial response to alcohol

Criteria for the diagnosis of essential tremor. Neurology 2000; 54(suppl 4):s7

Symptoms or signs suggestive of tremor other than essential tremor

Symptom or sign	Likely differential diagnosis
Unilateral tremor, leg tremor, rigidity, bradykinesia, rest tremor	Parkinson disease
Gait disturbance	Parkinson disease, cerebellar tremor
Focal tremor	Dystonic tremor
Isolated head tremor with abnormal posture (head tilt or turning)	Dystonic tremor
Sudden or rapid onset	Psychogenic tremor, toxic tremor
Current drug treatment that may cause or exacerbate tremor	Drug-induced or toxic tremor

Criteria for the diagnosis of essential tremor. Neurology 2000; 54(suppl 4):s7

Clinical Classification of Tremors
- Treatments for Essential Tremor

- **Beta-adrenergic blocking drugs**
  - Propranolol
  - Metoprolol
  - Nadolol

需藥？

- Primidone

- Clonazepam

- Botulinum toxin injection 肉毒桿菌毒素

- Stereotactic thalamic stimulation
  實體定位丘腦的刺激

Specific neurologic diseases

Clinical Classification of Tremors
- Tremors as part of specific neurologic diseases

- Parkinson's disease

- Cerebellar disease (multiple sclerosis)

- Wilson's disease

- Rare cases of peripheral neuropathy

Parkinson's disease

Diagnosis of Parkinson disease-UpToDate®
Pharmacologic treatment of Parkinson disease-UpToDate®
Nonpharmacologic management of Parkinson disease- UpToDate®

Demographics

Age

- Parkinson's disease is estimated to affect 1% of individuals >55 years of age in the US
- Peak age at onset is between 55 and 65 years. The prevalence increases with age.
- 5% of cases occur between 21 and 39 years of age
- Rare cases of juvenile Parkinson's disease are reported

Geography

- Except for living in rural conditions with exposure to well water and pesticides, no geographic vulnerability exists
- Parkinson's disease occurs throughout the world.

Demographics

Genetics

- Although Parkinson's disease is generally considered to be a <u>sporadic disease</u>, autosomal dominant and autosomal recessive inheritance have been documented

- Familial parkinsonism is estimated to be responsible for 5-10% of Parkinson's disease cases

- Vulnerability to environmental influences that may cause the disease may be genetically determined. Monozygotic twin studies support this concept.

Clinical features of Parkinson's disease

The first signs of PD are usually :

- a subtle fatigue

- discomfort or shakiness

- memory lapses, slower thinking

- depression become common

- Patients may develop a 'masked' or expressionless face

**Finally, the four primary symptoms appear**

■ Tremor at rest: Shaking or trembling begins in the hand, arm, leg, face, and it spreads, sometimes affecting only one side of the body.

– Tremors worsen when the muscles are <u>relaxed</u> or when the individual is <u>stressed</u>

– Tremor <u>disappears</u> during <u>sleep</u> or when the muscles are <u>intentionally moved</u>

■ Rigidity or hypertonia: permanent contraction of muscles

■ Akinesia or Bradykinesia: Spontaneous and automatic movement are lost and all movement becomes extremely slow.

■ Postural instability: Balance and coordination become impaired. Patients tend to lean forward or backward, and to develop a stooped posture. Walking with quick and small steps
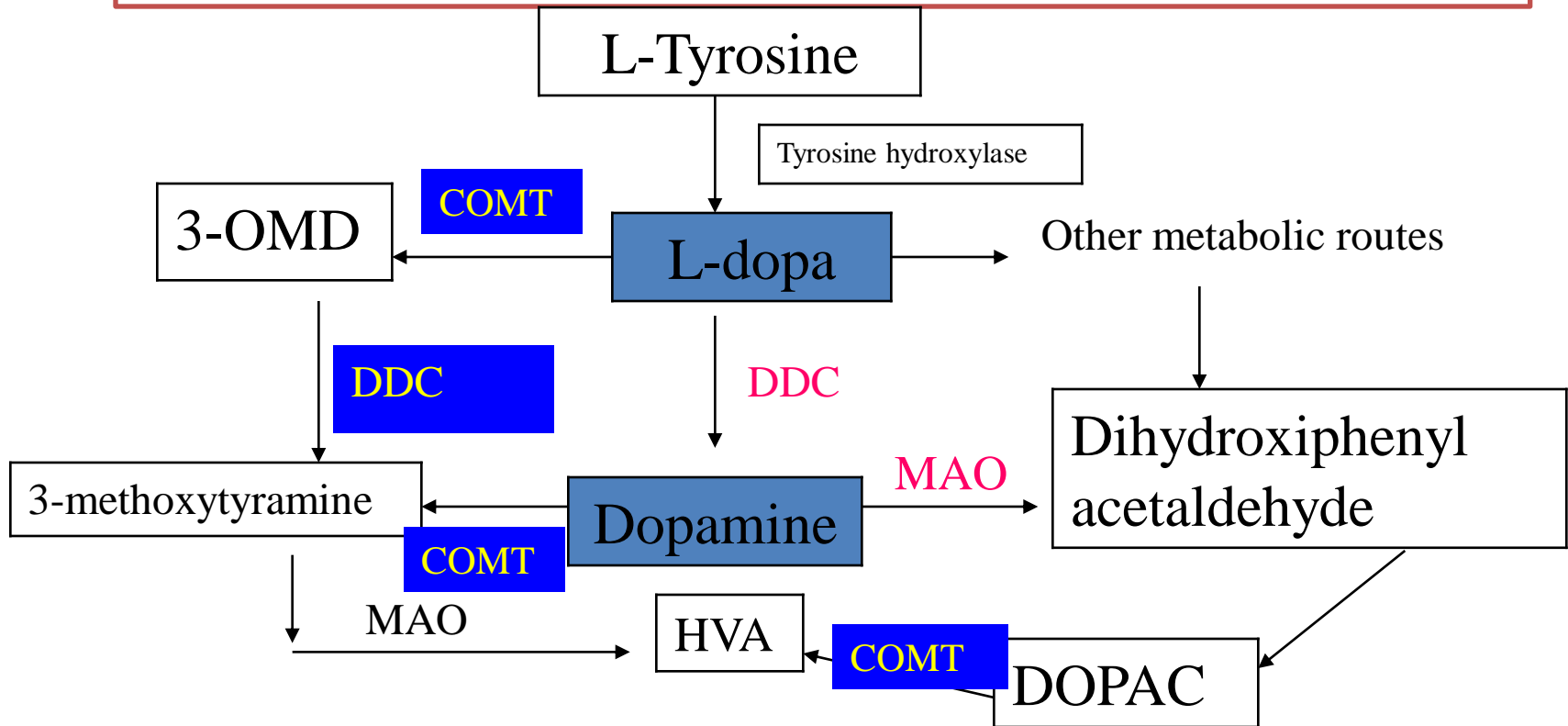
What causes Parkinson's disease ?

■ PD is caused by a loss of neurons in a part of the brain called the substantia nigra
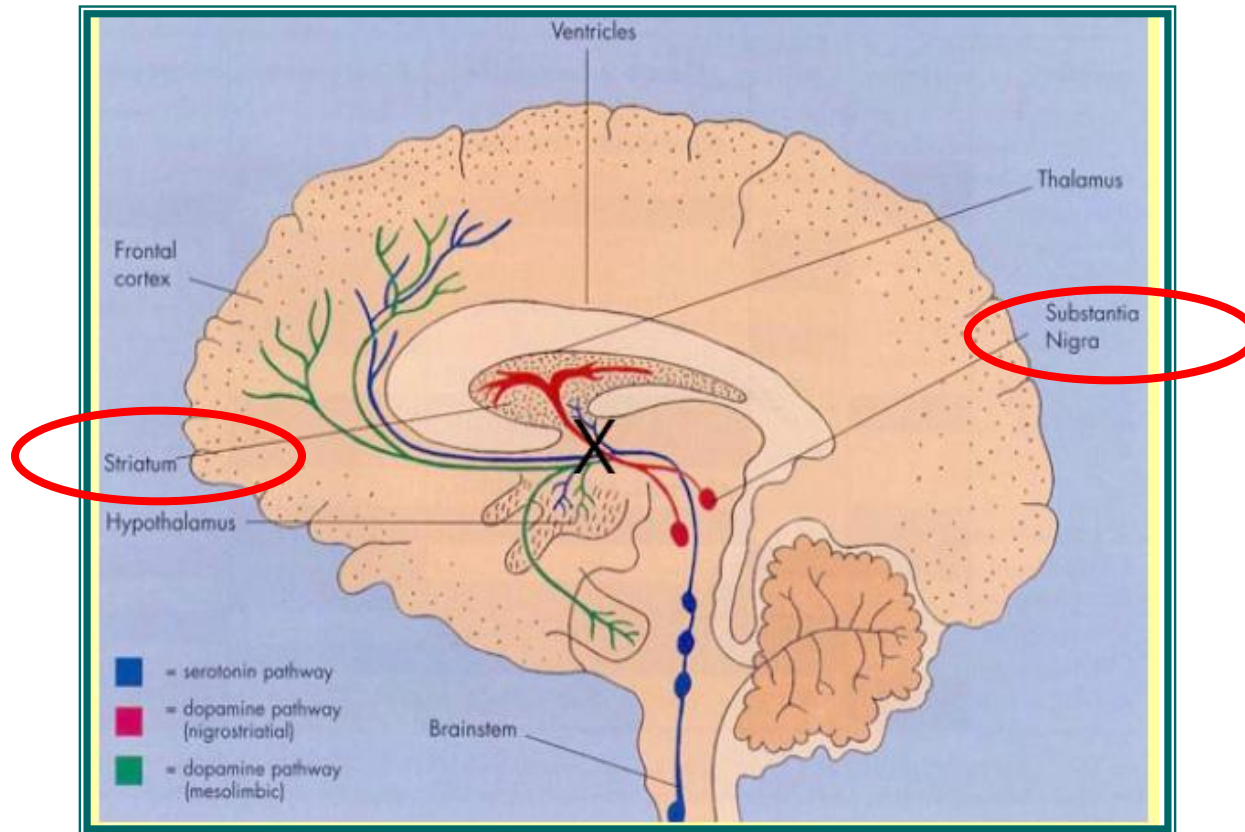
■ 巴金森病的主要病變是在腦部的黑質及紋狀體。黑質為製造並貯存紋狀體所需要的神經遞質─多巴胺的場所，並經黑質─紋狀體環路向紋狀體輸送多巴胺。

■ 多巴胺為紋狀體的抑制性神經遞質，乙醯膽鹼為紋狀體的興奮性神經遞質。

■ 在正常人，這兩種神經遞質處在一種動態平衡狀態。

■ 巴金森病患者的黑質細胞大量劣變而消失，多巴胺的製造減少，而乙醯膽鹼的作用相對亢進，所以，產生臨床上的諸多症狀。

由於Dopamine不能透過血腦屏障，因此，不能直接口服或注射多巴胺來治療，但可以口服易於透過血腦屏障的L-dopa來治療。L-dopa在腦內經過脫羧的作用，轉化為Dopamine，從而起到補充Dopamine的作用，以達到臨床治療巴金森病的目的

L-Tyrosine

Tyrosine hydroxylase

3-OMD

COMT

L-dopa → Other metabolic routes

DDC

DDC

3-methoxytyramine ← Dopamine — MAO → Dihydroxiphenyl acetaldehyde

COMT

MAO → HVA ← COMT ← DOPAC

COMT=cathechol O-methyltransferase   DDC= dopa decarboxylase
DOPAC=dihydroxyphenylacetic acid

HVA=homovanillic acid   MAO=monoamine oxidase   3-OMD=3-O-methyldopa

Disorders that can **mimic** Parkinson disease

Neurodegenerative causes
Alzheimer disease
Corticobasal degeneration
Dementia with Lewy bodies
Frontotemporal dementia
Huntington's disease
Multiple system atrophy
Parkinsonism-dementia-ALS complex of Guam
Progressive supranuclear palsy
Spinocerebellar ataxias

Disorders that can **mimic** Parkinson disease

Symptomatic
Drug-induced (neuroleptics, other dopamine receptor antagonists)
Infectious (post-encephalitic, Creutzfeldt-Jakob disease)
Metabolic (Wilson's disease, neurodegeneration with brain iron accumulation, hepatocerebral degeneration, parathyroid disorders)
Neoplastic
Post-traumatic
Toxic (carbon monoxide, manganese, MPTP)
Vascular
Other
Essential tremor
Normal pressure hydrocephalus

Causes of iatrogenic parkinsonism

Agent	Examples
Classic antipsychotic agents	Chlorpromazine (Thorazine), fluphenazine (Prolixen), haloperidol (Haldol), perphenazine (Trilafon), thioridazine (Mellaril), thiothixene (Navane), trifluoperazine
Atypical antipsychotic agents	Clozapine (Clozaril), risperidone (Risperdal), olanzapine (Zyprexa), aripiprazole (Abilify), quetiapine (Seroquel) ziprasidone (Geodon)
Antiemetics, motility agents	Prochlorperazine (Compazine), promethazine (Phenergan), metoclopramide (Reglan)
Chemotherapeutic agents	Fluorouracil (5-FU), vincristine, doxorubicin (Adriamycin)
Calcium channel blockers	Cinnarizine, Flunarizine
Others	Amiodarone, bethanechol, fentanyl, droperidol, lithium, meperidine (Demerol), pyridostigmine, reserpine, divalproex sodium (Depakote)