Overview of neurophysiology of Parkinson’s disease and other movement disorders

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Outline

• Introduction
• The motor system and movement disorders
• Coordination of movements
• The role of basal ganglia
• Causes of Parkinson Disease and other movement disorders
• Mechanism underlining the movement disorders
• Conclusion
Introduction & Learning objectives

• What are the motor systems and movement disorders?
• What are the parts of the body involved in locomotion
• Classes of movement
• Specific roles of each part
• Organization of the motor control system
• Basal ganglia: functions and pathways
• Role of Basal ganglia in the aetiology of:
  • Parkinson’s disease & other movement disorders
• Others types of movement disorders & their causes
The motor system and movement disorders

• Motor system of the body
  • Structure in the nervous system and the other parts of the body that supports movement

• Movement disorders
  • Group of neurological conditions that cause abnormal increase or decrease in movements, which may be voluntary or involuntary.
The motor systems of the body

• Functions
  • movement
  • Balance
  • Posture
  • communication

• They are guided by sensory systems
  • internal representation of world & the individual
  • Allow for detection of changes in the environment
    • external and internal changes
Body structures involved in motor control

- The muscles
- The bones
- Spinal Nerves
- Spinal Cord
- Nuclei in the brain stem
- Cerebellum
- Cerebral cortex
Motor coordination

- Co-ordinated movement is a process involving
  - Nerves, muscles and bones.

- Motor co-ordination start with the plan/intention
Spinal Motor Circuits: Reflexes

• Reflexes are involuntary unpremeditated but useful movements in response to stimuli.
• Muscle spindles initiate myotatic reflexes
• Proprioceptors detect a stretch and trigger a motor response to counteract the stretch.
  • The deep tendon and the flexor reflexes, are examples of this.
Pattern & Voluntary movements

• Rhythmic motor patterns
  • involves voluntary & reflexive movements
e.g. walking, running
  • once initiated, it becomes repetitive & reflexive

• Voluntary movement
  
  It is more complex, examples include reading, and writing
  It is usually purposeful, and goal-directed
Brain stem

• 1. serves as a main relay for descending motor fibres
• 2. contain many important motor controlling centres and nuclei e.g.
  • vestibular nuclei
  • Reticular nuclei
  • Red nuclei

a. Control of respiration
b. Control of the cardiovascular system
c. Partial control of gastrointestinal function
d. Control of many stereotyped movements of the body
e. Control of equilibrium
f. Control of eye movements
Basal ganglia

- These are groups of subcortical nuclei
- **Location:** Base of the forebrain
- **The nuclei includes**
  - Caudate nucleus
  - Putamen
  - Globus Pallidus
  - Substantial Nigra
  - Subthalamic

- **The caudate nucleus and putamen are commonly called the striatum**
Functions of Basal Ganglia

• The basal ganglia plays important roles in:
  • motor control, and
  • motor learning,
  • executive functions,
  • behaviors, and
  • emotions.
Pathways of Basal Ganglia

• To understand the pathophysiology of Parkinson’s disease it is necessary to look at the circuitry of the basal ganglia

• Two main pathways are identified
  • The direct, and
  • The indirect
The Direct Pathway

- Made up of projections from neostriatum, to medial pallidal segment, and to the cortex via the thalamus.
- The green pathways are from substantial nigra which releases dopamine which binds with D$_1$ and D$_2$ receptors in the neostriatum
- Red arrows are inhibitory
- Blue arrows are excitatory

Siegel, A. & Sapru H. N. Essential of Neuroscience. Wolters/Lippincott Williams & Wilkins (2011)
The Indirect Pathway

- Comprises of projections from neostriatum to lateral pallidal segment, to subthalamic nucleus, to medial pallidal segment, to the cortex via the thalamus
- Red arrows are inhibitory
- Blue arrows are excitatory

Siegel, A. & Sapru H. N. Essential of Neuroscience. Wolters/Lippincott Williams & Wilkins (2011)
Integrated normal activities of basal ganglia

- Interrelationship of the different basal nuclei to the thalamus and ultimately to the motor and premotor cortices
  - Dashed lines are inhibitory
  - Solid lines are excitatory
Parkinson’s disease a disorder arising from Basal ganglia: Hypokinetic disorder

• A model showing that PD is caused by reduction in the quantity of dopamine released

• Increase inhibition of \( \text{GP}_L \) (Indirect pathway, \( D_2 \)) Decrease inhibition of \( \text{GP}_M \) (Direct pathway, \( D_1 \))

Siegell, A. & Sapru H. N. Essential of Neuroscience. Wolters/Lippincott Williams & Wilkins (2011)
Role of Dopamine in Motor Coordination

• **Dopamine** is the main transmitter from the substantial nigra to the neostriatum

• Has opposing effects on the direct & indirect pathways
  • i.e. on the activation and inhibition

• **Dopamine** facilitate movement via excitation of dopamine $D_1$ receptors in the neostriatum

• It produces inhibition in the indirect pathways via the inhibition of $D_2$ receptors in the neostriatum,
  • inhibits the activities of subthalamic nucleus to the medial pallidal segment

• **Dopamine** facilitates movement
Other neurotransmitters

• In some instances,

• Patients with Parkinson’s disease may have reductions in

• Nor-adrenaline (loss in the locus coeruleus)

• Serotonin (loss in many parts of the brain, especially Striatum and the Raphe nuclei)
Factors underlying the development of Parkinson’s disease

• **Genetics**, such as mutations in the following genes
  • LRRK2 (Leucine-rich repeat kinase 2)
  • GBA (glucocerebrosidase)
  • SNCA (Synuclein Alpha)
    • (for about 10-15%), leads to eventual loss of neurons

• **Heredity**: having a relative with the diseases
• **Environmental triggers** like pesticides and other toxic products
• **Neurodegeneration** of nerve cells in substantial nigra
• **Loss of dopamine** in these cells
• **Age and gender**: >60yrs, men
Circuitry underlying hyperkinetic disorders, Huntington’s disease

Siegel, A. & Sapru H. N. Essential of Neuroscience. Wolters/Lippincott Williams & Wilkins (2011)
Other types of movement disorders

- **Ataxia**: could be due to neurodegeneration arising from metabolic disorders affecting central nervous system
- **Dystonia**: neurological disorder (of basal ganglia) leading to involuntary muscle spasm
- **Essential Tremor**: An uncontrolled shaking or trembling of one or the two hands caused by activativities of the thalamus
- **Multiple System Atrophy (MSA)**: progressive neurodegenerative diseases that affects movements and blood pressure
- **Myoclonus**: a twitching of the muscle in spasmodic manner; can results from several neurological ailments such as Alzheimer’s disease, or abnormalities from the sensorimotor area of the cerebral cortex
Other types of movement disorders

• **Rett Syndrome**: a progressive neurological disorder leading to reduced muscle tone and other symptoms

• **Secondary Parkinsonism**: this may be due to side effects of medications and different neurological disorders. Symptoms are similar to that of PD

• **Spasticity**: Increased muscle contraction, stiffness which could be from spinal cord injuries

• **Tardive Dyskinesia (TD)**: produces repetitive, involuntary movements. May be due to prolonged intake of some antipsychotic, and neuroleptic drugs

• **Tourette Syndrome**: a hereditary disorder of many parts of the brain (e.g. Basal Ganglia), characterized by repeated involuntary movements and uncontrollable vocal tics.
Other causes of movement disorders

- **Genetics**
  - E.g. Parkinson, and Huntington’s diseases
- **Alcohol**: may lead to ataxia, effects on cerebellum
- **Head injuries**
- **Stress, anxiety and emotional disturbances**
  - Especially in the aged, movement disorder may be transient
- **Pesticides and herbicides**
- **Iron deficiency**: e.g. restless leg syndrome
- **Excess copper in the body**: may lead to Wilson’s disease, abnormal body movement
- **Drugs**, such as antipsychotic drugs
  - like phenothiazines, prochlorperazine, thioridazine,
- **Chemicals** such as Polychlorinated Biphenyls (PCBs) and Trichloroethylene (TCE)
Conclusion

• Movement disorders can result from several causes.
• These factors acts on specific motor pathways/regulatory centers to achieve their effects