Textbook of MOVEMENT DISORDERS



Editor
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Foreword
Anthony E Lang

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Contents

1 History of James Parkinson and Kinnier Wilson **1**

Kalyan B Bhattacharyya

- James Parkinson (1755–1824) 1
- Samuel Alexander Kinnier Wilson (1878–1937) 5

2 Epidemiology of Parkinson's Disease **9**

Pragya Sinha, Ashok Kumar

- Descriptive Epidemiology 9
- Analytical Epidemiology 14

3 Basal Ganglia Circuit Related to Movement Disorders **24**

Priya Jagota

- Basal Ganglia Structures 24
- Basal Ganglia Circuit – the Motor Circuit 26
- Diseases of the Basal Ganglia 27

4 Pathophysiological Neuronal Oscillations: Invasive Recordings from the Basal Ganglia **28**

Arun Singh, Kai Bötzel

- Current Technologies for Invasive Recordings 28
- Oscillations 28
- Analysis 28
- Aberrant LFP Oscillations Recorded from Basal Ganglia 29
- Are there Medication /Lesion / DBS Effects? 30
- Synchronized Neuronal Activity in other Movements Disorders 30
- Oscillations During Motor Tasks 30
- Oscillations During Cognitive Functions 32

5 Animal Models of Parkinson's Disease **34**

Juan Sebastian Yakisich

- Toxin Models 35
- 6-OHDA 35
- MPTP 35
- Reserpine 36
- Rotenone 36
- Paraquat and Maneb 36
- LPS 36
- Methamphetamine 36

- Genetic Models 36
- Ubiquitin C-terminal Hydrolase L1 (UCH-L1) 37
- Combination Models (Fusion models) 38

6 Etiology and Pathogenesis of Parkinson's Disease 42
Paul Birinder S
- Genetic Factors 42
- Environmental Factors 45
- Pathogenesis of Parkinson Disease 46

7 New Insight into Parkinson's Disease Genetics 50
Ciprian Popescu

8 Nonmotor Symptoms of Parkinson's Disease 66
Rizaldy Pinzon

9 Cognitive Dysfunction in Parkinson's Disease 71
Vitor Tumas
- Neuropsychological Changes in Parkinson's Disease 72
- Recommendations 74

10 Psychosis in Parkinson's Disease 76
Ravi Yadav, Pramod Kumar Pal
- Prevalence 77
- Investigations 80

11 Impact of the Parkinson's Disease on the Heart 84
Ivica Scuric, Franjo Baborski
- Cardiac Denervation 84
- Effect of the PD Therapy 85

12 The Application of Motor Imagery in Patients with Parkinson's Disease: A State of the Art 87
Elke Heremans, Peter Feys, Alice Nieuwboer, Werner F Helsen
- Cardiac Denervation 84
- Motor Imagery: A new Technique within Neurological Rehabilitation 87
- Evaluation of Motor Imagery Ability 88
- Facilitation of Motor Imagery Quality 89

13 The Role of Tremor Analysis in Parkinson's Disease 92
Norbert Kovacs, Jozsef Janszky, Ferenc Nagy
- Introduction and Aims 92
- Physiological and Pathological Tremors 92
- Tremor Analysis 93
- Quantification of Tremor Characteristics 98
- Tremor Analysis for Differential Diagnosis 102
- Tremor Analysis for Measuring Efficacy of Pharmacological and Surgical Therapies 106
- Tremor Analysis in Clinical Research 106

14 Young Onset Parkinson's Disease **112**
Vinay Goyal, Bhavna Kaul

15 Management of Early Parkinson's Disease **115**
Pratap Sanchetee
- Diagnosis 115
- Drugs 116
- Selection of Drug 118
- Timing of Treatment 119
- Non Motor Symptoms 119
- Complementary and Supportive Therapies 120

16 Levodopa in Movement Disorders **122**
Sandeep Kaushal, Kanchan Gupta
- History of Levodopa (L-dopa) 122
- Pharmacological Effects 123
- Pharmacokinetics 123
- Therapeutic Uses of L-dopa 124
- Important Issues with the Use of L-dopa 126
- Important Drug Interactions 128
- Contraindications 129

17 Apomorphine, Duodopa or DBS—Last Line Treatment Options for Advanced Parkinson's Disease **131**
Dušan Flisar, Andreja Avberšek
- Duodenal Levodopa Infusion 131
- Continuous Subcutaneous Apomorphine Infusion 132
- Deep Brain Stimulation 133

18 Vascular Parkinsonism **137**
Deepak Gupta, Abraham Kuruvilla
- Historical Aspects 137
- Epidemiology 137
- Pathophysiology 137
- Pathology 139
- Clinical Features 139
- Imaging 142
- Diagnostic Criteria 142
- Differential Diagnosis 142
- Treatment 144
- Case Vignette 144

19 Progressive Supranuclear Palsy (PSP) **147**
Venkatesh Krishnamurthy
- Historical Perspective 147
- Genetics 147
- Epidemiology 148
- Clinical Features 148

- PSP—Clinical Subtypes 150
- Diagnostic Criteria 150
- Pathology 150
- Neuroimaging 151
- Diagnostic Workup 152
- Prognosis and Complications 152
- Treatment 153

20 Multiple System Atrophy **158**

Han-Joon Kim

- History 158
- Epidemiology 158
- Clinical Features 158
- Diagnostic Criteria 159
- Differential Diagnosis 160
- Pathology 160
- Investigations 161
- Pathogenesis 162
- Treatment 162
- Clinical Course and Prognosis 163

21 Corticobasal Degeneration **164**

Anhar Hassan

- Neuropathology 164
- Clinical Features 164
- Neuropsychology 166
- Neuroimaging 166
- Pathogenesis 167
- Biomarkers 167
- Treatment 167
- Future Approaches 168

22 Neuropsychology of Parkinson-Plus Syndromes **172**

Elena Baratelli, Cecilia Rassiga, Chiara Emilia Rosci

- Part One 172
- Part Two 179

23 Autonomic Functions in Parkinson's Disease and Other Movement Disorders **193**

TN Sathyaprabha, Kaviraja Udupa, Raju TR

- Pathophysiological Involvement of Autonomic Centers in PD 193
- Autonomic Symptoms in PD 194
- Gastrointestinal Symptoms 194
- Cardiovascular Symptoms 194
- Urogenital Symptoms 195
- Thermoregulatory Symptoms 195
- Studies Investigating Autonomic Involvement in PD 199
- Cardiac Autonomic Involvement as a Marker of Pre-PD 199
- Autonomic Functions in other Movement Disorders 199
- Future Directions 200

24 Tremors: Clinical Diagnosis and Treatment **203**
Prashanth LK, R Shiva Kumar, S Raghavendra, Abraham Kuruvilla
- Historical Aspects 203
- Clinical Definition 203
- Classification of Tremor 203
- Etiology of Tremors 204
- Tremor Assessment Scales 205
- Clinical Characteristics and Management of Various Types of Tremors 205

25 Essential Tremor **212**
Krishe Menezes, Selena C Nicholas Bublick, Lawrence W Elmer
- Definition of a Tremor 212
- Pathophysiology 212

26 MR Imaging in Essential Tremor **217**
Achyuta Nand Jha, Chandrajit Prasad, Santosh Kumar, Ashok Kumar

27 Wilson's Disease **222**
VM Dayal, Ashok Kumar
- Copper Metabolism 222
- Molecular Biology 222
- Clinical Features 223
- Pathologic Features 224
- Staging 224

28 Dystonia **230**
Tushar Gosavi, Kumar M Prakash
- Clinical Features of Dystonia in General 230
- Classification of Dystonia 230
- Etiology/Causes of Dystonia 232
- Primary Torsion Dystonia (PTD) 232
- Dsytonia Plus Syndromes 233
- Heredodegenerative Dystonias 234
- Clinical Features of Specific Dystonias 234
- Diagnostic Approach to Dystonia 236

29 Dopa Responsive Dystonia **242**
Nirendra K Rai, Ashok Kumar
- Introduction and Brief History 242
- Clinical Features 242

30 Writer's Cramp **250**
Brian D Berman
- Clinical Manifestations 250

31 Meige's Syndrome **257**
Prashanth LK, R Shiva Kumar, S Raghavendra, Abraham Kuruvilla
- Historical Aspects 257

- Epidemiology and Risk Factors 257
- Classification 257
- Pathophysiology 258
- Clinical Features 258
- Clinical Course 259
- Management 259

32 Catatonia **262**

Balram Pandit, AS Srivastava

- Historical Background 262
- Nosology 263
- Epidemiology 263
- Etiology 263
- Genetic Factors 263
- Biochemical Factors 263
- Psychosocial and Psychoanalytical Theories 265
- Modern Theorists 266
- Clinical Features 266
- Forms of Catatonia 267
- Course and Prognosis 271
- Prevention 272

33 Hemifacial Spasm: Clinical Features and Management **277**

Pavesi Giacomo, Costella Giovanni Battista, Zara Gabriella

- Functional Anatomy of the Facial Nerve 277
- Clinical and Epidemiological Features of Hemifacial Spasm (HFS) 278
- Differential Diagnosis 279
- Etiology of HFS 279
- Pathophysiology of HFS 280
- Quality of Life (Qol) Measures in HFS 280
- Diagnosis of HFS 280
- Pharmacological Treatment of HFS 281
- Neurosurgical Treatment of HFS 282

34 Chorea: An Update **287**

Fernando Vazquez-Sanchez, Adrian Ares-Luque

- Clinical Features 287
- Pathophysiology 287
- Treatment 293

35 Huntington's Disease **295**

Rohit Bhatia, Bhavna Kaul, Surekha Dabla

- Clinical Features 295
- Epidemiology 296
- Differential Diagnosis 296
- Treatment 297

36 Rheumatic Chorea **301**

Bhaskar Ghosh, Shyamal Kumar Das

- Epidemiology 301

- Pathogenesis 301
- Clinical Features 301
- Diagnosis 302
- Prognosis 302
- Treatment 303

37 Athetosis **305**

Sangeeta Chaal

- Introduction/Definition 305
- Clinical Features 305
- Drugs 307
- Management 309

38 Hemiballismus **310**

Lakshmi Narasimhan R, Kannan V, Venkatesh Perumalsamy, Jeyaraman R

- Definition 310
- Clinical Description 310
- Anatomical Localization 310

39 PANDAS **316**

Ashok Kumar

- Immune System and Psychiatric Disorders 316

40 Tics **321**

Tamar Ediberidze, Ashok Kumar

41 Myoclonus **325**

Anup Bhattacharya

42 Startle Syndrome **332**

Anita Arsovska, Zoran Arsovski, Ante Popovski

43 Stereotypies **344**

Kuljeet Singh Anand, Mina Chandra

- Historical Aspects 344
- Definition 344
- Differential Diagnosis 344
- Classification 345
- Primary Stereotypies 346
- Secondary Stereotypies 346
- Etiopathology 347
- Complications 348
- Investigations 348
- Treatment 348

44 Gait Disorders **351**

Amit Batla

- The Gait Cycle, Physiology and Examination for Clues to Diagnosis of Gait Disorder 351
- Gait Disorders 353
- Pathophysiology of Gait Disorders 353

- Classification of Gait Disorders 353
- Causes of Gait Disorders 353
- Specific Gait Disorders 353
- Dyskinetic Gait 354
- Assessment and Scoring of Gait 354
- Treatment of Gait Disorders 355

45 Hereditary Ataxias: An Overview and Indian Perspectives 362
Achal Kumar Srivastava, Mohammed Faruq
- Classification of Hereditary Ataxias 362
- Spinocerebellar Ataxia: Overview 363

46 Paroxysmal Dyskinesias 394
Tânia Lampreia, José Vale
- Historical Aspects 394

47 Psychogenic Movement Disorders 406
Sanjay Pandey

48 Movement Disorders and Epilepsy 410
Manjari Tripathi, Deepti Vibha
- Clinical Imitators 410

49 Structural MR Imaging in Movement Disorders 416
Robert Semnic, Aleksandar Jesic, Dusko Kozic, Marija Semnic
- Parkinsonism 416

50 Emergencies in Movement Disorders 426
Bindu Menon
- Disorders of Spinal Rigidity in Man 428
- Serotonin Syndrome 429

51 Movement Disorders in Children 431
R Shiva Kumar, Prashanth LK, S Raghavendra, Abraham Kuruvilla
- Description of Movement Disorders 432
- Clinical Approach to a Child with Abnormal Movements 432

52 Idiopathic Normal Pressure Hydrocephalus 447
Teruo Kimura, Masatsune Ishikawa, Nobumasa Kuwana
- Background 447
- Hypothesis 447
- Epidemiology – Incidence Rate 448
- Clinical Symptoms 448
- Prognosis and Outcome 464

53 Botulinum Toxin in Movement Disorder 469
Vinay Goyal, Ajanta Keshavraj, Chanchal Goyal
- Hemifacial Spasm 469
- Blepharospasm 470
- Oromandibular Dystonia 470
- Writer's Cramp 470

- Spasmodic Dystonia 470
- Adductor Laryngeal Breathing Dysphonia 470
- Cervical Dystonia (CD) 471
- Spasticity 471
- Sialorrhea 471

54 Deep Brain Stimulation in Movement Disorders 473
Pettarusp M Wadia
- Deep Brain Surgery for Parkinson's Disease 473
- Deep Brain Surgery for Dystonia 474
- Deep Brain Surgery for Tremors 476
- DBS in other Movement Disorders 476

55 Role of Physiotherapy in Parkinson's Disease 479
Josni Khah, Binay Pandey, Ashok Kumar
- Symptoms 479
- Examination 480
- Treatment Goals 480
- Therapeutic Interventions 480

Index 483

CHAPTER

3

Basal Ganglia Circuit Related to Movement Disorders

Priya Jagota

INTRODUCTION

Basal ganglia comprise a group of nuclei in the telencephalon, diencephalon and mesencephalon. These structures include caudate nucleus (Cd), putamen (Pt), globus pallidus (Gp), subthalamic nucleus (STN), nucleus accumbens (NA) and substantia nigra (SN) (Fig. 3.1). They are interconnected by complex circuits and loops. Caudate nucleus, putamen and NA are collectively called the striatum and have similar organization. Structurally, Cd and Pt are divided by the internal capsule. Putamen and Gp are together called the lentiform nucleus or lenticular nucleus. The globus pallidus is divided into two segments. The outer/lateral segment is called the globus pallidus pars externa (Gpe) and the inner/medial segment is called the globus pallidus pars interna (Gpi), separated by the medial medullary lamina. The Gpe lies medial to the putamen. Substantia nigra is also divided into two segments. The dorsal segment is substantia nigra pars compacta (SNc) and the ventral segment, which is functionally similar to the Gpi, is substantia nigra pars reticulata (SNr). Somatotopy and topographic organization is maintained in the basal ganglia.[1]

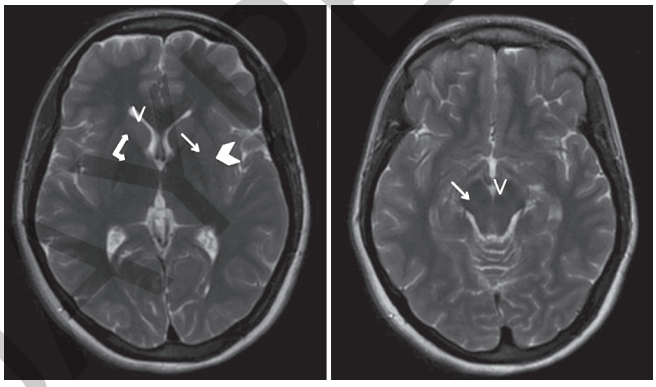

Fig 3.1. T2-weighted MRI showing parts of the basal ganglia. A) Thin arrow indicating globus pallidus, thick arrow head indicating putamen, thin arrow head indicating caudate nucleus and double arrow head indicating internal capsule. B) Arrow indicating substantia nigra and arrow head indicating red nucleus.

In the classical model of basal ganglia striatum is the input[2] structure of the basal ganglia which receives input from other parts of the brain and sends projections to structures within the basal ganglia. Globus pallidus pars interna and SNr are the output structures of the basal ganglia.[2] They receive input from other basal ganglia structures and send projections to structures outside the basal ganglia, mainly thalamus and brainstem.

Classically the basal ganglia has two major pathways – The direct pathway and the indirect pathway.[2] The direct pathway is the pathway in which the input structure of the basal ganglia connects directly to the output, i.e. the striatum sends projections directly to the Gpi and SNr. The indirect pathway is the pathway in which the striatum connects to the Gpi and SNr via Gpe and STN (Fig. 3.2).

Basal ganglia functions in the control of movement, procedural memory, habit formation, behavior and emotions.[3,4] This chapter deals with the motor circuit of the basal ganglia which is involved in the control of movements (Fig. 3.2). Disruption of this circuit causes abnormal, involuntary movements or impaired voluntary movements such as parkinsonism, chorea and dystonia.[5]

BASAL GANGLIA STRUCTURES

As mentioned above, basal ganglia are structures linked together by circuits. This section describes different structures of the basal ganglia and their connections.

Striatum

Striatum is the input structure of the basal ganglia. It receives information from most parts of the cerebral cortex and the centromedian-parafascicular (CM-Pf)[6] nuclei of the thalamus.[4] Striatum consists of two subcompartments – striosomes and matrix[7], and two main types of neurons. These are:

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Medium spiny neurons (MSNs)

MSNs constitute the majority of the striatal neurons. They are the projection neurons of the striatum. They receive inputs from the cerebral cortex, thalamus, SNc and striatal interneurons.[4,8] They project to both the Gpi/SNr forming the "direct pathway", and the Gpe forming the "indirect pathway". Apart from these, they also project to the SNc. Their main neurotransmitter is the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA). The MSNs that project to the direct pathway also contain substance P and dynorphin neuropeptides, and have D1 dopamine receptors on their dendrites.[7,8] The MSNs that project to the indirect pathway also contain enkephalin and have D2 dopamine receptors and A_{2A} adenosine receptors on their dendrites.[7,8]

The matrix and striosomes are differentiatied by their staining to acetylcholinesterase and opiate receptor binding.[9] The matrix contains the direct and indirect pathway MSNs and the striosomes contain neurons that project to the SNc.[7]

Interneurons

Interneurons are aspiny neurons and constitute a minor proportion of the striatal neurons. They include large aspiny tonically active neurons (TANs) and medium-sized aspiny fast-spiking interneurons.[4] TANs receive glutamatergic inputs from the cortex and the thalamus. They synapse on the MSNs and release acetylcholine (ACh) as their neurotransmitter, reducing the MSNs excitability.[4]

Fast-spiking interneurons are GABAergic neurons. They exert a powerful inhibitory signal on MSNs allowing only the neurons involved in the intended movements to be excited.[4]

Globus Pallidus

Globus pallidus is divided into two parts— The Gpe and the Gpi. Globus pallidus pars interna, along with the SNr, are the main outputs of the basal ganglia circuit. They receive inputs from the direct pathway MSN of the striatum, the Gpe, STN

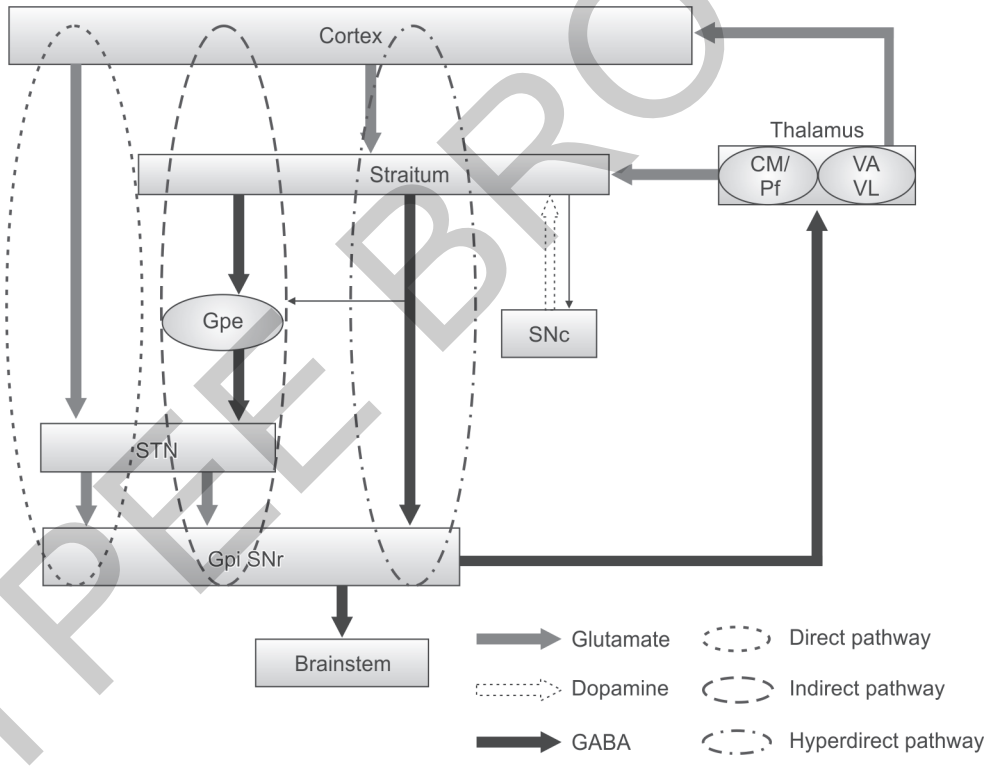

Fig. 3.2: Basal ganglia connections. The pathway from the cortex to the STN to the Gpi/SNr forms the 'hyperdirect' pathway and is the fastest conducting pathway. Next is the 'direct pathway which is the connection from the cortex to the straitum and then directly to the Gpi/SNr. 'Indirect' pathway is the projection from the cortex to the striatum to the Gpe, Gpe to the STN and finally to the Gpi/SNr. Thick arrows indicate the main direction of the pathways. Glutamate is an excitatory neurotransmitter, GABA is inhibitory, and dopamine's effect depends on the receptor subtype on the MSN. The direct pathway neurons consist of D1 dopamine receptors which exert excitatory effects, and the indirect pathway neurons consist of D2 dopamine receptors which exert inhibitory effects. Abbreviations: CM/Pf—centromedian-parafascicular nuclei of the thalamus, Gpe—globus pallidus pars externa, Gpi—globus pallidus pars interna, MSN—medium spiny neuron, SNc—substantia nigra pars compacta, SNr—substantia nigra pars reticulata, STN—subthalamic nucleus, VA—ventral anterior nuclei of the thalamus, VL—ventral lateral nuclei of the thalamus

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and the pedunculopontine nucleus (PPN). The Gpi projects its axons to the ventrolateral nucleus and parafascicular complex of the thalamus, the lateral habenula and the PPN.[9,10] It uses GABA as its neurotransmitter and controls the movements of the body down the neck. The Gpi does not appear to have interneurons.[10]

Globus pallidus pars externa is the "indirect pathway" of the basal ganglia circuit. It receives input from the indirect pathway MSNs of the striatum. In addition, it also receives inputs from the STN and collaterals from the direct pathway MSNs. There are two major types of neurons in the Gpe-parvalbumin-positive neurons and parvalbumin-negative neurons.[9] The parvalbumin-positive neurons send axons to STN, Gpi and SNr. Parvalbumin-negative neurons provide axons to the STN. Both are GABAergic.[9] It also projects back to the striatum. Apart from these, there are some cholinergic neurons as well that project to the cortex.[9]

Subthalamic Nucleus

The STN plays an important role in the control of movements. It is also considered to be an input nucleus of the basal ganglia,[10,11] forming the "hyperdirect pathway".[11] It consists of glutamatergic neurons and is thus, excitatory. It receives excitatory inputs from the cortex and CM-Pf nuclei of the thalamus.[12] Inhibitory inputs are mainly provided by the Gpe, forming the indirect pathway. It also receives dopaminergic input from the SNc.[12] It sends its glutamatergic projections to the Gpi/SNr and reciprocally to the Gpe and the cortex.[12]

Substantia Nigra (SN)

Substantia nigra lies in the midbrain. It consists of two distinct segments – Substantia nigra pars compacta (SNc) and substantia nigra pars reticulata (SNr). Substantia nigra pars compacta is in the dorsal segment, while SNr neurons are in the ventral segment.

Substantia nigra pars compacta contains densely packed pigmented dopaminergic neurons. Their major input is from striatal neurons in the striosomes[7] and the pallidum.[13] The input is GABAergic. They project mainly to the striosomes and matrix of the striatum.[7] Apart from the striatum, SNc also projects to other basal ganglia structures, namely, Gpe, Gpi, STN, SNr, and the thalamus.[14] Its degeneration or destruction causes parkinsonism.

SNr is an output structure of the basal ganglia circuit and is functionally similar to the Gpi. It receives inputs from the structures as Gpi and is GABAergic. The outputs, though, are somewhat dissimilar. It gives projections to the mediodorsal, parafascicular and ventromedial nuclei of the thalamus, superior colliculus and pedunculopontine nucleus (PPN).[9] It is involved in the control of head, neck and eyes movements.[9] The Gpi is involved in the control of limb and axial movements.[9]

BASAL GANGLIA CIRCUIT – THE MOTOR CIRCUIT

The classical model of the basal ganglia circuit, as mentioned above, consists of the "direct pathway" and the "indirect pathway".[2] In the direct pathway, the cortex and thalamus sends excitatory inputs (glutamate) to the striatum. The striatum releases GABA, an inhibitory neurotransmitter, to the Gpi/SNr (cortex-striatum-Gpi/SNr). Therefore, the Gpi/SNr neurons are inhibited and reduce their firing rate to the thalamus. As Gpi/SNr neurons contain the inhibitory neurotransmitter GABA, which in a normal state, would inhibit the thalamus from exciting the cerebral cortex, it will now release the thalamus of its inhibition. Therefore, the thalamus will increase its firing to the cerebral cortex. The neurons in the thalamus release glutamate which is an excitatory neurotransmitter, therefore, the cortex will be excited and produce movements. Hence, the "direct pathway" facilitates movements (Fig. 3.2).

The indirect pathway affects the cerebral cortex differently. The striatum receives excitatory inputs from the cortex and thalamus, and then sends inhibitory projections to the Gpe. The Gpe, mainly a GABAergic structure, is inhibited by the striatum. Thus, it will decrease firing its GABAergic neurons to the STN. As a result, the STN, which would normally be inhibited by the Gpe, will increase its firing rate to the Gpi/SNr. Subthalamic nucleus contains the neurotransmitter glutamate, an excitatory neurotransmitter. Therefore, Gpi/SNr will increase their firing rate too. This will increase Gpi/SNr's inhibition on the thalamus. Cerebral cortex receives reduced excitatory input from the thalamus and thus, does not produce movements. Hence, the "indirect pathway" (cortex-striatum-Gpe-STN-Gpi/SNr) is generally said to inhibit movements.

Medium spiny neurons in the striatum, apart from receiving glutamatergic inputs by the cerebral cortex and the thalamus, receive dopaminergic inputs from the SNc. Dopamine modulates cellular excitability of the MSNs[15] depending on the postsynaptic dopamine receptor subtype. D1 dopamine receptors increase the excitability of MSNs and D2 dopamine receptors reduce their excitability.[15–16] The direct pathway's MSNs express D1 receptors, thus, facilitating the pathway's activity, i.e. facilitating movements. The indirect pathway's MSNs express D2 receptors. The action of dopamine on the indirect pathway reduces inhibition of movements.

A third pathway, called the "hyperdirect pathway", has been added to this model.[11] In this model, the striatum and the STN receive parallel inputs from the cortex and the CM-Pf nuclei of the thalamus.[4,10] Hyperdirect pathway comprise of the cortical/thalamic projections to the STN, and then the STN projections to the output nuclei, the Gpi/SNr (cortex-

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STN-Gpi/SNr).[11] The cortical/thalamic projections excite the STN, which in turn excites the Gpi/SNr. Thus, the inhibitory Gpi/SNr neurons increase their firing to the thalamus. The thalamus is therefore, inhibited. This inhibits the cerebral cortex , inhibiting movements (Fig. 3.2).

The "hyperdirect pathway", of the three pathways, it is the fastest conducting pathway.[11] Before a movement is produced, the cortex projects to the striatum and the STN. As the hyperdirect pathway conducts the fastest, it inhibits the cortex first. It inhibits a wide area of the cortex,[1] including those involved in the desired movement.[11] The direct pathway is then conducted, disinhibiting the cortex, producing movements.[11] It disinhibits only a specific, more focused area of the cortex,[1] which releases the desired movements. Then the indirect pathway inhibits its target, cancelling the competing areas.[11] Thus, the basal ganglia is said to facilitate voluntary movements and inhibit competing movements.[1, 5]

DISEASES OF THE BASAL GANGLIA

In Parkinson's disease (PD) motor symptoms arise from loss of dopaminergic cells in the SNc. With the dopamine depleted in the striatum there is reduced excitation of the direct pathway. The inhibition of the indirect pathway is reduced resulting in overactivity of the pathway.[4] This results in decreased movements seen in parkinsonian patients.

Hyperkinetic movement disorders are disorders that cause excessive movements. Chorea disorders such as Huntington's disease (HD) and levodopa-induced dyskinesia (LID) result from relative overactivity of the direct pathway.[17] In HD, there is preferential loss of indirect pathway MSNs resulting in overactivity of the direct pathway MSNs in relation to the indirect pathway MSNs.[17] Therefore, it can generally be said that decreased/reduced movements occur from relative overactivity of the indirect pathway and chorea arises from relative overactivity of the direct pathway or lesion in one of the structures, respectively increasing or decreasing the ouput activity of the Gpi/SNr neurons. But there are limitations to this rate-based model of the basal ganglia. Levodopa-induced dyskinesia occurs when there is overactivity in the direct pathway induced by chronic levodopa administration.[17] According to this, dyskinesia should result from decreased firing rate of the Gpi/SNr. But in contrast, lesion in the Gpi abolishes the dyskinetic movements.[7] Therefore, current concepts involve studying firing rate and pattern of the basal ganglia structures in an attempt to explain clinical observations.[7]

REFERENCES

1. Mink JW. The basal ganglia: Focused selection and inhibition of competing motor programs. Progress in Neurobiology 1996;50(4):381–425.
2. Albin RL, Young AB, Penney JB. The functional anatomy of basal ganglia disorders. Trends in Neurosciences 1989; 12(10):366–75.
3. Budson AE, Price BH. Memory dysfunction. The New England Journal of Medicine 2005;352(7):692–9.
4. Obeso JA, Marin C, Rodriguez-Oroz C, Blesa J, Benitez-Temino B, Mena-Segovia J, Rodriguez M, Olanow CW. The basal ganglia in Parkinson's disease: Current concepts and unexplained observations. Annals of Neurology 2008;64 (Suppl 2):S30–46.
5. Mink JW. The basal ganglia and involuntary movements: Impaired inhibition of competing motor patterns. Archives of Neurology 2003;60(10):1365–8.
6. Smith Y, Raju D, Nanda B, Pare JF, Galvan A, Wichmann T. The thalamostriatal systems: Anatomical and functional organization in normal and parkinsonian states. Brain Research Bulletin 2009;78(2-3):60–8.
7. Brotchie JM, Obeso JA. Functional anatomy and pathophysiology of the basal ganglia. Movement disorders 4. Blue books of neurology;35 (Schapira AH, Lang AE, Fahn S-Elsevier Saunders) 2010,1–13.
8. Smith Y, Bevan MD, Shink E, Bolam JP. Microcircuitry of the direct and indirect pathways of the basal ganglia. Neuroscience 1998;86(2):353–87.
9. Gerfen CR, Bolam JP. The neuroanatomical organization of the basal ganglia. Handbook of basal ganglia structure and function. (Steiner H, Tseng KY-Academic Press Elsevier) 2010,3–28.
10. Kita H. Organization of the globus pallidus. Handbook of basal ganglia structure and function. (Steiner H, Tseng KY-Academic Press Elsevier) 2010,233–47.
11. Nambu A. A new dynamic model of the cortico-basal ganglia loop. Progress in Brain Research 2004;143:461–6.
12. Charpier S, Beurrier C, Paz JT. The subthalamic nucleus: From in vitro to in vivo mechanisms. Handbook of basal ganglia structure and function. (Steiner H, Tseng KY-Academic Press Elsevier) 2010;259–73.
13. Grace AA. Physiology of the normal and dopamine-depleted basal ganglia: Insights into levodopa pharmacotherapy. Movement Disorders 2008;23(Suppl 3):S560–9.
14. Smith Y, Villalba R. Striatal and extrastriatal dopamine in the basal ganglia: An overview of its anatomical organization in normal and parkinsonian brains. Movement Disorders 2008;23(Suppl 3):S534–47.
15. West AR, Grace AA. Opposite influences of endogenous dopamine d1 and d2 receptor activation on activity states and electrophysiological properties of striatal neurons: Studies combining in vivo intracellular recordings and reverse microdialysis. The Journal of Neuroscience 2002;22(1): 294–304.
16. Surmeier DJ, Day M, Gertler T, Chan S, Shen W. D1 and d2 dopamine receptor modulation of glutamatergic signaling in striatal medium spiny neurons. Handbook of basal ganglia structure and function. (Steiner H, Tseng KY-Academic Press Elsevier) 2010,113–32.
17. Centonze D, Bernardi G, Koch G. Mechanisms of disease: Basic-research-driven investigations in humans—The case of hyperkinetic disorders. Nature Clinical Practice, Neurology 2007;3(10):572–80.

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Textbook of MOVEMENT DISORDERS

This textbook is primarily intended for the practising neurophysicians and residents in neurology, with a balance between fundamentals and advancements in the field of neurology. The principal objective has been to present clearly some of the important and commonly encountered problems of movement disorders. Throughout the book, there is an emphasis on the need to obtain valid evidence by adopting reliable methods.



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