COMMENTARY

Recent developments in basal ganglia research and application to psychiatry

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Abstract

Functionally dopamine neurons can be organised into dorsal and ventral tiers. Dorsal tiers may be associated with schizophrenia. Ventral tiers may be associated with Parkinson's disease. Putamen circuit controls complex patterns of motor activity. Caudate circuit is responsible for cognitive control of sequences of motor patterns. Tremor, chorea, dystonia, athetosis and hemiballismus are involuntary movements associated with damage to basal ganglia. Movement disorders with basal ganglia as the location of primary neuropathology are idiopathic Parkinson's disease, parkinsonian syndromes, progressive supranuclear palsy, Huntington's disease, Wilson's disease and dystonia. Various antipsychotics are associated with medication-induced movement disorders. Neuroleptic-induced movement disorders are neuroleptic-induced parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia and neuroleptic-induced tardive dyskinesia.

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Historical aspects

Cecile and Oskar Vogt coined the term "corpus striatum." Von Sommering described the substantia nigra. Thomas Willis gave the first anatomical description of subcortical structures. Cajal and Samuel Wilson gave detailed anatomical descriptions of corpus striatum. Jules Bernard Luys described the subthalamic nucleus.

Major structures

Major structures are caudate nucleus, putamen, globus pallidus, subthalamic nucleus and substantia nigra. Other regions which may be considered part of basal ganglia are ventral striatum and ventral pallidum. Striatum is caudate nucleus and putamen; corpus striatum is caudate nucleus, putamen and globus pallidus; lenticular nucleus is putamen and globus pallidus.

Caudate nucleus and putamen are telencephalic in origin. Globus pallidus is diencephalic in origin. It is divided into external and internal segments by medial mamillary lamina. Subthalamic nucleus is also diencephalic in origin. Substantia nigra is mesencephalic in origin. It is present in midbrain. It consists of two components: pars compacta (dorsal, cell-rich, containing neuromelanin and dopamine) and pars reticulata (ventral, cell-sparse, containing gamma aminobutyric acid). Functionally dopamine neurons can be organised into dorsal and ventral tiers.

Dorsal tiers are distributed along medial ventral mesencephalon. They are dorsal to dense cell clusters in substantia nigra and lateral and caudal to red nucleus. There is less messenger ribonucleic acid (m-RNA) for dopamine transporter and dopamine type 2 (D2) receptor. They are calbindin positive and send projections to areas of striatum dominated by limbic related structures and association regions of the cerebral cortex. They may be associated with schizophrenia.

Ventral tiers are densely packed into substantia nigra. Cells penetrate into substantia nigra pars reticulate. There is more m-RNA for dopamine transporter and D2 receptor. They are calbindin negative and send projections to sensorimotor regions of the striatum. They may be associated with Parkinson's disease.

Functions of basal ganglia

Putamen circuit controls complex patterns of motor activity. Caudate circuit is responsible for cognitive control of sequences of motor patterns.

Involuntary movements associated with damage to basal ganglia

Tremor is rhythmic movements about a joint due to synchronous contraction of agonists and antagonists. Chorea is rapid, semi-purposeful, graceful, dance-like non-patterned involuntary movements involving distal or proximal muscle groups. Dystonia is sustained or repetitive involuntary muscle contractions frequently

causing twisting movements with abnormal postures. Athetosis is slow, writhing, involuntary movements with a propensity to affect arms and hands. Hemiballismus is a violent form of chorea that comprises wild, flinging, large-amplitude movements on one side of the body.

Movement disorders with basal ganglia as the location of primary neuropathology

They are idiopathic Parkinson's disease, parkinsonian syndromes, progressive supranuclear palsy, Huntington's disease, Wilson's disease and dystonia. Parkinson's disease is a neurodegenerative disease associated with loss of dopaminergic neurons in the substantia nigra pars compacta. In 1817, James Parkinson described paralysis agitans in his "Essay on the shaking palsy." The characteristic triad consists of resting tremor, rigidity and bradykinesia. It is also associated with gait and postural disturbances. Parkinson's disease is also associated with cognitive and psychiatric manifestations. Important psychiatric manifestations are depression, apathy, anxiety and psychosis.

Huntington's disease is an autosomal dominant neurodegerative disorder characterised by a relentlessly progressive course and a combination of motor, psychiatric and cognitive symptoms. It was first described by George Huntington in 1872. It is caused by CAG trinucleotide repeat expansion mutation. CAG repeat expansion is located on exon 1 of the Huntingtin gene on the short arm of chromosome 4. Phenomenon of anticipation i.e. younger age of onset in subsequent generations of a family is exhibited. Primary involuntary movement abnormality is chorea or choreoathetosis. Associated voluntary movement abnormalities are visual tracking, fine motor movements and gait disturbances. Psychiatric manifestations are higher rates of suicide, depression and mania.

Wilson's disease is an autosomal recessive disorder in which mutations in the gene ATP7B result in abnormal copper accumulation in the liver, basal ganglia and other tissues. Neurological findings are tremor, dystonia, rigidity, choreoathetosis, bradykinesia, masked facies and micrographia. Psychiatric manifestations are personality changes, depression, suicidality, anxiety disorders and psychotic disorders.

Various antipsychotics are associated with medication-induced movement disorders and impact on D2 receptors. Chlorpromazine, thioridazine, mesoridazine, clozapine, olanzapine and quetiapine cause low D2 blockade. Trifluoperazine, chlorprothixene, loxapine, molindone and ziprasidone cause medium D2 blockade. Fluphenazine, perphenazine, thiothixene, haloperidol, droperidol, pimozide, risperidone and aripiprazole cause high D2 blockade.

Neuroleptic-induced movement disorders

They are neuroleptic-induced parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia and neuroleptic-induced tardive dyskinesia. The classic triad of neuroleptic-induced parkinsonism is rigidity (continuous [leadpipe] or cogwheeling), akinesia (minimisation of spontaneous motor activity, slowed speech and shuffling gait) and tremor (resting rhythmic oscillations [three to six Hz]). Women are more susceptible and incidence is higher for those above 60 years.

Neuroleptic malignant syndrome is manifested by moderate to severe hyperthymia, rigidity and autonomic dysregulation. It is also associated with dysphagia, incontinence, tremor, altered sensorium (confusion to coma), mutism, leucocytosis and elevated creatinine phosphokinase (CPK) indicating severe muscle injury.

Neuroleptic-induced acute dystonia occurs in up to ten percent patients. It is more common in young men. Different symptoms are torticollis, trismus, impaired speaking and swallowing, tongue protrusion or dysfunction, oculogyric crisis and opisthotonus. Acute saturation of D2 receptors may play a role.

Neuroleptic-induced acute akathisia usually develops four weeks after starting medication or decreasing medications to treat extrapyramidal symptoms. There is a subjective sense of restlessness. It is also associated with fidgeting or swinging of legs, rocking from foot to foot while standing and inability to stand or sit in one place for several minutes. Dopamine neurons in ventral tegmental area may be associated in the pathogenesis.

Neuroleptic-induced tardive dyskinesia is characterised by involuntary movements of the tongue, jaw, trunk or extremities. It is commonly seen after one to two months of starting the neurolept medication and commoner in older patients. Patterns of movement are rapid, jerky and nonrepetitive; slow, continuous and sinuous; rhythmic.

Summary

The basal ganglia are a group of subcortical nuclei of varied embryonic origin. Its components are caudate nucleus, putamen, globus pallidus, subthalamic nuclei and substantia nigra. Its main functions are initiation and execution of complex patterns of motor activity and cognitive control of sequence of motor patterns. Abnormalities of the basal ganglia give rise to various abnormal involuntary movements. Important clinical syndromes resulting from the damage to the basal

ganglia are Parkinson's disease and parkinsonian syndromes, Huntington's disease and Wilson's disease. The importance of the basal ganglia from the psychiatric aspect is in the development of neuroleptic-induced movement disorders viz. drug-induced parkinsonism, neuroleptic malignant syndrome, acute dystonia, acute akathisia and tardive dyskinesia.

Further Readings

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