

**AN ESSAY ON
INVOLUNTARY MOVEMENTS**

**IN
INFANCY AND CHILDHOOD**

**Submitted for Partial Fulfilment of
the Master Degree of Pediatrics**

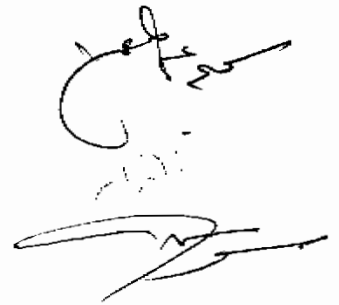
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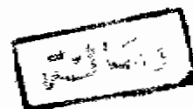
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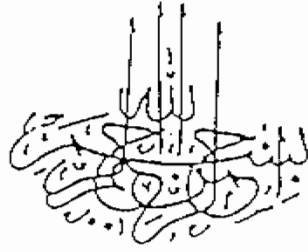
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INTRODUCTION

INTRODUCTION

The term involuntary movement disorders implies that the movements are not under volitional control; the patient cannot stop them at will. The movements are usually absent during complete relaxation especially during sleep; they are brought out by attempts to maintain a given posture or to carry out a skilled motor act. Furthermore, the movements are without apparent purpose. Involuntary movements occur principally in diseases of Basal Ganglia and of the Cerebellum.

Chorea consists of rapid, involuntary, nonrhythmic jerks of various parts of the body. The movements are seen to occur first in one part of the body and then another . They are marked by their irregularity and failure to be repetitive at a single site. Hypotonia is frequently present . (Lockman, 1982).

Athetosis is a slow writhing movement, often more marked in the distal extremities, consisting of alternating supination-pronation and flexion-extension of the limbs.

Dystonia is a tendency toward hyperextension of joints, brought out especially when the patient tries to walk. Typically, there is planter flexion of the feet, hyperextension of the legs, extension and pronation of arms, arching of the back, and extension and rotation

of the neck (Huttenlocher, 1983).

Myoclonus is an involuntary, repetitive, desultory, instantaneous, irregular contraction of a group of muscles or, occasionally a single muscle. The jerks of myoclonus may be symmetrically synchronus or asymmetric (Lockman, 1982).

Tics are sudden, purposeless, rapid, repetitive , highly stereotyped involuntary movements which occur irregularly. They preferentially involve the muscles of the face, neck, and upper extremities.

Tremors are purposeless, rapid, repetitive, highly stereotyped movements. They differ from tics in being both more constant and rhythmic, whereas tics are irregular. In addition, the movement of tremors is generally of smaller amplitude (Golden and Hood, 1982).

REVIEW
OF
LITERATURE

BASAL GANGLIA

Neuroanatomy:

The main structures of the basal ganglia are the caudate nucleus and the lentiform nucleus with its two subdivisions, the putamen and globus pallidus (pallidum). In addition to the caudate and lenticular nuclei, one usually includes the claustrum, the subthalamic nucleus (Corpus luyssii), and the substantia nigra. Insofar as the caudate and putamen are really a single continuous structure, which is cytologically and functionally distinct from the pallidum, a more meaningful division of these nuclear masses is into the neostriatum (or striatum), comprising the caudate and putamen, and the paleostriatum or pallidum, with its medial (internal) and lateral (external) segments. The striatum and pallidum lie on the lateral aspect of the internal capsule, which separates them from the subthalamic nucleus and substantia nigra on its medial side (Adams and Victor, 1977).

The well-established pathway from the dentate nucleus of the cerebellum via the red nucleus, through the ventral nucleus of the thalamus (anterior half), to the primary motor cortex is joined by a pathway from the striatum, globus pallidus, and substantia nigra to the same region of the thalamus and then to the primary motor cortex. Thus the afferent component of the "extrapyramidal system" - that is, the pathway from the striatum to the thalamus to the cortex and the pathway from the substantia nigra to the thalamus to the cortex - is joined by the "ascending cerebellar system" at the level of the thal-

amus (Carman, 1968).

There apparently are also connections from the cortex to the striatum, red nucleus, and substantia nigra. Direct corticopallidal connections are unproved. The important interconnections of the basal ganglia are shown in Fig-1. Movement disorders are attributed to abnormalities in the structure and function of these nuclear masses (Lockman, 1982).

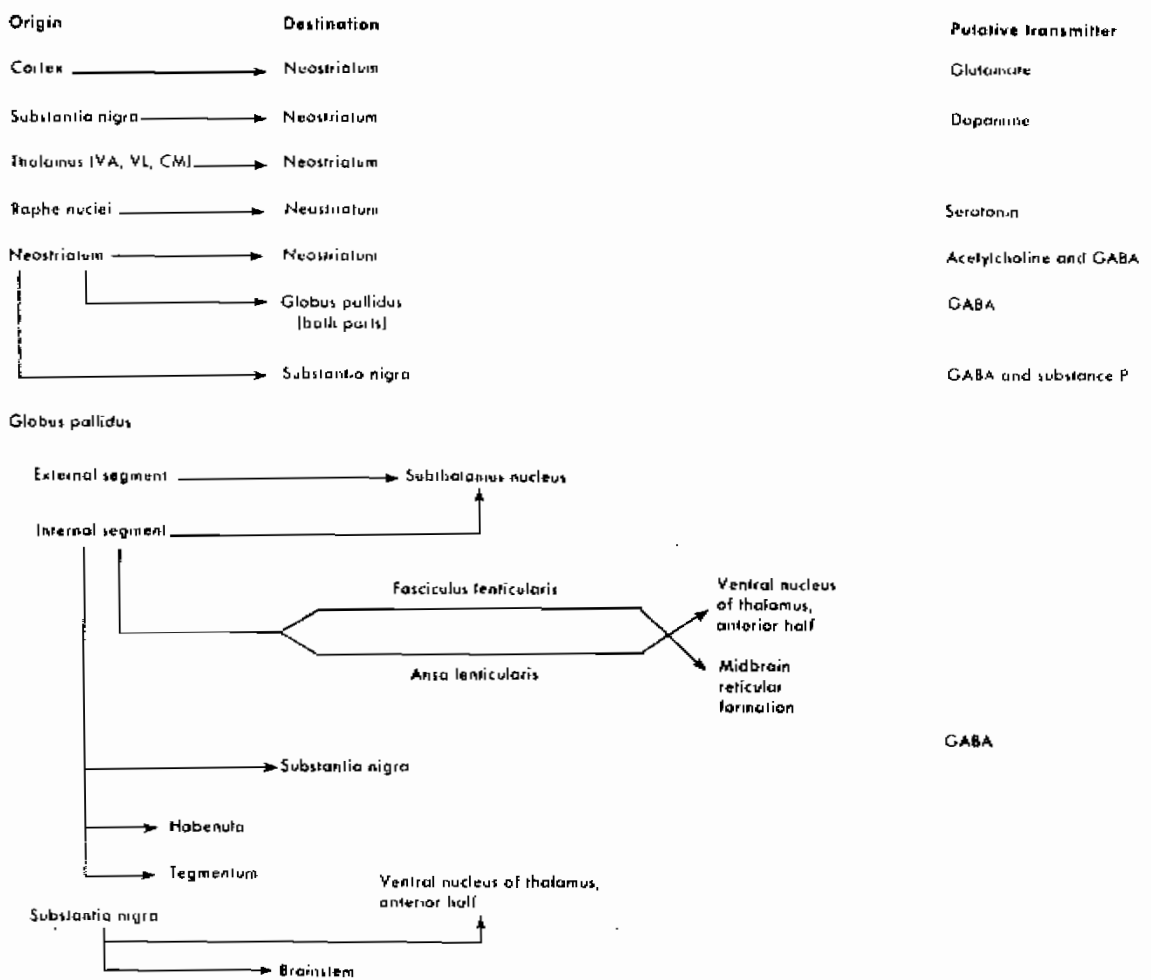


Fig. 1: Simplified scheme of connections of the basal ganglia (Lockman, 1982).

Neuropharmacology:

A feature of the basal ganglia is the rich but differential concentration of neurotransmitters within these grey masses along with mechanisms for their synthesis, storage, release, and inactivation. Neurotransmitter substances including dopamine, acetylcholine, serotonin (5-hydroxytryptamine), histamine norepinephrine, and γ -aminobutyric acid (GABA) are highly concentrated within the basal ganglia, although they are present in other parts of the brain. Current therapeutic strategies involve attempts at enhancing or reducing the effects of one or another of the neurotransmitter substances in an attempt to reestablish the delicate balance essential for the normal tone and movement (Lockman, 1982)

Dopamine:

Dopamine has a specific function in the central nervous system, apart from being a precursor of norepinephrine and melanin. There is a prominent system of dopaminergic neurons, the nigrostriatal dopaminergic system, with cell bodies in the substantia nigra and axonal endings in the caudate nucleus. The dopamine released at these endings appears to inhibit cells in the caudate, whereas acetylcholine released from other cells excites them. A feedback circuit from the caudate to the substantia nigra is made up of neurons that secrete γ -aminobutyric acid (Ganong, 1983,a).

The symptom most closely associated with dopamine depletion is bradykinesia; in the treatment of patients with parkinson disease,

the akinesia responds first (Barbeau, 1974).

Conversely, hyperkinetic movement disorders, particularly chorea, have been described in parkinson disease patients treated with L-dopa and have been attributed to denervation sensitivity of dopaminergic neurons in the brain. Gilles de la Tourette syndrome has also been induced by L-dopa. The metabolic breakdown product of dopamine is homovanillic acid (HVA), which can be assayed in spinal fluid and urine . Decreased HVA concentrations in spinal fluid and urine have been used as an indicator of decreased dopamine metabolism particularly in parkinson disease. Certain drugs, for example, tetrabenazine and reserpine, deplete the presynaptic granules of dopamine and inhibit the reuptake. Other pharmacologic agents, such as haloperidol, other butyrophenones, and pimozide, specifically block the dopamine receptor site. Both haloperidol and pimozide have been used clinically to treat hyperkinetic dyskinesia (Lockman, 1982).

Acetylcholine:

Acetylcholine is present throughout the brain. The highest concentration is in the neostriatum, where acetylcholine is localized to nerve endings and specifically in synaptic vesicles. The activity of choline acetylase and acetylcholinesterase, the enzymes necessary for the synthesis and degradation of acetylcholine, is also high in the striatum. These facts suggest that acetylcholine is a physiologically potent substance and that the striatum is probably the major site of cholinergic activity. Acetylcholine appears to have an excitatory

effect on neostriatal neurons, which can be counteracted by dopamine. It is likely that the effectiveness of the belladonna alkaloids, which had been used empirically for many years in the treatment of parkinson's disease, also depends on their capacity to antagonize acetylcholine centrally (Adams and Victor, 1977).

Gamma aminobutyric acid (GABA):

GABA has been known to be present in the central nervous system for many years, and its function as an inhibitory neurotransmitter now seems without doubt. Glutamic acid is metabolized to GABA by the enzyme glutamic acid decarboxylase (GAD). High concentrations of GABA are found in the substantia nigra, globus pallidus and hypothalamus, with lesser amounts in the putamen and the caudate. The transmitter is degraded by action of the enzyme GABA transaminase (GABA-T) to succinic semialdehyde. It may be an important inhibitory neurotransmitter in the interneurons of the neostriatum. It probably also is implicated in the striatonigral pathway, as well as probably being a neurotransmitter in the pathway descending from the globus pallidus to substantia nigra (Lockman, 1982).

Serotonin;

Serotonin is formed in the body by hydroxylation and decarboxylation of the essential amino acid tryptophan. After release from serotonergic neurons, much of the released serotonin is recaptured by an active uptake mechanism and inactivated by monoamine oxidase to form 5-hydroxyindoleacetic acid (5-HIAA). This substance is the

principal urinary metabolite of serotonin, and the urinary output of 5-HIAA is used as an index of the rate of serotonin metabolism in the body (Ganong, 1983 b).

Serotonergic neurons are located primarily near the midline or raphe regions of the pons and upper brain stem and project downward to the medulla and spinal cord and also upward to the telencephalon, diencephalon, limbic system, and the neostriatum. Serotonin appears to have primarily an inhibitory effect on the post synaptic cell (Lockman, 1982).

The tricyclic antidepressant inhibit the reuptake of serotonin into neuronal tissue and also are known to decrease parkinsonian rigidity and tremor. Conversely, increase in brain serotonin concentration leads to rapid exacerbation of both tremor and rigidity (Barbeau, 1974).

Substance P:

Substance P, is a peptide found in the spinal cord and also is present in substantia nigra, caudate, putamen, amygdala, and hypothalamus, as well as the cerebral cortex. It appears to have prolonged excitatory action (Lockman, 1982).