بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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STUDY OF SOME BIOCHEMICAL FACTORS IN PATHOGENESIS OF PARKINSONISM

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By

HAZEM FARAG MANNAA

MBBCh, Alex.

Faculty of Medicine

Alexandria University

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SUPERVISORS

Prof. Dr. ENAYAT M. HASHEM

Professor of Medical Biochemistry

Faculty of Medicine

University of Alexandria

Prof. Dr. SABAH A. MAHMOUD

Professor of Medical Biochemistry

Faculty of Medicine

University of Alexandria

Dr. MOHAMED F. BORAEY

Assistant Professor of Neuropsychiatry,

Faculty of Medicine

University of Alexandria

CO-WORKER

Dr. EMAN A. SHAAT

Lecturer of Medical Biochemistry

Faculty of Medicine

University of Alexandria

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ABBREVIATIONS

AD:	Alzheimer
ATP:	Adenosine triphosphate
CO:	Carbon monoxide
DA:	Dopamine
DNA:	Deoxyribonucloeic acid
FAD:	Flavine adenine dinucleotide
Fe^{2+}:	Ferrous iron
Fe^{3+}:	Ferric iron
FMN:	Flavine mononucleotide
GSH:	Reduced Glutathione
GSSG:	Oxidized Glutathione
GSH-PX:	Glutathione peroxidase
H_2O:	Water
MAO:	Monoamine oxidase
Mn	Manganese
MPP+:	1-methyl-4-phenyl-pyridinium ion
MPTP:	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
NAD:	Nicotinamide adenine dinucleotide
O_2:	Molecular oxygen
PD:	Parkinson's disease
SN:	Substantia nigra
SOD	Superoxide dismutase
UQH_2:	Ubiquinol

ERRATA

Page	Line	Wrong word	Correct word
5	5	Norepinephrin	Norepinephrine
5	5	Epinephrin	Epinephrine
7	14	Unbiquinol	Ubiquinol
12	8,15,17	Unbiquinol	Ubiquinol
14	13	Form	From
15	3	Independance	Independant
37	18	Substatntia	Substantia
36	21	Substatntia	Substantia
38	2	Substatntia	Substantia
50	21	Duroeuinone	Duroquinone

INTRODUCTION

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In 1817, James Parkinson; a physician of Hoxton in London, gave the first description of the major clinical features of what today is recognized as a symptom complex manifested by any combination of six cardinal features: (1) tremor at rest, (2) rigidity, (3) bradykinesia-hypokinesia, (4) flexed posture, (5) loss of postural reflexes, and (6) the freezing phenomenon. At least two of these features, with at least one being either tremor at rest or bradykinesia must be present for a diagnosis of definite parkinsonism.[1-3]

Aetiology

Parkinsonism is caused by lesions in the basal nuclei and is associated particularly with the interconnecting system between the substantia nigra and the corpus striatum. The nigrostriatal pathways utilize dopamine as a neurotransmitter, and parkinsonism is associated with dopamine deficiency.[1-3]

The many causes of parkinsonism are divided into four categories: idiopathic, symptomatic, parkinson-plus syndromes, and other neuro-degenerative diseases in which parkinsonism is a manifestation (table 1).[1,4,5]

Table 1. Classification of major parkinsonian syndromes

Idiopathic Parkinsonism
Parkinson disease
Symptomatic Parkinsonism
Drug-induced: dopamine antagonists and depletors
Hemiatrophy-Hemiparkinsonism
Hydrocephalus: normal pressure hydrocephalus
Hypoxia
Infectious; postencepalitic
Metabolic; parathyroid dysfunction
Toxin: Mn, CO, MPTP, Cyanide
Trauma
Tumor
Vascular; multi-infarct state
Parkinson-plus syndromes
Cortical-basal ganglionic degeneration
Dementia syndromes
Alzheimer disease
Diffuse Lewy body disease
Lytico-Bodig (Guamanian Parkinsonism-Dementia-ALS)
Multiple system atrophy syndromes
Striatonigral degeneration
Shy-Drager syndrome
Sporadic olivopotocerebellar degeneration (OPCA)
Motor neuron disease- parkinsonism
Progressive pallidal atrophy
Progressive supranuclear palsy
Heredodegenerative diseases
Hallervorden-Spatz disease
Huntington disease
Lubag (X-linked dystonia- parkinsonism)
Mitochondrial cytopathies with striatal necrosis
Neuroacanthocytosis
Wilson disease

Drug-induced parkinsonism

Secondary parkinsonism may be caused by variable drugs. Neuroleptics (antipsychotic drugs) are the commonest among this actiological group of secondary parkinsonism. Neuroleptics include; haloperidol (safinace), chlorpromazine (neuroazine), resperidone, clozapine (lebonex), and fluphenazine (mellaril).[5]

Pentoxifylline is a synthetic derivative of xanthine and it may cause imbalance between dopamine receptors producing pharmacologic parkinsonism, or rather, may unmask the subclinical Parkinson's disease.[6]

Amiodarone; an antiarrhythmic drug, was reported to produce some features of parkinsonism.[7]

Valproate (antiepileptic drug), some of the calcium channel blockers[8] as deltiazim and amlodipine, and cinnarzine (a piperazine derivative with calcium antagonist and anticonvulsant properties)[9] were reported to induce parkinsonism.

Incidence of Parkinson's disease

It is estimated that Parkinson's disease (PD) makes up approximately 80% of the cases of parkinsonism.[1]

The age at onset assumes a bell-shaped curve with a mean age of 55 years in both sexes and a wide range from 20 to 80 years. Onset at younger than 20 years is known as juvenile Parkinsonism which is often hereditary or caused by Huntington disease or Wilson's disease.[1,10] Reports tell that 1% of people over the age of 50 years have this condition.[11]

Parkinson's disease is more common in males with a male/female ratio of 3/2. But as women live longer and the incidence increases with age, there are more affected older women.[4]

Monoamine oxidase and Dopamine Biochemistry

Monoamine oxidase (MAO) is an enzyme that oxidatively deaminates many amines. It is found in all human tissues except red blood cells.

In the 1960's, 2 isoenzymes of MAO were identified; MAO-type A (MAO-A) and MAO-type B (MAO-B). MAO-A prefers as substrates, the hydroxylated amines; norepinephrin, epinephrin, and serotonin, while MAO-B preferentially acts on nonhydroxylated amines such as phenylethylamine.[27]

MAO-A and MAO-B, differ in their amino acid sequences and are encoded and transcriptionally controlled at separate gene loci.[28,29] Both proteins are constituents of mitochondrial outer membranes but are also found in the cytosol.[30,31] MAO-A is resident in most neurons, while MAO-B is found in non-neuronal cells, particularly astrocytes.[31]

Figure(1) shows the main metabolic pathways of dopamine. Infusion of radiolabelled dopamine has shown that most is metabolized to homovanilic acid, and a lesser proportion through the catecholamine pathway to norepinephrin, epinephrin, and vanillyl mandilic acid.[29-32]