STUDY OF THE AETIOLOGY AND PATHOGENESIS OF MOTOR NEURONE DISEASE

Thesis

Submitted for the Partial Fulfilment of the Master Degree in Psychological Medicine and Neurology

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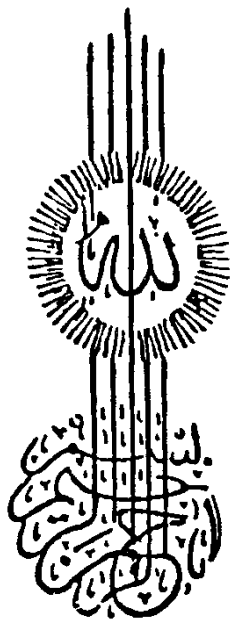
1986



قالوا

سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا

إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

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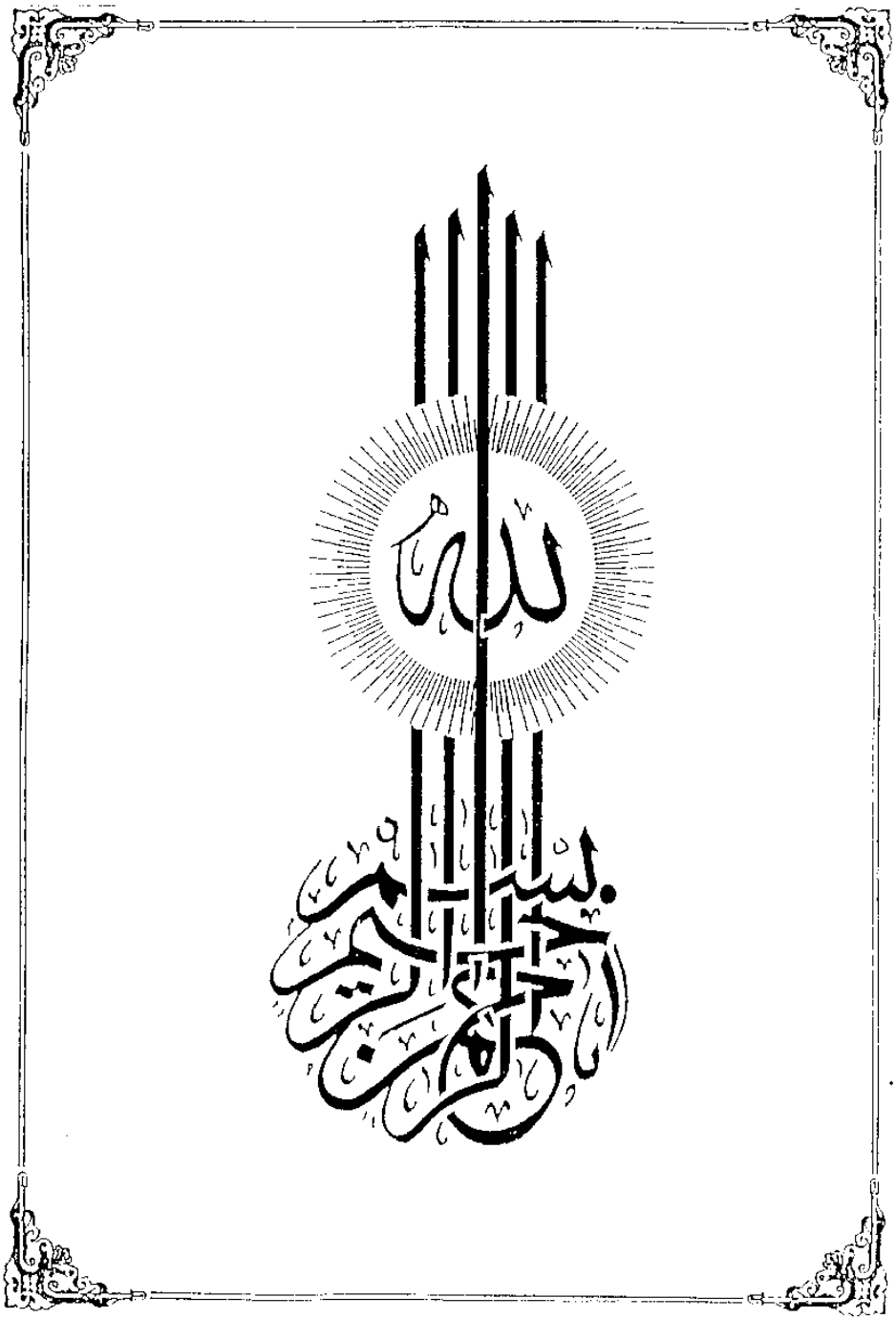

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ACKNOWLEDGEMENT

I would like to express my sincerely felt gratitudes to ***Professor Dr. Yousif Ali Abu Zied*** *who suggested the subject. His constant encouragement, patience, constructive criticism, warm kindness and guidance helped me very much to carry on this work. His unintrusive guidance have a great value for me to grasp the basis and techniques of scientific work.*

I owe special thanks and much regards to ***Dr. Amira Ahmed Zaki*** *for her guidance, understanding and supply of important references which helped me much to overcome many difficulties.*

My cordial appreciation to my wife and children for their patience and cooperation.

God bless them all.

Dr. M. E. Khalid

August, 1986.

Aim of the Work

The tremendous discoveries and research work in basic sciences started to discover the obscure aetiologies of some neurological diseases, such as Creutzfeldt - Jakob disease. It was claimed that neurology has benifited perhabs more than any branch of medicine from the applications of basic sciences.

It is aimed by this work to review the literature about research progress in the aetiology and pathogenesis of motor neurone disease, so as to deduce epidemiological and laboratory data which may prove helpful in prevention, early diagnosis and management.

INTRODUCTION

INTRODUCTION

Motor neurone disease is a disorder of unknown aetiology till now. There have been many theories concerning its pathogenesis ranging from toxic factors to immunological disturbances.

It is aimed by this study to review the literature to:

- Study the epidemiology and antecedent events to find any possible causative factors.

Review the theories and postulations about the aetiology, pathogenesis and factors which make motor neurones vulnerable for the degenerative process of the disease.

To complete the picture about the disease, short notes will be written about pathology, clinical picture and trials of treatment and management.

The thesis will be ended by a chapter of conclusions and comments.

Motor neurone disease is so called because, it is characterized by selective degeneration of motor neurones, involving the cortico spinal pathways and those which originate in the motor nuclei of the brain stem and the anterior horn cells of the spinal cord. (Bannister, 1977). This definition goes with earlier recommendation for definition of motor neurone disease proposed by Mackay (1963) who said to be in a clinicoanatomic terms.

The above apparent simple concept of motor neurone disease is far form universally accepted within the constellation of motor neurone diseases. Kurtzke (1982) stated that "motor neurone diseases" refer to all disorders characterized primarily by progressive weakness attributed to leisons of the anterior horn cells, whether or not any other parts of the neuraxis are affected. The major groupings included in his definition are the heredofamilial spinal muscular atrophies, with their own subtypes both eponymal and numerical and motor, neurone disease.

The term motor "neurone disease" and not diseases is restricted to include:

- Amyotrophic lateral sclerosis.
- Progressive spinal muscular atrophy.
- Progressive bulbar palsy.
- Primary lateral sclerosis.
- Special types of familial, progressive muscular atrophy e.g. Werdnig-Hoffman type (Adams and Victor, 1977).

Campbell and Liversedge, (1981) gave clear and comprehensive clinical classification of motor neurone diseases (Table I), including with it the types which are grouped under the term "motor neurone disease", to be either:

a) Sporadic form

b) Familial form

c) Western pacific form.

It should be noted that, in united kingdom the inclusive

Table (I): Motor Neurone diseases:

1. **Motor neurone disease:**

   Includes: - Amyotrophic lateral sclerosis.
   - Progressive bulbar palsy.
   - Progressive muscular atrophy.

   a. Sporadic form
   b. Familial form
   c. Western pacific forms

2. **Spinal muscular atrophies:**
   a. Proximal forms
   b. Distal forms.
   c. Scapuloperoneal form.
   d. Facioscapulohumeral form.
   e. Juvenile progressive bulbar palsy.

3. **Motor neurone disease associated with other diseases of the central nervous system:**

   a. mental disorder
   b. Extrapyrimidal disorders.
   c. Spinal disease including the hereditary spinocerebellar ataxias.

4. **Miscellaneous diseases:**
   a. Infections.
   b. Metabolic including hypoglycaemia.
   c. Toxicity-heavy metals, organophosphorus compounds.
   d. Ischaemic myelopathy including radiation damage.
   e. Trauma including electrical injury.
   f. Non-metastatic carcinomatous neuromuscular disease (Campbell & Liversedge, 1981).

term commonly used to identify this disease, which embraces: progressive muscular atrophy, progressive bulbar palsy and amyotrophic lateral sclerosis is motor neurone disease (M.N.D.). In the United States of America by contrast, motor system disease or more often amyotrophic lateral sclerosis (A.L.S.) is occationally used to cover the whole disease spectrum (Campbell & Liversedge, 1981).

Rose Clifford, (1977) preferred to restrict the term amyotrophic lateral sclerosis (A.L.S.) to those cases in which upper motor neurone signs predominate, and illustrated the clinical types of M.N.D. as follows:

1. Progressive muscular atrophy; in which lower motor neurone signs predominate.

2. Amyotrophic lateral sclerosis; in which upper motor neurone signs predominate.

3. Progressie bulbar palsy:

   a. Chronic: Lower motor neurone.

   b. Psuedobulbar: upper motor neurone.

Primary lateral sclerosis has virtually, disappeared as a concept. (Rowland & Layser, 1971). But some authors still retain it as a clinical variant e.g. Mawdsley and Simpson (1977) defined primary lateral sclerosis as an uncommon entity in which progressive paraparesis usually antedates lower motor neurone signs, may

be by months.

The western pacific form:

Following the occupation by the American Forces of the Island of Guam in the Second World War, an abnormally high prevelance of the otherwise typical form of amyotrophic lateral sclerosis was discovered among the indigenous population of Chamorro Indians (Koerner, 1952).

This variant of motor neurone disease is also known as "Guamanian amyotrophic lateral sclerosis", or "the Marian Islands form of amyotrophic lateral sclerosis" or "the Western Pacific form of amyotrophic lateral sclerosis". The entity is clinically and-initially-pathologically appeared identical with sporadic motor neurone disease. It is known to affect natives of Rota and Saipan and there are also foci of the identical disease within the küPeninsula of South-eastern, Honshu, Japan. Plus another focus, without pathological proof, in certain villages of West New Guinea-thus "Western Pacific" - (Kurtzke, 1982).

Familial Types :-

The familial incidence of motor neurone disease outside the Western Pacific Islands is generally 5-10 percent with an autosomal dominenant pattern of inheritance showing high pentrance (Kurland and Mulder, 1955; Bobowick and Brody, 1973).

The clinical picture is similar to that of sporadic forms except that some patients have shown additional features of dementia

or extrapyrimidal disease (Hirano A, Kurland L.T. et al., 1967; Bonduelle, 1975). However there are other reports of regular involvement of Clarke's nucleus in sporadic amyotrophic lateral scierosis (Averback Paul and Crocker, 1982).

Madras Motor Neurone Disease (M.M.N.D.):

It is reported that there is another variant of motor neurone disease (MND) found in India and specifically in Madras (Kurtzke, 1982).

Srinivas K. et al (1984) reported that, it is clearly seems to be two distinict entities clinically, the Madras Motor Neurone Disease (M.M.N.D.) and convential Motor Neurone Disease. Biochemical differences are noted but their significance is largely unknown. Poor nutritional status is common to all their patients and not related in any way to the primary neurological disorder. The striking feature is the occurance of M.M.N.D. exclusively in the younger age groups as well as some cases of conventional M.N.D. below the age of thirty years. Kurtzke (1982) considered it as a variant of sporadic motor neurone disease and characterized by sensorineural deafness.

From this short introduction we can conclude that the term " motor neurone disease although sometimes equated with the term "amyotrophic lateral sclerosis" as mentioned before, it has these forms: the sporadic form including the Madras type, the familial and the Western Pacific forms. These forms can present

clinically in one of these clinical subtypes; amyotrophic lateral sclerosis, progressive muscular atrophy and progressive bulbar palsy.

EPIDEMIOLOGY