Clinical Appraisal of Genetics in Dementia

Essay submitted for partial fulfillment of the M.Sc. Degree in Neuropsychiatry

Presented by

AMIRA NASSIEB EL-BATRAWY

M.B., B.Ch.

Under the supervision of

PROF. DR. MAHAMMAD OSSAMA ABDULGHANI

Professor of Neuropsychiatry

Faculty of Medicine-Ain Shams University

PROF. DR. NAGLAA NAGY EL-MAHALAWY

Professor of Neuropsychiatry

Faculty of Medicine-Ain Shams University

DR. SAMIA ASHOUR

Assistant Professor of Neuropsychiatry

Faculty of Medicine-Ain Shams University

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

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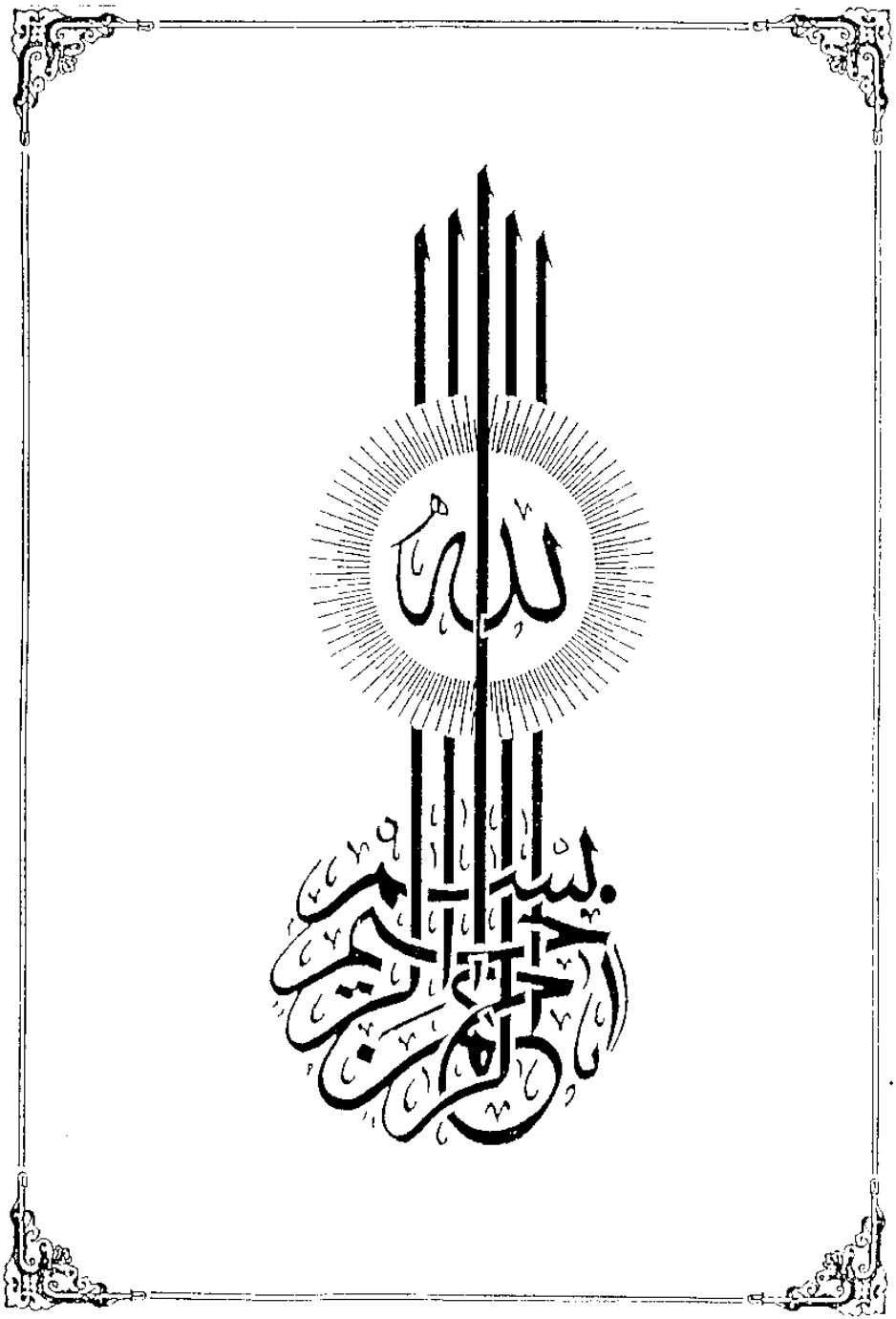
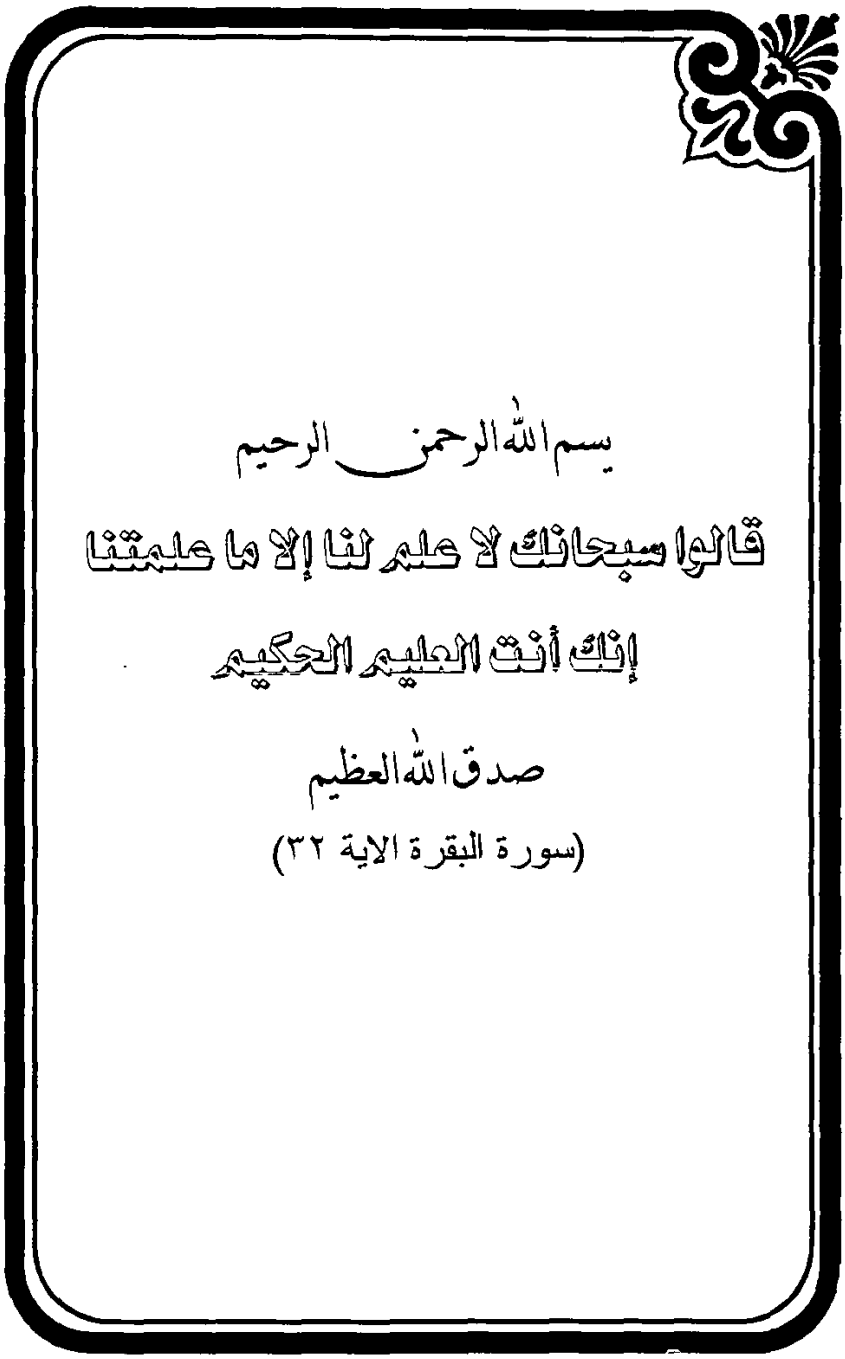




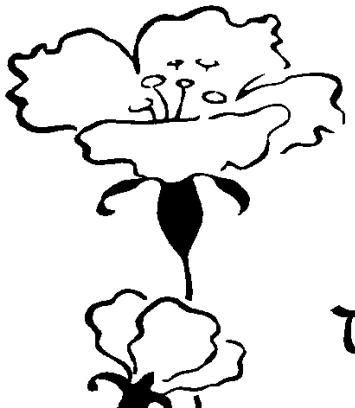
بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا

إنك أنت العليم الحكيم

صدق الله العظيم

(سورة البقرة الاية ٣٢)



Dedication

To My Family

and

to Ahmed

my Beloved Fiancé

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List of Abbreviations

A: Adenine

AD: Alzheimer's disease

ADAS-Cog: Alzheimer's disease assessment scale cognitive.

ADAS-non Cog: Alzheimer's disease assessment scale non-cognitive.

ADL: Activities of daily living.

AIDS: Acquired immune deficiency syndrome.

APoE: Apolipoprotein E.

APP: Amyloid precursor protein

BSE: Bovine spongiform encephalopathy

C: Cytosine

CADASIL: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoence-phalopathy.

cDNA: Complementary DNA

CDR: Clinical dementia rating.

CJD: Creutzfeldt Jacob disease

cM: CentiMorgan

CT: Computerized tomography

DIST: Dihycholipoyl succinyl transferase.

DNA: Deoxyribonucleic acid

DSM IV: Diagnostic and statistical manual of mental disorders IV.

Dz: Dizygotic

ε: Epsilon

FAD: Familial Alzheimer's disease.

FAQ: Functional assessment questionnaire

FTDP: Fronto-temporal dementia with parkinso-nism.

G: General criteria for dementia.

G: Guanine

GDS: Global deterioration scale.
GoM: Granular osmophilic material.
HD: Huntington's disease.
IADL: Instrumental activities of daily living scale.
ICD 10: International classification and diagnosis of mental behavioural disorders.
MBDS: Modified blessed dementia scale.
MMSE: MiniMental state examination
MR: Morbidity risk
MRI: Magnetic resonance imaging
mRNA: Messenger RNA
Mz: Monozygotic
NFT: Neuro-fibrillary tangles
P: Prior probability
p: Short-arm.
PCR: Polymerase chain reaction.
PD+D: Parkinson's disease with dementia.
PD: Parkinson's disease.
PD-D: Parkinson's disease without dementia.
PET: Positron emission tomography
PHF: Paired helical filaments
PrP: Prion protein
Ps: Presenilin
q: Long-arm
RFLPs: Restriction fragment length polymorphism
RNA: Ribonucleic acid
rRNA: Ribosomal RNA
SPs: Senile plaques
T: Thymine
tRNA: Transfer RNA
U: Uracil
Vs: Versus

Introduction and Aim of the Work

to function effectively as a worker or head of family because of certain diseases of aging e.g. dementia and modern medicine offers the means of treating such conditions and in same instances restoring the patient to normal health and effectiveness ***(Adams and Victor, 1997).***

At the present time, no treatment has been proven to alter the relentless deterioration of the disease. A number of attempts have been made at neurotransmitter replacement therapy, concentrating particularly on cholinergic drugs and there is some evidence of minor symptomatic benefit from anticholinesterase drugs. As modern neurology has been greatly influenced by developments in molecular genetics. By the positional cloning approach a number of genes responsible for inherited neurological diseases have been mapped in the human genome and some of them have already been identified ***(Hyman and Nestler, 1993)***.

By identifying and cloning the aberrant genes, it has become possible to study the defective problems responsible for the disorders such advances in molecular medicine have begun to revolutionize diagnosis and should eventually have a profound impact on the treatment and even prevention of serious diseases in humans. Vulnerability to many of the most severe neuropsychiatric disorders e.g. dementia appears to be