THE ROLE of GENETIC FACTORS IN THE ETIOLOGY OF AUTISTIC DISORDER

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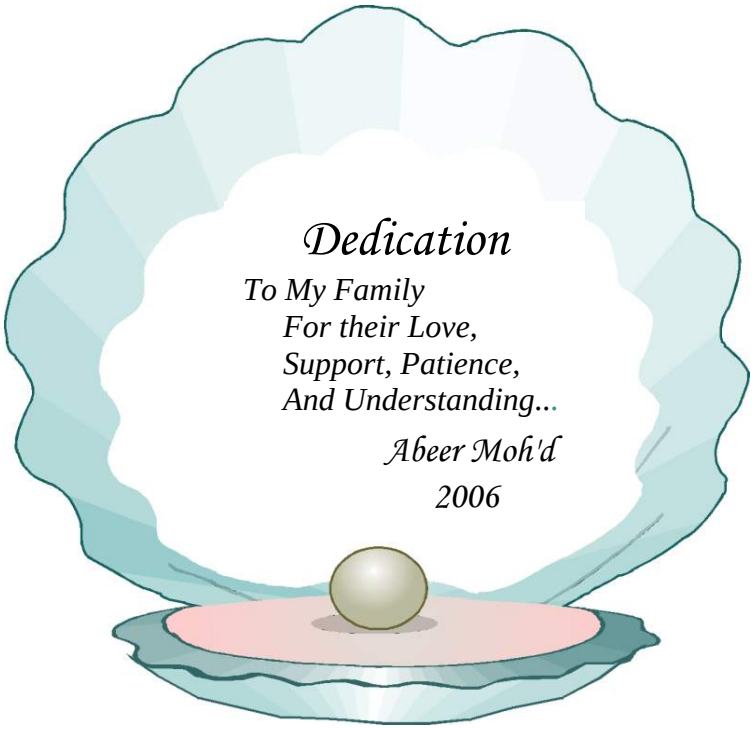
بسم الله الرحمن الرحيم

"و قل ربی زدنی علما "

صدق الله العظيم

سورة طه. آية 114

And say,' My Lord!
Increase My Knowledge'



Dedication

To My Family
For their Love,
Support, Patience,
And Understanding...

Abeer Moh'd

2006

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Abstract

Autistic disorder **(AD)** is a pervasive developmental disorder beginning before the age of 3 ys and lasting over the whole life time. It is characterized by a triad deficit: qualitative impairments in social interactions, communication deficits & repetitive and stereotyped pattern of behavior. Recent studies show prevalence rates ranging from 10 to 20 per 10,000. Although the etiology of AD is unknown, genetic predisposition is evident from family and twin studies, and heritability is estimated over 90%. The genetic component is best described by a multilocus model that takes into account epistatic interactions between several susceptibility genes. To date, suggestive autism susceptibility loci have been identified on almost every chromosome.

Key Words: **Autistic Disorder (AD); Candidate genes; Cytogenic Regions of Interest (CROI); Linkage; Association; Genome Scan; Multifactorial Inheritance.**

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List of Abbreviations

A:	**Adenine.**
ABC:	**Autism Behavior Checklist.**
ADA:	**Adenosine Deaminase.**
AD:	**Autistic Disorder.**
ADI-R:	**Autism Diagnostic Interview Revised.**
ADOS:	**Autism Diagnostic Observation Schedule.**
AGTR2:	**Angiotensin II Receptor.**
AIT:	**Auditory Integration Training.**
AKAP:	**A-kinase Anchoring Protein.**
APA:	**American Psychiatric Association.**
APOE:	**Apolipoprotein E.**
ARP:	**Affected Relative Pairs.**
AS:	**Asperger's Disorder.**
AS*:	**Angelman Syndrome.**
ASD:	**Autism Spectrum Disorder.**
ASDSQ:	**Autism Spectrum Disorder Screening Questionnaire.**
ASP:	**Affected Sib-Pair.**
ASQ:	**Autism Screening Questionnaire.**
AVP:	**Arginine-Vasopressin.**
BAP:	**Broader Autism Phenotype.**
BDNF:	**Brain-Derived Neurotrophic Factor.**
C:	**Cytosine.**

cen:	**Centromere.**
CGH:	**Comparative Genomic Hybridization.**
CGRP:	**Calcitonin Gene Related Peptide.**
CHARGE:	**Coloboma, Heart disease, Atresia Choana, Retarded growth & development, Genital anomalies, Ear anomalies.**
CHAT:	**Checklist for Autism in Toddlers.**
CLSA:	**Collaborative Linkage Study of Autism.**
cM:	**cent Morgan.**
CNS :	**Central Nervous System.**
CROI:	**Cytogenetic Regions of Interest.**
CT:	**Computed Tomography.**
DBH:	**Dopamine Beta-Hydroxylase.**
del:	**Deletion.**
DLD:	**Developmental Language Disorder.**
DMG:	**N, N-Dimethylglycine.**
DNMTs:	**DNA Methyltransferases.**
DNA:	**Deoxyribonucleic Acid.**
DSM-III:	**Diagnostic and Statistical Manual of Mental Disorders, 3rd edition.**
DSM-IV:	**Diagnostic and Statistical Manual of Mental Disorders, 4th edition.**
DSM-IV-TR:	**Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision.**
dup:	**Duplication.**

DZ:	**Dizygotic.**
FISH:	**Fluorescence In Situ Hybridization.**
fra:	**Fragile site.**
FXS:	**Fragile X Syndrome.**
E^*:	**Epinephrine.**
E:	**Environmental.**
EEG:	**Electroencephalogram.**
G:	**Guanine.**
GABA:	**Gamma-Aminobutyric Acid.**
GABA-T:	**Gamma-Aminobutyric Acid Transaminase.**
GIT:	**Gastrointestinal Tract.**
GluR6:	**Glutamate Receptor 6.**
GRPR:	**Gastrin-Releasing Peptide Receptor.**
h^2:	**Broad- Sense Heritability.**
HDACs:	**Histone Deacetylases.**
HLA:	**Human Leukocyte Antigen.**
5-HT:	**Serotonin.**
HTR2A:	**Serotonin 2A Receptor.**
HTT:	**Serotonin Transporter Gene.**
i:	**Isochromosome.**
IBD:	**Identical By Descent.**
IC:	**Imprinting Center.**
IgA:	**Immunoglobulin A.**

IGF-II:	**Insulin-like Growth Factor II.**
IMGSAC:	**International Molecular Genetic Study of Autism Consortium.**
inv:	**Inversion.**
IQ:	**Intelligence Quotient.**
ish:	**In situ hybridization.**
Kb:	**Kilobase.**
λs:	**Sibling Recurrence Risk Ratio.**
LD:	**Linkage Disequilibrium.**
LKS:	**Landau –Kleffner Syndrome.**
LOD:	**Logarithm Of the Odds.**
MAOA:	**Monoamine Oxidase A.**
MeCP2:	**Methyl-CpG-Binding Protein.**
MEGDI:	**Mixed Epigenetic and Genetic and Mixed De novo and Inherited.**
MHC:	**Major Histocompatibility Complex.**
MHPG:	**3-Methoxy-4-Hydroxy-Phenylglycol.**
ms:	**Millisecond.**
MLS:	**Maximum LOD Score.**
MMR:	**Measles, Mumps, and Rubella.**
MMTV:	**Mouse Mammary Tumor Virus.**
MRI:	**Magnetic Resonance Imaging.**
MRS:	**Magnetic Resonance Spectroscopy.**
mtDNA:	**Mitochondrial DNA.**