Study of TGFβ1 in a sample of Egyptian Children with Autism Spectrum Disorder

Thesis

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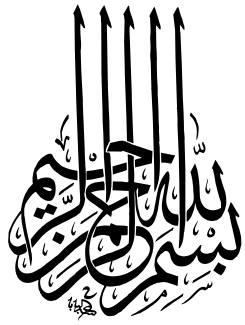

" قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا ﷺ
إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ "

سورة البقرة (آية ٣٢)

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List of Abbreviations

Abb.	Full Term
3di	Developmental, Dimensional and Diagnostic Interview
AAI	Animal-Assisted Therapy
ABA	Applied Behavior Analysis
ADHD	Attention deficit hyperactivity disorder
ADOS	Autism Diagnostic Observation Schedule
AEDs	Antiepileptic drugs
ALA	Alpha-linoleic acid
APA	American Psychiatric Association
APLS	Antiphospholipid Syndrome
ASDs	Autistic spectrum disorders
ATEC	Autism treatment evaluation checklist
ATX	Atomoxetine
BBB	Blood brain barrier
BMP	Bone morphogenetic proteins
CAM	Complementary and Alternative Medicine
cAMP	Cyclic adenosine monophosphate
CARS	Childhood autism rating scale
CARS2-HF	CARS2-High Functioning Version
CARS2-ST	CARS2-Standard Version
CBMNC	Cord blood mononuclear cell
CBT	Cognitive Behavioral Therapy
CC	Corpus Callosum
CDC	Center for Disease Control and prevention
CKIs	Cyclin-dependent kinase inhibitors
CMV	Cytomegalovirus
CNS	Central nervous system

CSF	Cerebrospinal fluid
DAT	Dopamine active transporter
DC	Dendritic cell
DDT	Dichlorodiphenyltrichloroethane

List of Abbreviations (Cont…)

Abb.	Full Term
DHA	Docosahexaenoic acid
DIR	Relationship-based model
DISCO	Diagnostic Interview for Social and Communicative Disorders
DNA	Deoxyribonucleic acid
DPT	Diphtheria, Tetanus, Pertussis Vaccine
DSM	Diagnostic and statistical manual of mental disorders
DSM-III-R	Diagnostic and statistical manual of mental disorders third edition-revised
DSM-IV	Diagnostic and statistical manual of mental disorders – fourth edition
DSMIV-TR	Diagnostic and statistical manual of mental disorders – fourth edition – text revision
DSM-V	Diagnostic and statistical manual of mental disorders – fifth edition
DT	Diphtheria and tetanus toxoidsVaccine
DTT	Discrete Trial Training
DUI	Daytime urinary incontinence
EAAT	Equine-assisted activities and therapies
EC	The endothelial cell
EEG	Electroencephalography
eg	For example
EIBI	Early Intensive Behavioral Intervention
ELISA	Enzyme-linked immunosorbent assay
EPA	Eisosapentaenoic acid
EPS	Extrapyramidal symptoms
ESDM	Early Start Denver Model
FDA	Food and Drug Administration
FI	Fecal incontinence
GABA	Gamma amino butyric acid
GARS 2	Gilliam Autism Rating Scale Second Edition

List of Abbreviations (Cont…)

Abb.	Full Term
GD	Gestational diabetes
GDF	Growth and differentiation factors
GFCF	Gluten free casein free
GI	Gastrointestinal
GIT	Gastrointestinal Tract
HAH	Halogenated Aaromatic Hy-drocarbons
HBOT	Hyperbaric oxygen therapy
IFN-ɣ	Interferon gamma
Ig	Immunoglobulines
IGF-1	Insulin-like growth factor
IL	Interleuken
IQ	Intelligent quotient
ITC	Infant Toddler Checklist
IU	International unit
ITP	Idiopathic thrombocytopenic purpura
LAP	latency associated peptide
lb	Pound
LEAP	Learning Experiences, An Alternative Program
LTBPs	Latent TGF-β binding proteins
mcg	Micrograms
M-CHAT-R	Modified Checklist for Autism in Toddlers-Revised
mg	milligram
miRNA	Micro RNA
MMR	Measles, Mmumps,Rrubella Vaccine
MPH	Methylphenidate
MR	Mental retardation
MRI	Magnetic resonance imaging
mRNA	Messenger ribonucleic acid
NAC	N-Acetylcysteine
nAChR	Nicotinic acetylcholine receptor
NE	Nocturnal enuresis

List of Abbreviations (Cont…)

Abb.	Full Term

NK	Natural killer
NO.	Number
NTFs	Neurotrophic factors
NREMS	Non-rapid eye movement sleep
OT	Occupational therapy
p	Probability of variance
PCP	Primary care pediatrician
PDD	Pervasive developmental disorders
PDD-NOS	Pervasive developmental disorders not otherwise specified
PECS	Picture Exchange Communication System
PET	Positron emission tomography
Pg/ml	Picograpm per meliliter
PGD	Pregestational diabetes
PIT	Parent implemented training
PM	Particulate matter
PPARγ	Peroxisome proliferator activated receptor gamma
PRT	Pivotal Response Training
PT	Parent training
PUFAs	Polyunsaturated fatty acids
RDI	Relationship Development Intervention
ROS	Relative Oxygen Species
RRB	Restrictive, Repetitive Behavior
SCD	Specific carbohydrate diet
SCI	Social communication and interaction
SD	Standard deviation
SGAs	Second generation antipsychotics
SI	Sensory Integration
SIB	Self-injurious behaviors
SP	Streptavidin-Peroxidase
SRS	Social Responsiveness Scale

List of Abbreviations (Cont…)

Abb.	Full Term
SSRIs	**Selective serotonin reuptake inhibitors**
TGFβ1	Transforming growth factor beta 1
Th	T helper cell
TLE	Temporal lobe epilepsy

TMS	Transcranial Magnetic Stimulation
TNF-α	Tumor necrosis factor alpha
TPN	Total parenteral nutrition
TPO	Thyroid disease with anti-thyroid peroxidase
TZDs	Thiazolidinediones
UCMSC	Umbilical cord-derived mesenchymal stem cells
US	United States
USA	United States of America
VBI	Verbal Behavior Intervention
VEGF	Vascular endothelial growth factor
VPA	Valporic acid
WHO	World Health Organization

Introduction

Autism spectrum disorders (ASDs) represent a group of neurodevelopmental disorders characterized by impairments in verbal and non-verbal communication, social withdrawal and stereotypical behaviors, which may or may not be associated with cognitive deficits, self-injurious behaviors and other neurological comorbidities ***(Salmi et al., 2013).***

A dramatic rise in incidence of ASDs has occurred in the past 25 years. ASD has a current estimated prevalence of about 1 in 68 children aged 8 years; estimated prevalence was significantly higher among boys (23.6 per 1000) than among girls (5.3 per 1000) ***(Christensen et al., 2016).*** The exact etiology of autism remains unknown, it is likely to result from a complex combination of genetic, immunological and environmental susceptibility ***(Cohen et al., 2005).***

There is growing awareness of an immunological involvement in children with ASD. Evidence of immune dysregulation has been observed in some individuals with ASD including increase levels of pro-inflammatory cytokines in brain tissue, CSF and plasma and increased production of pro-inflammatory cytokines by peripheral blood mononuclear cell culture when compared to typically developing control ***(Ashwood et al., 2008).***

Also, immunosuppressive cytokines are critical for immune homeostasis and transforming growth factor beta 1 (TGFβ1) is one of them and it is the most important immune regulator that can effectively control diverse aspects of the immune response. TGF-β1 is a multifunctional immunosuppressive cytokine and has pivotal neurodevelopmental functions with potential therapeutic effects ***(den Haan et al., 2007).***