Fragile X Mental Retardation 1 Gene and Metabolic Biomarkers in Autism and Fragile X Syndrome

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ABSTRACT

Fragile X is the most common single gene cause of autism, responsible for 2% to 6% of all cases of autism, Approximately 30% of males with FXS have full autism. Genes known to be causes of ASD interact with the translational pathway defective in FXS , and it has been hypothesized that there will be substantial overlap in molecular pathways and mechanisms of synaptic dysfunction between FXS and ASD. The present study aimed at detection of molecular and neurobiological similarities between FXS and ASD. Also it aimed at detection of certain metabolic biomarkers that could be specific to autism, Fragile X. The present study included 4 groups of subjects, 2 diseased groups (20 males patients with Autism and 20 males Fragile X syndrome) and 2 control groups (20 Normal healthy males controls and 20 Down Syndrome males patients). The present study concluded that low serotonin levels was exclusively and unique to autistic patients and it can be consider as a metabolic marker for autism. Also we found that autism and FXS share neurobiological similarities as GABA was significantly high in both disorders than normal control children , meanwhile it was specific to Autism and Fragile X Syndrome as GABA level was not high in D.S. On the contrary Down Syndrome showed lower (non significant) GABA levels than normal healthy children. Regarding Glutamate, it was high in the 3 disorders but with the highest levels in Autism followed by Fragile X and Down Syndrome, respectively. The present study didn't find a significant difference between autism and controls regarding CGG repeats numbers.

Key words:

Autism

Fragile X

GABA –Serotonin- Glutamate

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List of Abbreviations

ABC	Autism Behavior Checklist
ABA	Applied Behavior Analysis
ACC	Anterior Cingulate Cortex
ACh	Acetylcholine
Ach E	Acetylcholine Esterase
AGC1	Aspartate/Glutamate carrier
AMPA	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
ADHD	Attention Deficit Hyperactive Disorder
ADI-R	Autism Diagnostic Interview, Revised
ADOS	Autism Diagnostic Observation Schedule
APA	American Psychiatric Association
AD	Autistic Disorder
ASDs	Autism Spectrum Disorders
AS P	Aspargine
CO	Carbon Monoxide
CHAT	Checklist for Autism in Toddlers
CARS	Childhood Autism Rating Scale
CDD	Childhood Disintegrative Disorder
CSN	Children with Special Needs
CY-BOCS	Children's Yale-Brown Obsessive Compulsive

	Scale
CAM	Complementary and Alternative Medical
CGH	Comparative Genomic Hybridization
CNTNAP2	Contactin-Associated protein-like 2
CNV	Copy Number Variation
CYFIP1	Cytoplasmic *FMR1* Interacting Protein
DAN	Defeat Autism Now
DHCR7	Dehydrocholesterol Reductase
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition
DA	Dopamine
D.S	Down Syndrome
ESI	Electro Spray Ionization
ECD	Electrochemical Detection
EN2	Engrailed 2 Gene
ELISA	Enzyme-linked Immunosorbent Assay
EDTA	Ethylenediaminetetraacetic Acid
ERPs	Event Related Potentials
EAAT 1	Excitatory Amino Acid Transporter 1
FISH	Fluorescent In-situ Hybridization

FMR	Fragile X Mental Retardation
FMRP	Fragile X mental Retardation Protein
FX DNA	Fragile X DNA
FXS	Fragile X syndrome
FXTAS	Fragile X-Associated Tremor Ataxia Syndrome
GABA	Gama Aminobutyric acid
GABA-T	GABA-Transaminase
GC/MS	Gas Chromatography/ Mass Spectrometry
GIS	Gastrointestinal Symptoms
GWA	Genome wide Association
GLN	Glutamine
GLU	Glutamic
GluR6	Glutamate Receptor 6
GAD	Glutamic Acid Decarboxylase
GF/CF diet	Gluten- and Casein-free
HPLC	High Performance Liquid Chromatography
HFA	High-Functioning Autism
HIAA	Hydroxyindoleacetic Acid
5-HTP	5-Hydroxytryptophan

ID	Intellectual Disability
IQ	Intelligence Quotient
ICD-10	International Classification of Diseases, Tenth
KO mouse	knockout Mouse
LTD	Long Term Depression
LTP	Long-Term Potentiation
MECP	Methyl –CPG-binding protein 2
MEG	Magnetoencephalography
m TOR	Mammalian Target of Rapamycin
MS/MS	Mass Spectrometry/ Mass Spectrometry
MMR	Measle, Mumps, Rubella Vaccine
MR	Mental Retardation
mGluR5	Metabotropic Glutamate Receptor 5 Pathway
M-CHAT	Modified Checklist for Autism in Toddlers
MAO	Monoamine Oxidase
MPEP	2-methyl-6-(phenylethynyl)-pyridine
MBP	Myelin Basic Protein
NA	Noradrenaline
NF1	Neurofibromatosis Type 1
NO	Nitric Oxide
NMDA	N methyl D Aspartate

OAS	Overt Aggression Scale
OT	Occupational Therapy
OXTR	Oxytocin receptor gene
PI3 Kinase	Phosphatidyl Inositol Kinase
PPARg	Peroxisome Proliferator-Activated Receptors Gamma
PDD-NOS	Pervasive Developmental Disorder Not Otherwise Specified
PDDST	Pervasive Developmental Disorder Screening Test
PDDs	Pervasive Developmental Disorders
PKU	Phenylketonuria
PTEN	Phosphatase and Tensin Gene
PSL	Platelet Serotonin Levels
PPP	Platelet-Poor Plasma
PCR	Polymerase Chain Reaction
PWP	Prader-Willi Phenotype
PPI	Prepulse Inhibition
PCPs	Primary Care Practitioners
POI	Primary Ovarian Insufficiency
PLP	Pyridoxal Phosphate
RELN	Reelin Gene

R S	Rett Syndrome
SAD	Seasonal Affective Disorder
SIDS	Sudden Infant Death Syndrome
SSA	Succinic Semialdehyde
SSRIs	Selective Serotonin Reuptake Inhibitors
SE, 5-HT	Serotonin
SERT	Serotonin Transporter
SNP	Single Nucleotide Polymorphism
SPECT	Single Photon Emission Computed Tomography
SLO	Smith–Lemli–Opitz Syndrome
SCQ	Social Communication Questionnaire
SCID	Structured Clinical Interview for the DSM-IV
TBE	Tris/Borate/EDTA
TEACCH	Treatment and Education of Autistic and Related Communication Handicapped Children
TCA	Trichloroacetic Acid
TSC	Tuberous Sclerosis
UPD	Uniparental Disomy
UTR	Untranslated Region