بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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MONA MAGHRABY

NMDA (N-Methyl D- Aspartate) Receptor Antibody in Relation to ASD (Autism Spectrum Disorder): Presence and Association with Symptom Profile

Thesis

Submitted for Partial Fulfilment of

PhD Degree in ***Psychiatry***

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Mohammad Abdullah ElshieKh

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Abb.	Full term
ADHD	Attention-deficit and hyperactivity disorder
ADOS-2	Autism diagnostic observation schedule-2nd edition
ANA	anti-nuclear antibody
ASD	Autism spectrum disorder.
BDNF	Brain derived neurotrophic factor.
COVID	Corona virus disease-19
DNA	Deoxyribonucleic acid
DSM5	Diagnostic and statistical manual, 5th edition
EEG	Electroencephalogram.
ELISA	Enzyme-linked immunosorbent assay
ESR	Erythrocyte sedimentation rate
GARS	Gilliam Autism rating scale
HS	Highly significant
IQR	Interquartile range
MBP	Myelin basic protein
NMDA	N-Methyl-D- Aspartate.
NMDAR	N-Methyl-D-Aspartate Receptor.
NS	Nonsignificant
PC	personal computer
Pg	pico gram
RPM	Rotation per minute
S	Significant
SD	Standard deviation
SPSS	Statistical package for Social Science

INTRODUCTION

Autistic disorder is a pervasive developmental disorder characterized by impairment in communication and reciprocal social interaction, as well as stereotypic/repetitive behaviours. Causes of autism remain elusive, yet clearly combine genetic, developmental, and environmental factors ***(Belmonte et al., 2004).***

In addition to these core symptoms, there are few other behaviour disturbances which are commonly seen in the autistic individuals, such as anxiety, depression, sleeping and eating disturbances, attention issues, temper tantrums, and aggression or self-injury ***(Yang et al., 2011).***

A review of global prevalence of ADS by ***Elsabbagh et al. (2012)*** reported a median of 62 cases per 10,000 people with average 4.3:1 male-to-female ratio. There is a lack of evidence from low- and middle income countries.

Prevalence of autism spectrum disorders among children with developmental disorders in Egypt was documented to be 33.6 % ***(Seif el din et al., 2008),*** although no prevalence studies was found to point out prevalence of autism spectrum disorders in general population ***(Nagwa, 2015).***

Several neurobiological models have been proposed including the existence of a glutamatergic dysfunction

(Rubenstein et al., 2003) and excessive oxidative stress ***(Kern et al., 2003)*** to find a possible model of autism etiology.

Because there is no completely effective treatment for autism at present, many researchers are trying to find novel therapeutic agents based on the neurobiological defects underlying autism spectrum disorders (ASD) ***(Kumar et al., 2012).***

Given the apparent etiologic heterogeneity of autism, it is possible that different interventions will be efficacious in different autistic subgroups. Interventions related to molecules or processes demonstrating clear developmental differences in autism as compared to typical development may be particularly effective. However, it is also possible that the developmental periods when such interventions would have been effective will have ended prior to diagnosis of autism ***(Terrence and Linmarie, 2007).***

Atypical features – which may suggest an alternative diagnosis and warrant further investigations to exclude both congenital and acquired causes – include severe learning difficulties, the presence of an early onset epileptic syndrome, or an associated movement disorder. The onset of symptoms outside the usual age, or a sudden acute onset of autism with or without fluctuation of symptoms, would also point to an alternative diagnosis ***(Hacohen et al., 2016).***

Several studies have suggested that abnormalities in GABAergic and glutamatergic transmission contribute to the development of autism spectrum disorders ***(Mori et al., 2012; Chez et al., 2007).***

Glutamate is the predominant excitatory neurotransmitter in the brain and comprises about half of all synapses in the forebrain ***(Herlenius and Lagercrantz 2004).*** There are three families of ionotropic receptors with intrinsic cation permeable channels [N-methyl-D-aspartate (NMDA), a-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) and kainate].

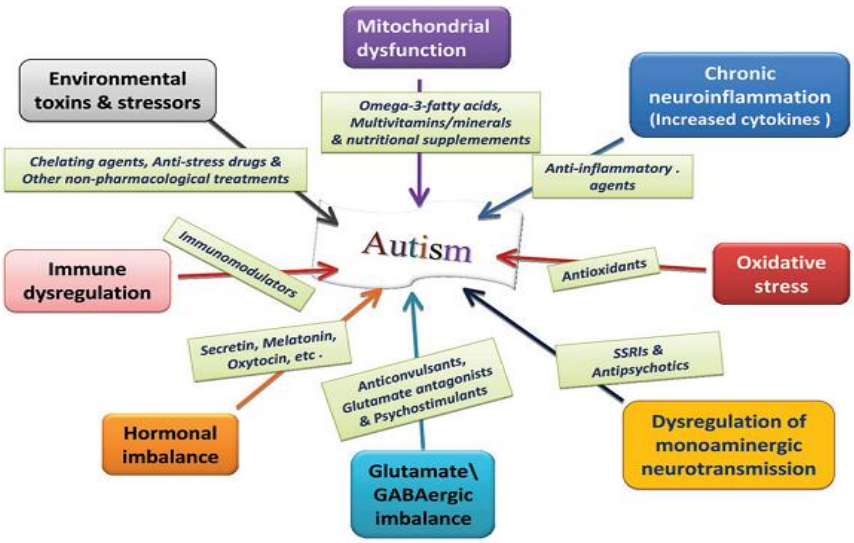

Figure 1: Summarization of different postulated theories of etiology of ASD and possible interventions ***(Terrence and Linmarie, 2007).***

There are three groups of metabotropic, G protein–coupled glutamate receptors (mGluR) that modify neuronal and glial excitability through G protein subunits acting on membrane ion