

Screening of vitamin B12 in children diagnosed as Autism Spectrum Disorder

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List of Abbreviations

ABR	Auditory brain stem response
AD	Attention deficit
ADHD	Attention-deficit hyperactivity disorder
AdoCbl	Adenosylcobalamin
aCGH	Array comparative genomic hybridization
ASD	Autism spectrum disorder
CARS	Childhood Autism Rating Scale
Cbl	Cobalamin
CNCbl	Decyanation of cyanocobalamin
CNV	Copy number variants
DNA	Deoxyribonucleic acid
DSM	Diagnostic and Statistical Manual of Mental Disorders (5 th edition)
EPA	Environmental Protection Agency
GSH	Glutathione
HCY	Homocysteine
IQ	Intelligence quotient
MeCbl	Methylcobalamin
MMACHC	Methylmalonic aciduria type C and homocystinuria
MMR	Mumps, Missiles and Rubella
mRNA	Messenger Ribonucleic acid
MPS	Mucopolysaccharidosis
MS	Methionine synthase
NADPH	Nicotinamide adenine dinucleotide phosphate
PDDs	Pervasive developmental disorders
PDD-NOS	Pervasive developmental disorder not otherwise specified
SAH	S adenosylhomocysteine
SAM	S adenosylmethionine
SLI	Specific language impairment
TC	Transcobalamin

Introduction

Autism spectrum disorder (ASD) is a pervasive developmental disorder, defined by impairments in social and communication function, repetitive and stereotyped behavioral patterns (*American Psychiatric Association 2013*).

Autism spectrum disorders characterize a heterogeneous group of neurodevelopmental disorders, including autism, Asperger syndrome, Rett's disorder, childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified, and are characterized by social and communication deficits accompanied by repetitive and stereotype actions (behaviors), with onset before 3 years of age (*Caglayan, 2010*).

It appears that genetic predisposition plays a main role in the etiology of autism although environmental influences are also implicated. Heritability contributes about 90% of the risk of a child developing autism, but the heritability of autism is complex and typically it is unclear which genetic factor are responsible (*Freitag, 2007*).

The signs usually develop gradually, but some autistic children first develop more normally and then regress. Diagnosis is made subjectively and based on a cluster of performances observed clinically as there is currently no laboratory test to diagnose autism (*Ratajczak, 2011*).

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-IV) outlines criteria for the diagnosis of attention deficit (AD) and related Pervasive developmental disorders (PDDs) (*Ratajczak, 2011*).

Vitamin B12 is necessary for cell formation, proper digestion, absorption of foods, protein synthesis, and metabolism of carbohydrates and fats. Vitamin B12 deficiency is most often due to a defect in absorption and not dietary lack except in strict vegetarians, since it is only available from animal sources. Deficiency is common in those with digestive disorders, and is present in almost all ASD children (*Jaquelyn et al., 2002*).

Cobalamin (vitamin B₁₂) deficiency is a simply treated disorder that often goes undiagnosed in newborns and children, placing them at high risk for irreversible brain injury. It is well documented that B₁₂ deficiency can cause developmental delay, hypotonia, tremor, seizures, failure to thrive, reduced intelligence quotient (IQ), and mental retardation. Children with B₁₂ deficiency exhibit language, and social delays, behavioral issues, and problems with fine and gross motor movement (*Sally and Pacholok, 2014*).

Vitamin B12 (cobalamin, Cbl) exists in multiple forms, including methylcobalamin (MeCbl) and adenosylcobalamin (AdoCbl), serving as cofactors for MS and methylmalonylCoA mutase, respectively (*Yiting et al., 2016*).

Lack of vitamin B12 in the maternal diet during pregnancy has been revealed to cause severe retardation of myelination in the nervous system. (*Lovblad et al., 1997*).

Aim of the work

The aim of this work to investigate level of vitamin B₁₂ in ASD children in an attempt to reach such etiological factor and to be incorporated in management if proved.

Autism

A neurodevelopmental disorder, it characterized by an impairment of the growth and development of the brain or central nervous system. A narrower use of the term refers to a disorder of brain function that affects emotion, learning ability and memory and that unfolds as the individual grows. The term is sometimes erroneously used as an exclusive synonym for autism and autism spectrum disorders. Autism affects information processing in the brain by altering how nerve cells and their synapses connect and organize; how this occurs is not well understood (*Levy et al., 2009*).

The term “Autism” was first defined in 1911 by the Swiss psychiatrist Eugen Bleuler (1857—1939) (*Gillberg and Coleman, 2000*) as extreme withdrawal from outside into the self-associated with schizophrenia. Then in 1943, the American psychiatrist Kanner described autism as a psychiatric developmental condition in which there is a combination of social isolation, language expression difficulty and unusual behavioral action in children. In 1980, the third edition of the Diagnostic and Statistical Manual of Mental Disorders, known as DSM-III, was published by the American Psychiatric Association: in which, the term 'pervasive developmental disorder' was used for the general category of autism and related conditions (*APA, 1980*). Parents usually notice signs in the first year of their child's life (*Landa, 2008*).

These delays or atypicality in social development, communication, neurocognition, and behavior vary in severity of symptoms, age of onset, and association with other childhood disorders (*National Research Council, 2001*). The Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association) and the 10th edition of the International Classification of Diseases World Health Organization [WHO] list categories of pervasive developmental disorders (PDD) which include autism and four other associated disorders (*WHO, 1993*) (*APA, 2000*).

The five pervasive developmental disorders are (*Wilkinson and Lee., 2010*):

- 1) autistic disorder.
- 2) Asperger's disorder.
- 3) Rett's disorder.
- 4) Childhood disintegrative disorder.
- 5) Pervasive developmental disorder not otherwise specified (PDD-NOS).

Autism affects individuals throughout the world. There is international and cross-disciplinary agreement on the primary characteristics and validity of autism as a diagnostic category. In fact, there is no other developmental disorder for which internationally accepted criteria exist (*Volkmar, 2005*). Autistic disorder is the clinical term for what is frequently called autism. First described by Leo Kanner over 60 years ago, autism is the most common and typical of the ASD/PDD subtypes. It is generally described as a developmental disorder of neurobiological origin defined on the basis of behavioral and developmental features.