European Journal of Neurodegenerative Diseases
ISSN 2279-5855 / 2021

AUTISM SPECTRUM DISORDER – NEW FRONTIERS

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KEYWORDS: *autism, brain, disability, developmental disorder, ASD*

INTRODUCTION

Autism spectrum disorder (ASD) is defined by the Centers for Disease Control and Prevention as "a developmental disability caused by differences in the brain" (1). ASD is heterogeneous, highly heritable, and can co-occur with other conditions (2). It includes autistic, pervasive developmental and Asperger's disorders and the category was created for containing a broad spectrum of social communication deficits.

ASD is frequently diagnosed in early childhood and is a common neurodevelopmental disorder. Over the past 20 years, the rates of diagnosis have increased drastically, with the modern prevalence rate in diagnosed children between 1.5%-2% (3)(4). ASD is more frequent in males, with a ratio of 4 boys to every affected girl (5)(6).

The disorder manifests with dysfunctional social communication and interaction, repetitive behaviors, attention, cognitive, learning, and sensory defects (7). There can be varying levels of intellectual disability. Psychiatric and neurological disorders can often occur with ASD and include anxiety, depression, epilepsy, and attention-deficit/hyperactivity disorder (ADHD).

ASD is a developmental disorder, with the onset of symptoms in the first three years of life. In some cases, symptoms are apparent within a child's first year of life, while in others, development can be normal and then switch to delay in the acquisition of new skills or their loss (7). Diagnosis is based on behavioral and developmental presentation, with clinical specifiers such as language, intelligence, comorbidity, and support taken into consideration. A reliable diagnosis can be made by the age of two years old. Early intervention is critical to enhancing communication skills.

Risk factors

Those who have a family history of ASD, have older parents, were born at very low birth weight, or have particular genetic conditions such as Down or Fragile X syndrome, have a higher risk of ASD (8). In the majority of ASD cases, the exact etiology is unknown, although development may be affected by the combination of genetics and environmental aspects acting together (9). Recent twin studies have suggested 40-50% variance of environmental factors in ASD (10-12).

Prenatal, natal, and postnatal environmental risk factors have been identified, although they are not causal, being considered reactive or contributory at best (2)(13). Advanced parental age, small gestational age, pregnancy and birth complications, gestational diabetes mellitus, and the use of valproate during pregnancy are some of these risk factors.

Inflammation

Received: 24 March, 2021
Accepted: 04 June, 2021

2279-5855 (2021)

Disclosure: all authors report no conflicts of interest relevant to this article.

So far, the pathogenesis of ASD is unknown, but it is hypothesized that some immune and autoimmune inflammatory diseases are involved. We recently reported that in children with ASD there is a presence of immune dysfunction and inflammation in the brain (14). In fact, we found that the anti-inflammatory cytokine IL-37, and pro-inflammatory cytokines IL-18 and TNF, are increased in the amygdala and dorsal lateral prefrontal cortex of children with ASD, demonstrating that inflammation is important in this disease (14). In addition, IL-37 inhibits neurotensin, stimulated secretion and gene expression of IL-1β and cytokine CXCL8.

The elevation of IL-37 in the brain of ASD could signify a defensive strategy for fighting the pro-inflammatory IL-1 family members which are potent mediators of inflammation and are harmful to the brain.

Genetics

Genetics have a strong influence on ASD, with a 50% risk for development (15), and a wide range of genetic variation is involved. The most common genetic abnormalities are synaptic gene mutations (16)(17), which are also seen in other neuropsychiatric disorders (18). Mutations reported in synaptic genes include neurexin (NRXN) families, neuroligins (NLGN), SH3 and multiple ankyrin repeat domains (SHANK), and contactin-associated protein-like 2 (CNTNAP2) (19) and indicate that ASD may result from synaptic plasticity abnormalities.

CONCLUSION

Different neurodevelopmental disorder theories have been proposed to explain the pathophysiology of autism, for example, the theory of mind and social motivational deficit theories, and are helpful for clinicians and cognitive behavioral therapy (2). It is believed that different causes of ASD act together to affect a person's development (1). MRI studies seem to show the disruption of neural pathways in the brains of children before behavioral symptoms are presented (20)(21).

Early developmental and behavioral intervention is important in ASD to improve impairments in social communication and interaction. Some approaches include parent-mediated interventions and the Early Start Denver Model, an intensive therapist-guided intervention that instructs parents on the usage of beneficial modes of communication and interaction. Therapy continues with school-based strategies and then aims to promote independence in adults with ASD. Medication is primarily used to treat associated symptoms such as agitation and irritability, and the common mental health conditions that accompany ASD, such as ADHD.

Quality of life (QoL) has been reported as lower in adults with ASD when compared to the general population (22). Being female, having a co-current mental health condition, and experiencing severe autism symptoms tend to lower QoL, while employment, relationships, and support tend to raise QoL (23).

Autism research continues to evolve with genetic and neurobiology studies, as the numbers of diagnosed children have risen steadily over the last two decades, increasing from a diagnosis of 1 in 150 children in 2000 to 1 in 44 children at present. This drastic rise in numbers most likely stems from an increase in awareness and diagnoses of ASD.

Currently, there is no therapy for ASD and new research is needed to further our understanding of the disease and improve the QoL for patients.

Conflict of interest

The authors declare that they have no conflict of interest.

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