Immune System Dysregulation and Its Potential Role in Autism Spectrum Disorder (ASD)

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Abstract:

The complex neurological disorder known as autism spectrum disorder (ASD) is typified by repetitive behaviors, limited interests, and difficulties with social communication. There is growing evidence that the pathophysiology of ASD is significantly influenced by immune system dysfunction. These include autoimmune, cytokine imbalance, neuroinflammation, microglial activation, maternal immune activation (MIA), and disruptions of the gut flora. According to research, people with ASD have malfunctioning microglia, high levels of pro-inflammatory cytokines (IL-6, TNF-α, and IFN-γ), and autoantibodies that target brain proteins, all of which may be linked to aberrant neurodevelopment. Furthermore, because inflammatory reactions can impair fetal brain development, maternal immune activity during pregnancy has been associated with a higher incidence of ASD in offspring. Another important consideration is the gut-brain axis; symbiosis in people with ASD may exacerbate systemic inflammation and change the synthesis of neurotransmitters. In light of these findings, a number of therapeutic approaches are being investigated to lessen immune-related dysfunctions in ASD, including probiotics, dietary changes, immunomodulatory therapy (such as IVIG), and anti-inflammatory medications. To enhance patient outcomes, further research is required to clarify the processes driving immune system dysregulation in ASD and create focused treatment strategies

Keywords: Immune Dysregulation, Autism, nervous system, microglial dysfunction

Introduction:

Immune Dysregulation and Comorbidities with High Incidence in ASD. Among the current findings in ASD, studies underline the coexistence of immune-mediated comorbidities that could predispose one to later-life autoimmunity linked to more aberrant behavioral conditions and the incidence of a major disease severity.

The complex neurodevelopmental disorder known as autism spectrum disorder (ASD) is typified by repetitive behaviors, communication problems, and social interaction deficits. Although the precise cause of ASD is still unknown, new research indicates that immune system dysregulation may be a major factor in the pathophysiology of the disorder. People with ASD have been found to have immunological abnormalities, such as autoimmunity, cytokine imbalances, maternal immune activation, and chronic neuroinflammation. These findings suggest a potential connection between immune dysfunction and aberrant brain development.

Through processes including synaptic pruning, neuronal signaling, and inflammatory responses, the immune system and the central nervous system (CNS) are intimately related and have an impact on neurodevelopment. Immune dysregulation-induced disruptions in these systems could be a factor in the behavioral and cognitive symptoms of ASD. Furthermore, during pregnancy, maternal immune activation (MIA) is brought on by An elevated risk of ASD in offspring has been linked to infections or autoimmune disorders. ASD is characterized by disrupted neuronal connections, which may be caused by microglial dysfunction and increased pro-inflammatory cytokine activity.

Gaining insight into how immune system dysregulation contributes to ASD may pave the way for more focused therapy interventions and early identification. Novel approaches to treating the symptoms of ASD may be provided by examining gut-brain axis interactions, immunological biomarkers, and inflammatory response modulation. Investigating the causes behind immunological dysregulation in ASD, emphasizing its probable effects on neurodevelopment, and identifying novel immunomodulatory treatments are the goals of this study.

In Autism Spectrum Disorder (ASD), microglial activation and neuroinflammation

It is becoming more well acknowledged that neuroinflammation plays a significant role in the pathophysiology of autism spectrum disorder (ASD). Activation of microglia and astrocytes, two glial cell types that are essential for immunological defense, synaptic pruning, and neuronal maintenance, is one of the primary causes of neuroinflammation. According to research, people with ASD frequently display aberrant activation of these cells, which might cause abnormalities in normal neurodevelopmental processes. (1)

Activation and Dysfunction of Microglia in ASD

The central nervous system's (CNS) main immune cells are called microglia. By removing cellular trash, controlling synaptic connections, and reacting to infections, they serve as the brain's first line of defense. However, microglia frequently exhibit a deregulated or hyper activated state in ASD, which can lead to disrupted neural connections and persistent inflammation. Research looking at postmortem brain tissue from people with ASD has discovered:

increased microglial density and activity in the cerebellum and prefrontal cortex, two areas of the brain linked to social and cognitive functioning.

Prolonged inflammation and neuronal injury are caused by elevated levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ). (2)

altered microglial morphology, which can disrupt normal brain growth and indicates excessive or extended activation.

Additionally, microglia play a role in synaptic pruning, a critical process in the early stages of brain development that optimizes neuronal circuits by removing superfluous synapses. The aberrant brain connections seen in ASD may result from disruptions in this mechanism caused by either hyperactive or underactive microglia. Some of the sensory, social, and cognitive challenges observed in ASD may be caused by either an excess or a lack of neural connections, which could be a result of an imbalance in synaptic pruning.

ASD and Astrocyte Dysfunction

Another kind of glial cell that supports neuronal activity, preserves the blood-brain barrier, and controls neurotransmitter balance are astrocytes. Astrocytes in people with ASD also exhibit dysfunctional characteristics, such as:

elevated neuroinflammatory state as a result of increased inflammatory chemical synthesis. (3)

diminished capacity to sustain neurons, which has an impact on synaptic plasticity and neuronal repair.

ASD-related cognitive and behavioral symptoms have been linked to altered glutamate control, which results in excitotoxicity (excessive neuronal excitement).

Neuroinflammation Effects on ASD

Targeting neuroinflammatory pathways may be a viable treatment approach given the existence of persistent neuroinflammation and glial cell dysfunction in ASD. Among the potential interventions are:

Anti-inflammatory treatments that may lessen excessive microglial activation include cytokine inhibitors and no steroidal anti-inflammatory medications (NSAIDs).

Intravenous immunoglobulin (IVIG) therapy is one example of an immunomodulatory medication that attempts to restore immunological equilibrium. (4)

Focusing on the gut-brain axis, probiotics and dietary therapies may help reduce neuroinflammatory effects because gut bacteria affect immune responses and microglial function.

In autism spectrum disorder (ASD), cytokine imbalance

Signaling proteins called cytokines control inflammation, immunological responses, and intercellular communication. They are essential for synaptic plasticity, neuroprotection, and brain development. But more and more data points to a cytokine imbalance in people with autism spectrum disorder (ASD), especially an increase in pro-inflammatory cytokines including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ). ASD's abnormal neurodevelopment and behavioral symptoms may be exacerbated by this instability.

Cytokine imbalance evidence in ASD

Significant cytokine abnormalities have been found in studies examining the cerebrospinal fluid (CSF), blood plasma, and postmortem brain tissue of people with ASD. These abnormalities include:

A prolonged inflammatory state in the brain and body is suggested by elevated levels of pro-inflammatory cytokines, such as IL-6, TNF-α, IFN-γ, and IL-1β.

An imbalance between pro-inflammatory and regulatory immune responses results from changes in the amounts of anti-inflammatory cytokines (such as TGF-β and IL-10). (5)

increased cytokine levels in the brain areas linked to social behavior, communication, and sensory processing—the amygdala, cerebral cortex, and cerebellum.

A chronic inflammatory state that may impact brain function and connection in ASD is indicated by this dysregulation of cytokines.

Pro-inflammatory cytokines' effects on neurodevelopment

1. Interference with Synaptic Plasticity and Function

Cytokines affect neuroplasticity, neurotransmitter release, and synaptic pruning. Unbalanced cytokine levels can interfere with these processes:

Overexpression of TNF-α and IL-6 might cause excessive synaptic pruning, which may decrease neuronal connection in areas of the brain related to cognition and social communication. (6)

Neurotransmitter systems like dopamine, serotonin, and glutamate—which are essential for mood regulation and learning—may be hampered by IFN-γ dysregulation.

Long-term potentiation (LTP), a process crucial to memory and learning, can be hampered by elevated cytokines.

2. Effect on Brain Structure and Neural Circuitry

ASD is frequently characterized by aberrant brain connections, which has been connected to cytokine imbalance. Cytokines that promote inflammation can:

have an impact on white matter tract development, which impairs connectivity between various brain regions.

Modify neuronal migration and differentiation, two processes essential to healthy brain structure.

Increased excitotoxicity and oxidative stress can harm neurons and interfere with neurological processes. (7)

3. The Development of the Fetal Brain and Maternal Immune Activation (MIA)

The developing fetus may be exposed to increased cytokines during pregnancy due to immune system activation or maternal illnesses. This disorder, called maternal immune activation (MIA), has been linked to a higher chance of ASD in children.

By changing neurogenesis and synapse formation, elevated levels of IL-6 and TNF-α during pregnancy can impair the development of the foetus' brain.

Pregnant mice who have experimentally induced MIA exhibit repetitive behaviors and impaired social interactions, among other ASD-like traits, according to animal research.

According to certain epidemiological research, a higher prevalence of ASD in offspring is associated with maternal bacterial or viral illnesses during pregnancy. (8)

Possible Therapeutic Consequences

Researchers are looking into immune-modulating therapies as possible therapy approaches because of the role that cytokine imbalance plays in ASD:

Anti-inflammatory Drugs

Ibuprofen is one example of a no steroidal anti-inflammatory medicine (NSAID) that may help lower inflammation.

Studies are being conducted to examine the possible neuroprotective effects of cytokine inhibitors, such as anti-IL-6 antibodies.

Immunomodulatory Treatments

In certain cases of ASD, intravenous immunoglobulin (IVIG) therapy has demonstrated promise in lowering inflammation and enhancing behavioural signs.

The potential of stem cell therapy to control immunological responses and stimulate neurogenesis is being investigated. (9)

Interventions for the Gut Micro biome and Diet

By altering the gut micro biota, probiotics and prebiotics may aid in the regulation of cytokine levels.

Systemic inflammation may be lessened by anti-inflammatory diets high in antioxidants and omega-3 fatty acids.

Maternal Immune Activation (MIA) and Its Role in Autism Spectrum Disorder (ASD)

Maternal Immune Activation (MIA) refers to the activation of a pregnant mother's immune system in response to infections, autoimmune conditions, or environmental factors such as stress and inflammation. During pregnancy, the maternal immune system plays a critical role in supporting fetal development, but excessive or deregulated immune responses can have long-term consequences on fetal brain development. (10)

A growing body of research suggests that MIA is a significant risk factor for Autism Spectrum Disorder (ASD). Studies have found that exposure to infections, pro-inflammatory cytokines, or maternal antibodies during pregnancy may alter neurodevelopmental processes, increasing the likelihood of ASD-related behaviors in offspring.

Mechanisms of MIA and Its Effects on Fetal Brain Development

MIA can disrupt fetal brain development through several mechanisms, primarily involving inflammatory cytokines, microglial activation, and synaptic alterations.

1. Pro-Inflammatory Cytokines and Neurodevelopmental Disruptions

When the maternal immune system is activated, it releases pro-inflammatory cytokines such as:

Interleukin-6 (IL-6)

Tumor Necrosis Factor-alpha (TNF-α)

Interleukin-1 beta (IL-1β)

Interferon-gamma (IFN-γ)

These cytokines can cross the placenta and enter the fetal brain, disrupting critical developmental processes:

IL-6 elevation has been directly linked to altered neuronal differentiation and connectivity in the fetal brain.

TNF-α and IL-1β contribute to excessive neuroinflammation, which can lead to abnormal synaptic pruning and altered neurotransmitter function. (11)

IFN-γ affects the development of inhibitory neurons, potentially contributing to ASD-like hyper connectivity patterns in the brain.

2. Microglial Activation and Synaptic Pruning

Microglia, the brain's resident immune cells, play a key role in synaptic pruning, which ensures proper neural connectivity. When MIA occurs:

Microglia become over activated, leading to excessive synaptic elimination.

This excessive pruning may result in weakened neuronal networks, which are often observed in ASD. (12)

Alternatively, some studies suggest that MIA may cause under-pruning, leading to hyper connectivity, which is associated with sensory sensitivities and cognitive dysfunction in ASD.

3. Disruption of Excitatory and Inhibitory Balance in the Brain

MIA can lead to altered neurotransmitter levels, including glutamate (excitatory) and GABA (inhibitory) imbalance.

This imbalance is a common feature in ASD and is associated with difficulties in sensory processing, communication, and social interaction.

Evidence from Animal Studies on MIA and ASD

Animal models have provided strong evidence that MIA can cause ASD-like behaviors in offspring:

Mouse models: Pregnant mice injected with viral or bacterial mimics (such as poly(I:C) or lipopolysaccharide) produced offspring with impaired social behavior, repetitive behaviors, and altered communication, mimicking ASD symptoms. (13)

Non-human primate studies: Studies on monkeys exposed to maternal inflammation showed deficits in social interaction and abnormal brain connectivity, similar to findings in human ASD cases.
Cytokine-blocking studies: When IL-6 was inhibited in MIA-exposed mice, ASD-like behaviors were significantly reduced, confirming its critical role in ASD development.
These studies suggest that elevated maternal immune activity during pregnancy can lead to long-lasting neurodevelopmental changes in offspring.

Human Evidence Linking MIA to ASD

Epidemiological studies have found correlations between MIA and ASD in humans:

Maternal Infections and ASD Risk
Viral and bacterial infections during pregnancy (such as influenza, rubella, and COVID-19) are associated with a higher prevalence of ASD in children.
Studies have shown that first-trimester infections may be particularly harmful to fetal brain development. (14)

Autoimmune Disorders and ASD Risk

Mothers with autoimmune conditions such as rheumatoid arthritis, lupus, and Type 1 diabetes have a higher likelihood of having children with ASD.
The presence of maternal autoantibodies targeting fetal brain proteins has been linked to altered neurodevelopment and autism-like traits.

Maternal Inflammatory Biomarkers and ASD

Increased levels of C-reactive protein (CRP), an inflammatory marker, have been detected in pregnant women who later give birth to children with ASD.
Elevated IL-6 and TNF-α in maternal blood samples have also been associated with a higher risk of ASD diagnosis in children.
Potential Therapeutic Strategies to Mitigate MIA Effects
Given the evidence linking MIA to ASD, researchers are exploring strategies to reduce maternal inflammation and protect fetal neurodevelopment:

1. Anti-Inflammatory Therapies

Omega-3 fatty acids: These have anti-inflammatory properties and may help modulate maternal immune responses.
Aspirin and NSAIDs: Some studies suggest that low-dose aspirin use during pregnancy may reduce inflammation-related risks. (15)
Cytokine inhibitors: Blocking IL-6 and TNF-α pathways may be a potential therapeutic approach, though more research is needed.

2. Immunomodulatory Interventions

Intravenous Immunoglobulin (IVIG) therapy: Being investigated as a treatment to modulate maternal immune activity.

Probiotics and micro biome-targeted therapies: Since gut micro biota influence maternal immune function, probiotic supplementation may reduce inflammation.

3. Prenatal Screening and Monitoring

Regular monitoring of inflammatory markers during pregnancy may help identify high-risk pregnancies where maternal immune activation is a concern.

Early interventions such as anti-inflammatory diets and stress reduction techniques may reduce the risk of excessive immune activation. (16)

Immune dysfunction and autoimmunity in autism spectrum disorder (ASD)

According to new research, autism spectrum disorder (ASD) may be significantly influenced by immunological abnormalities and autoimmune processes. Autoantibodies against neural proteins are present in some people with ASD, which may interfere with normal brain growth and function. ASD-related symptoms may also be exacerbated by broader immunological dysregulation, which is indicated by anomalies in T-cell and B-cell activity. These results imply that ASD might include immune system dysregulation that impacts brain function in addition to neurodevelopmental abnormalities.

1. Autoimmune Responses to Neural Proteins in Autism

Immune proteins called autoantibodies unintentionally attack the body's own tissues, including brain cells. According to research, some people with ASD have autoantibodies that react with brain proteins, which may indicate that the disease has an autoimmune component. (17)

Autoantibody Evidence in ASD

Mothers of children with ASD have been found to have higher levels of maternal autoantibodies that target proteins in the fetal brain. These antibodies have the potential to disrupt fetal brain development by crossing the placenta.

Blood samples from people with ASD have been shown to include autoantibodies against particular brain proteins, such as myelin basic protein (MBP), neuron-axon filament proteins, and synaptic proteins. (18)

Research on postmortem brain tissue from people with ASD shows evidence of immunological activity and possible neuroinflammation caused by antibodies.

Autoantibodies' Possible Impact on Brain Development

Autoantibodies can cause anatomical and functional problems in the brain by interfering with myelination, synapse formation, and neuronal signaling. Common symptoms of ASD that may be exacerbated by these abnormalities include:

Communication and social interaction problems

heightened sensitivity to sensory information

Repeated actions and narrow interests

ASD and Maternal Autoantibodies Danger

Mothers of children with ASD are more likely to have anti-brain autoantibodies, according to research. These antibodies have the potential to cross the placenta and impact the development of the fetal brain by:

altering synapse development and neuronal connection by targeting important brain proteins.

causing neuroinflammation, which results in aberrant patterns of brain growth.

changing neurotransmitter systems, which has an impact on cognition and behavior.

This theory is supported by research on animals. ASD-like behaviors, including repetitive movements and decreased social interactions, were observed in offspring of pregnant mice or monkeys exposed to human maternal ASD-associated autoantibodies. (19)

2. ASD and T-Cell and B-Cell Dysfunction

The adaptive immune system relies heavily on T-cells and B-cells. B-cells make antibodies, but T-cells control immunological responses. Individuals with ASD have been found to have abnormalities in these immune cells, indicating immunological dysfunction that could be a contributing factor to neurodevelopmental anomalies.

ASD T-Cell Abnormalities

Decreased T-cells that regulate (Trigs): Trigs aid in preventing autoimmunity and managing inflammation. Trig insufficiency may be a factor in ASD's hyper activated immune system. (20)

Changed balance of T-helper cells (Th1/Th2): Increased inflammation may result from an imbalance between pro-inflammatory Th1 cells and anti-inflammatory Th2 cells, according to certain research.
Increased T-cell production of pro-inflammatory cytokines: A heightened immune response is shown by elevated levels of IL-6, TNF-α, and IFN-γ, which may be a contributing factor to neuroinflammation in ASD.

Abnormalities of B-Cells and Dysregulation of Antibodies

Some people with ASD have hyperactive B-cells, which causes them to produce too many antibodies, including possible autoantibodies against brain proteins.
Changes in immunoglobulin levels (IgG, IgA, and IgM): Research has shown that humeral immunity is deregulated when immunoglobulin levels are either increased or decreased.
Gastrointestinal (GI) dysfunction, frequently noted in people with ASD, has been linked to reduced IgA levels in ASD. (21)

3. Neuroinflammation and Immune Dysfunction in ASD

Immune dysregulation in ASD may be a factor in long-term neuroinflammation, which impacts behavior and brain function. Autoantibodies, T-cell/B-cell malfunction, and over reactive immunological responses can result in:
excessive activation of microglia, which interferes with synaptic pruning.
changed the permeability of the blood-brain barrier (BBB), which made it possible for cytokines and immune cells to reach the brain.
ASD symptoms are associated with alterations in neurotransmitter systems, including glutamate, GABA, and serotonin.

4. Possible Treatment Approaches for Immune Dysfunction and Autoimmunity in ASD

Researchers are looking into immunomodulatory therapies to treat ASD symptoms because of the immunological dysregulation that contributes to the disorder. (22)

1. Immunotherapy

Intravenous Immunoglobulin (IVIG) Therapy: In certain cases of ASD, IVIG has been used to lower the development of autoantibodies and modify immunological responses.
NSAIDs and corticosteroids are examples of anti-inflammatory treatments that may help control neuroinflammation in people with ASD.

2. Autoantibody Targeting

Plasma Exchange Therapy, or plasmapheresis: This method eliminates dangerous autoantibodies from the blood in autoimmune diseases.

Blocking particular immunological mechanisms implicated in autoimmunity is the goal of some experimental therapies, such as monoclonal antibodies.

3. Interventions Based on Nutrition and the Gut

Gut micro biome regulation and probiotics: Since the gut micro biota affects immune function, gut health therapies may lessen autoimmune.

Anti-inflammatory diets and omega-3 fatty acids may help reduce inflammation and promote brain function. (23)

The Micro biome and Gut-Brain Axis in Autism Spectrum Disorder (ASD)

The central nervous system (CNS) and the gastrointestinal (GI) tract communicate with each other in both directions through the gut-brain axis. Neurodevelopment, immunological regulation, and behavior are all significantly impacted by this relationship, which is mediated by neurological (vague nerve), immune, and endocrine pathways.

Growing research indicates that symbiosis, or abnormalities in the gut micro biota, may be a factor in immunological dysfunction, neuroinflammation, and altered neurotransmitter synthesis in people with autism spectrum disorder (ASD), all of which can affect symptoms of the disorder. Comprehending the function of the gut-brain axis in ASD could result in new therapeutic approaches, including as immunomodulatory therapies, probiotics, and dietary changes.

1. The Gut Micro biota Affects Brain Development and Immune System Function

The intestinal system is home to trillions of bacteria, fungi, and viruses that make up the gut micro biome. These microorganisms are essential to:

controlling immunological reactions (keeping pro- and anti-inflammatory pathways in balance).

generating neurotransmitters, including GABA, dopamine, and serotonin.

altering behavior and neurodevelopment by use of microbial metabolites. (24)

How Microbial Metabolites and Neurotransmitter Production in the Gut Micro biome Impact Brain Function in ASD

Short-chain fatty acids (SCFAs), which affect brain function, are produced by specific gut bacteria and include butyrate, acetate, and propionate.

In animal models, excessive propionic acid production has been connected to repetitive behaviors and social deficiencies that resemble those of ASD.

Serotonin and GABA, which are essential for mood, thought, and social interactions, are also produced by gut microorganisms. In ASD, imbalances in these neurotransmitters are frequently seen.

Modulation of the Immune System

A balanced immune response is ensured by the gut micro biome's regulation of immunological homeostasis.

Chronic low-grade inflammation brought on by symbiosis may be a factor in neuroinflammation and aberrant brain development in ASD.

The integrity of the blood-brain barrier (BBB) and the gut barrier

Systemic inflammation is brought on by toxins, germs, and inflammatory chemicals entering the bloodstream through a leaky gut (intestinal permeability). (25)

The blood-brain barrier (BBB) may be weakened by increased inflammation, allowing dangerous chemicals to enter the brain and impair neuronal function.

2. Symbiosis (Unbalanced Gut Micro biota) in Autism Spectrum Disorder and Its Effects

An imbalance in the gut micro biome, known as symbiosis, is typified by an overabundance of pathogenic microorganisms and a decrease in helpful bacteria. According to studies, people with ASD have altered gut micro biomes, including:

reduced concentrations of Lactobacillus and Bifid bacteria, two types of helpful bacteria.

increased concentrations of dangerous bacteria that create neurotoxic compounds, like Clostridium and Desulfovibrio.

Decreased microbial diversity is linked to more gastrointestinal (GI) problems, such as bloating, diarrhea, and constipation, which are frequently reported in people with ASD.

Symbiosis's Effects on ASD

Inflammation of the System: Chronic inflammation that impacts the brain is a result of symbiosis, which causes an imbalance between pro- and anti-inflammatory cytokines.

Modified Neurotransmitter Production: Deficits in serotonin and GABA, which are critical for mood and cognition, can result from disturbances in microbial communities. (26)

Increased GI Symptoms: Anxiety and worsening behavioral symptoms are associated with gastrointestinal issues, which are common in people with ASD.

3. Possible Treatment Consequences

Researchers are looking at a number of therapeutic strategies to restore gut micro biome balance and lessen neuroinflammation in ASD because of the close connection between gut health, immunological function, and brain development.

A. Treatments to Reduce Inflammation

Researchers are looking at anti-inflammatory therapies to lessen neuroinflammation and alleviate symptoms because persistent inflammation is a major contributing factor to ASD. (27)

NSAIDs, or non-steroidal anti-inflammatory drugs

Ibuprofen is one NSAID that may help lessen immunological over activity and neuroinflammation.

To prove their efficacy in ASD, more research is required, and prolonged treatment may have negative effects.

Anti-inflammatory biologics, or cytokine modulators

Cytokine-targeting medicines are being investigated because people with ASD frequently have higher levels of pro-inflammatory cytokines (IL-6, TNF-α, and IFN-γ).

Treatments for ASD may use monoclonal antibodies that target inflammatory pathways, such as anti-TNF or anti-IL-6 medications.

B. Dietary Measures and Probiotics to Restore the Balance of the Gut Micro biome

Probiotic supplements and dietary changes may help restore microbial balance and lower inflammation because symbiosis is widespread in ASD.

Live Beneficial Bacteria, or probiotics

Probiotic supplementation with strains of Lactobacillus and Bifidobacterium has demonstrated potential in enhancing immunological balance, gastrointestinal health, and behavior in individuals with ASD.
Probiotic use has been linked in studies to improvements in anxiety, gastrointestinal problems, and social interactions. (28)
Dietary fibers that nourish beneficial bacteria are known as prebiotics.
Foods high in prebiotics, like whole grains, garlic, onions, and bananas, encourage the development of good gut flora.

Particular Diets

Gluten-Free, Casein-Free (GFCF) Diet: According to some research, eliminating casein (a milk protein) and gluten (a wheat protein) may help reduce the symptoms of ASD.
Ketogenic Diet: Low-carb, high-fat diets may enhance cognitive performance and lessen inflammation.
Mediterranean Diet: Packed in fiber, polyphenols, and omega-3 fatty acids, this diet promotes both brain and gut health. (29)

C. Immunomodulatory Treatments (IVIG for Autism Spectrum Disorder)

An immune-based treatment called intravenous immunoglobulin (IVIG) therapy modifies immune responses by injecting donors' healthy antibodies.
The Function of IVIG in ASD
Reduces Autoimmunity: In ASD, autoantibodies that target brain proteins may be neutralized with IVIG.
Modulates Inflammation: IVIG has been demonstrated to reduce pro-inflammatory cytokines, which may lessen immunological dysfunction and neuroinflammation.
Restores immunological Balance: Following IVIG therapy, certain ASD cases with immunological dysregulation have demonstrated improvements in behavior, language, and social interaction.

Evidence and IVIG Therapy's Drawbacks

Positive effects on ASD symptoms, such as enhanced social interactions and cognitive function, have been documented in certain clinical investigations.
IVIG is costly, though, and it might not be effective for everyone with ASD.
To determine which ASD subgroups gain the most, more research is required. (30)

Conclusion:

The pathophysiology of autism spectrum disorder (ASD) is significantly influenced by immune system dysfunction. The development of symptoms of ASD has been linked to a number of immune-related problems, such as neuroinflammation, microglial dysfunction, cytokine imbalance, maternal immune activation, autoimmunity, and gut micro biota symbiosis. These immunological abnormalities could lead to changes in synapse pruning, neurotransmitter function, and brain connectivity, which would ultimately impact behavior and cognition.

Therapeutic approaches that focus on immunological modulation are becoming more popular as evidence of the involvement of immune dysfunction in ASD grows. By lowering inflammation and re-establishing immunological balance, anti-inflammatory medications, probiotics, dietary changes, and immunomodulatory treatments like intravenous immunoglobulin (IVIG) therapy have demonstrated promise in alleviating symptoms associated with ASD. Even if these treatments have potential, more study is required to ascertain their long-term effectiveness, find biomarkers for patient stratification, and enhance individualized therapeutic approaches.

To create innovative interventions that could improve the quality of life for people with ASD, it is crucial to comprehend the complex interactions that exist between the immune system, neurodevelopment, and ASD pathology. In order to develop a thorough understanding of ASD and create efficient, focused treatments for this complicated disorder, future research should concentrate on combining immunological, genetic, and environmental variables.

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اختلال تنظيم الجهاز المناعي ودوره المحتمل في اضطراب طيف التوحد(ASD)

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مستخلص البحث:
يُعد اضطراب طيف التوحد (ASD) من الاضطرابات العصبية المعقدة التي تتّسم بسلوكيات تكرارية، واهتمامات محدودة، وصعوبات في التواصل الاجتماعي. وتشير الأدلة المتزايدة إلى أن خلل الجهاز المناعي يلعب دورًا جوهريًا في الفيزيولوجيا المرضية لهذا الاضطراب. تشمل هذه الاضطرابات المناعية كلاً من أمراض المناعة الذاتية، واختلال توازن السيتوكينات، والالتهابات العصبية، وتنشيط الخلايا الدبقية الصغيرة، وتفعيل الجهاز المناعي للأم خلال فترة الحمل، بالإضافة إلى اضطرابات في توازن البكتيريا المعوية. وقد أظهرت الدراسات أن الأفراد المصابين بالتوحد يعانون من خلل في وظيفة الخلايا الدبقية الصغيرة، وارتفاع في مستويات السيتوكينات الالتهابية)مثل IL-6 و TNF-α وIFN-γ(، ووجود أجسام مضادة ذاتية تستهدف بروتينات الدماغ، وهو ما يرتبط على الأرجح باضطرابات في النمو العصبي. كما يرتبط تنشيط الجهاز المناعي للأم أثناء الحمل بزيادة احتمال إصابة الأبناء بالتوحد، نظرًا لأن الالتهابات قد تؤثر سلبًا في تطور دماغ الجنين. ويُعد محور الأمعاء–الدماغ عاملًا مهمًا آخر؛ حيث يمكن أن يؤدي اختلال توازن البكتيريا المعوية لدى المصابين بالتوحد إلى تفاقم الالتهاب الجهازي وتغيير إنتاج النواقل العصبية. وبناءً على هذه النتائج، يجري حالياً استكشاف عدد من الأساليب العلاجية للتخفيف من اختلالات الجهاز المناعي المرتبطة بالتوحد، منها استخدام البروبيوتيك، وتعديلات النظام الغذائي، والعلاجات المناعية التعديلية) مثل العلاج بالأجسام المناعية الوريدية(IVIG ، والأدوية المضادة للالتهابات. ولا يزال هناك حاجة ماسة إلى مزيد من الأبحاث لفهم الآليات الكامنة وراء هذا الخلل المناعي في التوحد، بهدف تطوير استراتيجيات علاجية موجّهة تُحسّن نتائج المرضى.
الكلمات المفتاحية:اختلال التنظيم المناعي، التوحد، الجهاز العصبي، خلل الخلايا الدبقية الصغيرة.