

Autism pathogenesis: Piecing it all together, from end to beginning ...

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Abstract

Increased extra-axial cerebrospinal fluid (EA-CSF) have been observed in imaging studies of infant brains, who go on to develop autism. Folate deficiency can cause defects in neural development that can affect CSF production and drainage. Folate receptor alpha antibodies (FRAA) are observed in 75% of autism patients. Maternal FRAA have also been observed in the case of neural tube defects.

Folate deficiency can cause aluminum accumulation in the brain. Autistic brains have been shown to accumulate aluminum. FRAA in the child or mother can therefore explain all the observations.

Further, autism patients have a higher genetic risk for cancer but have lower cancer rates. Many cancer cells express folate receptor alpha to transport folate required for rapid growth. Once again FRAA in autism can thus explain lower rates of cancer occurrence as FRAA block FRA expressed on cancer cells, affecting folate transport.

A majority of FRAA are of the IgG4 subclass and bind with higher affinity to the bovine folate receptor than the human folate receptor. The human and bovine FR have 90% protein sequence homology.

From allergies and parasite infections we know that IgG4 is the second stage of the immune response. The first stage is IgE against FRA. The US Institute of Medicine concluded that antigens in vaccines do cause IgE mediated sensitization. Many vaccines contain cow's milk proteins, one of which is the bovine folate receptor protein. Bovine casein and casamino acids used as growth media for vaccine manufacture are derived from cow's milk.

The solution for vaccine-induced IgE against FRA, is to immediately remove all non-target proteins from all vaccines by using processes such as affinity chromatography.

Keywords Autism, children, folate receptor alpha, bovine milk, IgG4, IgE, vaccines, aluminum, allergy, helminth infection

INTRODUCTION

Autism spectrum disorder (ASD) is a neurological and developmental disorder. It affects communication, behavior and is usually diagnosed in the first few years of life. In the US, the prevalence is 1 in 59 children.(1) Like for many other diseases, there is too much emphasis on finding a genetic basis. The rapid increase in prevalence of diseases such as ASD simply cannot be explained by genes.(2)

in any disease. People who suffer measles complications, for example, likely have a genetic susceptibility. The focus in that case is not in analyzing the genes, but on preventing measles infection. We know that IgE and IgG4 antibodies are involved in allergy and helminth infections. A genetic susceptibility to allergy means the individual has a strong helminth defense capability. Until very recently, even in developed countries, such a capability would have been an asset for survival, not a liability. The focus needs to shift and be directed at environmental factors in ASD.

DISCUSSION

Increased Extra-axial Cerebrospinal Fluid (EA-CSF)

Shen et al.(3) report increased EA-CSF in infants who later develop autism. Maternal folate receptor alpha antibodies (FRAA) have been associated with neural tube defects.(4) The CSF protects the brain, supplies nutrients and removes waste. Any defect in the plumbing during development can affect the production and drainage of CSF. Folate imbalance in CSF was reported as a cause of "unequal production and drainage of cerebrospinal fluid (CSF)".(5) Folate deficiency induced defects can also result in hydrocephalus.(5) □

Aluminum accumulation in the brain

Mold et al.(6) report that aluminum accumulates in autistic brains. A reason aluminum accumulates in the brain could be folate deficiency.(7-9) □

Folate receptor alpha antibodies

So all observations above can be explained by folate receptor alpha antibody (FRAA) mediated folate deficiency in the brain.(10,11) □ A child could be synthesizing FRAA or maternal

FRAA can impact the fetus.(12) □ FRAA bind/block folate receptors in the choroid plexus and block folate transport. Folic acid can be used to supply folate via an alternate pathway to improve the deficiency.(13) □

Lower cancer rate in autism

Autism patients are known to have higher genetic susceptibility to cancer. However, cancer rates are lower in autism patients.(14) □

Genetic susceptibility is not for a rapid growth. So they express more

folate receptor alpha (FRA) proteins on their surface that helps transport folate. Thus treatments that target these FRA proteins with antibodies are an experimental cure for cancer.(15) □ Since many autism patients are already making FRAA, it is easy to see why cancer rates will be lower.

The bovine connection

A majority of FRAA are of the IgG4 subclass and bind with higher affinity to the bovine folate receptor than the human folate receptor. The human and bovine FR have 90% protein sequence homology.(10) □

The worm and allergy connection

We know that IgE and IgG4 are involved naturally in helminth defense and now in allergies. IgE dominates in mild helminth infections. IgE mediated histamine release, itching and mucus generation are strategies to physically remove helminths/parasites and prevent major infections. If infection intensifies, an IgE mediated reaction can be dangerous leading to anaphylaxis. So naturally the body downregulates IgE and switches to an IgG4 dominated defense state. A chronic low intensity battle ensues with the helminth to avoid immunopathology of an IgE dominated aggressive defense.(16) □

This process is used in food allergy immunotherapy. A slow increase in the allergen exposure, modifies an allergen specific IgE dominated food allergy to an allergen specific IgG4 mediated "tolerant" state, reducing the risk of anaphylaxis.(17,18) □

Thus autism patients making bovine folate receptor alpha specific IgG4 (FRAA) are in this "tolerant" state. When they consume bovine milk which contains the bovine folate receptor protein, they make more IgG4 FRAA, aggravating autism symptoms. A

milk-free diet reduces FRAA levels and improves symptoms.(10)□

Working back from food allergy immunotherapy and helminth infections, autism patients started with an IgE mediated allergy to bovine folate receptor protein. Josephs et al. show that IgE FRAA are involved in cancer defense.(19)□ Such IgE are likely responsible for the lower cancer rate in autism patients as described above. How did autism patients, or their mothers develop IgE mediated allergy to bovine folate receptor proteins?

Bovine milk protein containing vaccines

Bovine milk protein containing aluminum adjuvanted vaccines that bias for a Th2 (allergy) dominated response. Bovine casein and casamino acids are growth media used in many vaccines and are derived from cow's milk.(20)□ Children allergic to milk make for excellent bovine milk protein detectors. They react to these vaccines.(21)□

The US Institute of Medicine (IOM) reviewed the entire literature from 1950 to 2011 and concluded that antigens in vaccines do induce IgE mediated sensitization.(22)□

Injecting egg proteins causes IgE mediated sensitization to egg - egg allergy.(23,24)□

Injecting gelatin causes IgE mediated sensitization to gelatin - gelatin allergy.(25,26)□

Injecting hepatitis B surface antigen the same.(27)□

Injecting influenza virus proteins(28–31)□, toxoids(32)□, dengue virus(33)□, bee venom(34)□, the same result.

Therefore, bovine milk protein containing vaccines inducing IgE directed against bovine folate receptor alpha proteins, is where it all begins. This could happen in the child or in the mother, before or during pregnancy. The mechanisms leading to abrogation of peripheral tolerance due to immunization with animal proteins was previously described.(35,36)□

CONCLUSION

The reason epidemiological studies failed to link vaccines and autism was previously described.(37)□

While FRAA are the primary mechanism causing autism, NMDA receptor autoimmunity is another contributor.(38)

The solution is to immediately remove all non-target proteins from all vaccines by using processes such as affinity chromatography.(39) □

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