REVIEW ARTICLE

A POSSIBLE CENTRAL MECHANISM IN AUTISM SPECTRUM DISORDERS, PART 1

Russell L. Blaylock, MD

The autism spectrum disorders (ASD) are a group of related neurodevelopmental disorders that have been increasing in incidence since the 1980s. Despite a considerable amount of data being collected from cases, a central mechanism has not been offered. A careful review of ASD cases discloses a number of events that adhere to an immunoexcitotoxic mechanism. This mechanism explains the link between excessive vaccination, use of aluminum and ethylmercury as vaccine adjuvants, food allergies, gut dysbiosis, and abnormal formation of the developing brain.

It has now been shown that chronic microglial activation is present in autistic brains from age 5 years to age 44 years. A considerable amount of evidence, both experimental and clinical, indicates that repeated microglial activation can initiate priming of the microglia and that subsequent stimulation can produce an exaggerated microglial response that can be prolonged.

It is also known that one phenotypic form of microglia activation can result in an outpouring of neurotoxic levels of the excitotoxins, glutamate and quinolinic acid. Studies have shown that careful control of brain glutamate levels is essential to brain pathway development and that excesses can result in arrest of neural migration, as well as dendritic and synaptic loss.

It has also been shown that certain cytokines, such as TNF-α, can, via its receptor, interact with glutamate receptors to enhance the neurotoxic reaction. To describe this interaction I have coined the term *immunoexcitotoxicity,* which is described in this article. (*Altern Ther Health Med.* 2008;14(6):46-53.)

Russell L. Blaylock, MD, is a retired neurosurgeon and visiting professor of biology at Belhaven College, Jackson, Mississippi.

Editor's note: The following is part 1 of a 3-part series. Part 2 will appear in the Jan/Feb 2009 issue of Alternative Therapies in Health and Medicine.

Autism spectrum disorders (ASD) are an increasingly common group of neurodevelopmental disorders without a clearly defined cause. This spectrum of disorders is characterized by a collection of neurobehavioral and neurological dysfunctions often occurring before age 36 months, which include a loss of eye contact, deficiencies in socialization, abnormal theory of mind function, language dysfunction, repetitive behaviors, and some difficulties with executive prefrontal lobe functions.[1,2]

The disorder has a prevalence of males to females of 4:1. A regressive loss of developmental skills occurs in 30%, most often between the ages of 18 months and 24 months. It also has been noted that autistic boys are more likely to experience an early onset of puberty.[3-5] Recent epidemiological evidence indicates a rapid rise in the prevalence of autism, with a 1 in 150 to a 1 in 160 incidence.

Neuropathological studies have shown abnormalities in the architecture of the autistic brain affecting cortical, subcortical, limbic, and cerebellar structures.[6-8] One of the most consistent findings has been hypoplasia of the inferior vermis of the cerebellum with variable but substantial loss of Purkinje cells in the cerebellar cortex.

The bulk of the evidence indicates that immune factors play a major role in these disorders.[9-11] Likewise, abundant evidence implicates mercury neurotoxicity from previously high levels of ethylmercury used as a preservative (thimerosal) in a number of childhood vaccines, as well as other sources of mercury.[12,13]

A host of other observations related to ASD has been aired, including abnormalities in organic acids, opioid-like substances from gliadin and gluten metabolism, intestinal dysbiosis, and trace element imbalances. A strong genetic influence is also known to exist.[14]

Neuroscience has discovered one mechanism that explains most of the findings in ASD: the excitotoxic cascade. New studies have linked a number of seemingly unrelated events to this cascade, such as immune activity, neurohormone abnormalities, and a host of biochemical events.[15,16] Examination of the pieces to this puzzle demonstrate that most fit well into this mechanism.

THE EXCITOTOXIC CASCADE

In 1957, Lucas and Newhouse discovered that monosodium glutamate (MSG)–exposed rats developed degeneration of the inner ganglion layers of the retina.[17] John Olney in 1969 discovered that the food additive MSG could produce delayed neuron death when animals were fed the substance in higher concentrations.[18] He observed not only destruction of the animals' retinal neurons but also destruction of selected nuclei in the hypothalamus and other brain structures. He coined the name *excitotoxin* based on the early observation that the neurons seemed to excite themselves to death in a delayed manner.

The glutamate receptor system consists of 3 ionotropic receptors