

Vitamin D as Nutritional Strategy to Treat Autism



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Letter to the Editor

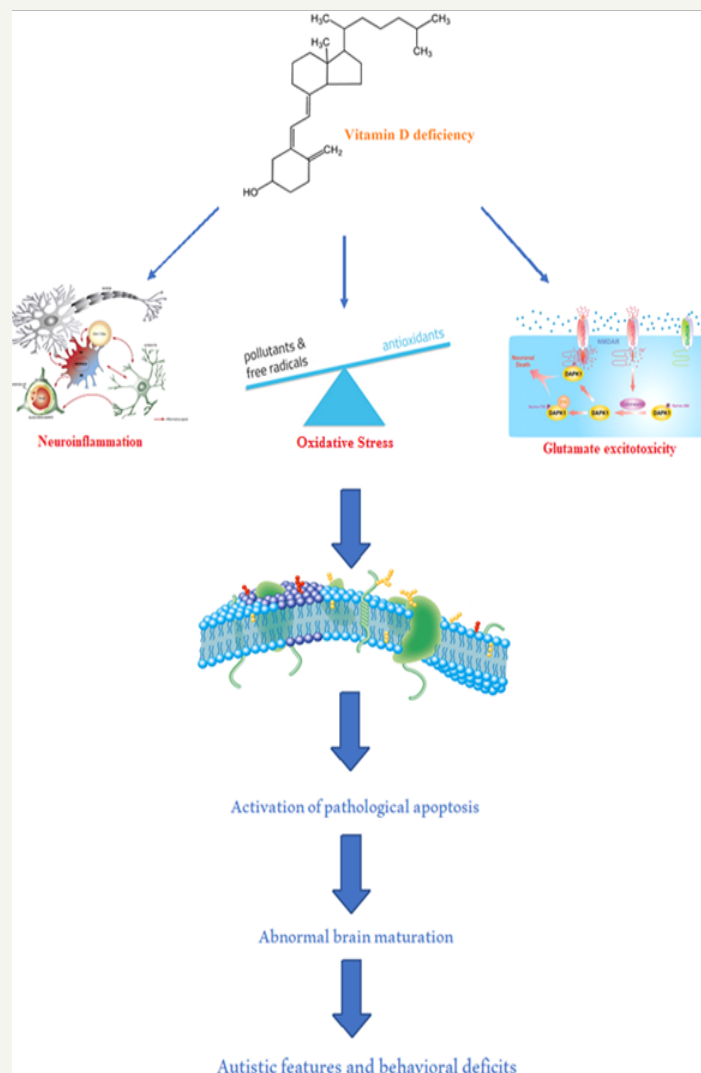


Figure 1: Demonstrates the suggested relationship between vitamin deficiency and neuro inflammation, oxidative stress and glutamate excite toxicity. It is Illustration of the relationship between vitamin D deficiency and neuro inflammation, oxidative stress, and glutamate excite toxicity as three etiological mechanisms in autism).

Autism is a neuro developmental disorder that is caused by many factors such as genetics, environment and maternal condition. There are a lot of environmental risk factors that influence autism

pathogenesis by their epigenetic effects [1]. Among the risk factors of autism as a multifactorial disorder is the low vitamin D status in early development. The concurrent increase of prevalence of

vitamin D deficiency and autism during the last 20 years might help to suggest vitamin D deficiency/insufficiency during pregnancy or in the first year of life as a contributor which can be related to different etiological mechanisms of autism. Confirmation of the role of vitamin D status in autism may provide strategy for primary and secondary preventive interventions. This manuscript is an attempt to solve the contradiction related to the role of vitamin D deficiency/insufficiency in autism and to find its relationship with oxidative stress; neuro inflammation, autoimmunity and glutamate excite toxicity and apoptosis as pathos-physiological mechanisms. It is well known that iron and zinc-induced oxidative stress in rat brain through depletion of glutathione and subsequent generation of reactive oxygen and nitrogen inflammatory species can be ameliorated by activated vitamin D. Repletion of glutathione by vitamin D can be easily related to detoxification of mercury and lead heavy metal burden repeatedly reported in individuals with autism as poor detoxifiers [2-4].

Based on the fact that pro-inflammatory cytokines and chemokines such as MCP-1, TNF- α , IFN- γ , IL-6, and IL-12, are consistently elevated in individuals with autism [5-7], serum levels of vitamin D is significantly lower in autistic patients [8,9], and that vitamin D has a profound anti-inflammatory action, so supplementation with vitamin D can help to reduce the neuro-inflammatory insult in autism [8,10]. Anti-inflammatory action of vitamin D is also demonstrated as inhibition of the synthesis and biological effects of prostaglandins as inflammatory lipid mediator and NF- κ B, which is involved in aberrant signaling in autistic brains [11,12]. A significantly elevated levels of anti-myelin-associated glycoprotein (anti-MAG) auto-antibodies were found in children with autism and were negatively correlated with vitamin D levels, showing the relationship between vitamin D deficiency/insufficiency and autoimmunity as etiological mechanism in autism [13,14].

Glutamate excite toxicity as etiological mechanism in autism is due to overstimulation of glutamate receptors and down regulation of glutamate transporters, as proteins critically needed for the clearance of the excitatory neurotransmitter, glutamate from the synaptic cleft [15,16]. Based on our understanding of glutamate signaling in children with autism and the recently reported enhancement of glutamate transporter (EAAT3) expression by activated vitamin D as the legend for the Vitamin D Receptor (VDR), vitamin D supplementation can be of remarkable help in the regulation of the excite toxic glutamate handling in autism [17]. Using animal modeling of autism, Al-Fawaz 2014 were able to show the protective effects of vitamin D through the remarkable amelioration of the impaired biochemically measured parameters representing neuro chemical (Serotonin), inflammation (IFN- γ) and detoxification processes (Glutathione-s-transferase) [18].

As vitamin D deficiency in autistic children is confirmed, randomized controlled trials are urgently needed. A recent randomized controlled trial, published in the Journal of Child Psychiatry and Psychology, found that high dose vitamin D (300 IU/KG/day) had a significant treatment effect on the core symptoms

of autism [8]. In a more recent trial, Cannell 2017 reported that younger children and those children whose final vitamin D level exceeded 40ng/ml responded best to vitamin D supplementation. If these trials are replicated, it would make the early diagnosis of autism very critical, because effective treatment with vitamin D may be possible [19] (Figure 1).

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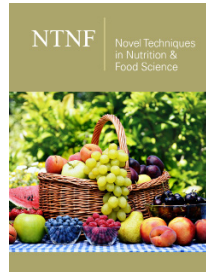
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