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Environmental Toxicants and Autism Spectrum Disorders

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It is widely believed that Autism Spectrum Disorders (ASD) is associated with environmental factors and genetic susceptibility. This gene, by environment interaction, is believed to affect neural development and leads to the behavioural phenotype of autism spectrum disorders (ASD) which is characterized by impaired social reciprocity and communication as well as restricted interests and behaviours. The list of potential neurotoxicants as candidates is long and includes metals, solvents, herbicides, pesticides, and drugs. Likewise, the list of gene candidates includes those involved in neuronal development, neurotransmitter synthesis and degradation, toxicant metabolism, and management of reactive oxygen species (see review by Miles [1]). Genes involving xenobiotics metabolism are reported to be associated with ASD [2-8]. However, no single toxicant and no single gene alteration have been identified as causal.

Many studies assessing the etiology of ASD have examined the body burden of one or more environmental chemicals in the affected individual and/or the mother of the affected individual. With very few exceptions, the limitations of such studies include failure to identify dose, frequency of exposure, and timing of exposures to the various toxicants. The general mobility of families makes it difficult to identify the local environment during which the critical exposures might have occurred, nevertheless, various studies have reported a possible association of environmental exposure in autistic individuals. For example, much interest has been focused on mercury in the environment and its potential contribution to increased prevalence of ASD [9-12]. Ming and her colleagues found a possible association between the number of toxic landfill sites in loci in New Jersey and the frequency of ASD in New Jersey [9].

Another line of investigating potential candidate toxicants could be focused on the type of environmental chemicals that are used at industrial levels and by most households world-wide. One such chemical stems from the use of plastic products, of which phthalates are the predominant toxicants. The potential sources of airborne phthalates are multiple, ranging from polyvinyl chloride (PVC) flooring, building materials, cleaning products, to toys and cosmetics [13]. Exposure to phthalates has been recently linked to ASD in two studies. One of these studies, performed in New York City, found a relationship between increased maternal prenatal exposure and behavioural problems in the children some years later [14]. Autism, itself was not documented. However, the umbrella term 'behavioural problems' could include ASD. Phthalate exposure was estimated from maternal urine phthalate metabolite levels. Phthalate measurements on spot urine specimens with controlling for creatinine are often used as a proxy estimate of total exposure to phthalates [14-17].A large scale Swedish epidemiological study serendipitously observed that the presence of PVC flooring material in the home, when the child was 1–3 years of age, was associated with ASD five years later [18]. Indoor dust samples are contaminated by phthalates [19]. Although not implicating phthalates directly, a study by Kalkbrenner et al. [20] found perinatal exposure to the mixture of air pollutants as defined in the National Air Toxics Assessment (NATA) program to be associated with 8 year old children with ASD. Exposure to phthalate esters in indoor dust is also associated with childhood asthma in a dose–response relationship [21-24].

In addition to increased exposure to environmental chemicals, there is evidence from literature suggesting that detoxification is different in some individuals with ASD. One study found that 90% of autistic children with known food/chemical intolerance showed a deficiency in phenol sulfotransferase, a liver enzyme involved in detoxification [25,26]. A study by Edelson and Cantor reported an increased urinary glucaric acid, a biomarker for xenobiotics contamination in ASD children together with abnormal liver detoxification profiles [27]. Another study found decreased acetaminophen conjugation (sulfation) by the liver in 20 low functioning ASD children [28]. James et al. [29] reported an abnormal methylation in autistic children and parents. Glutathione S-transferases (GST) are enzymes that catalyze conjugation of glutathione to toxicants, thereby detoxifying the toxicants. Genetic polymorphism of GST M1or GST P1 may be implicated in reduced or absent GST enzyme function, have been described in families with autistic children [29-32]. Another detoxification enzyme, glutathione peroxidase, was found to be polymorphic with potential functional consequence in families of autism [33].

Exposure to xenobiotics may or may not be significantly higher in families of autistic children [34-37]. A combination of impaired detoxification mechanisms and increased toxicant loads is more plausible in contributing to autism phenotypes; therefore, research on both causes in the same ASD population may be more productive.

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