

## Neurodevelopmental Disorders in Children

### Autism and ADHD

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Autism, ADHD, learning disabilities, developmental delays and intellectual retardation are among the neurodevelopmental disorders that exact an enormous emotional, mental and financial toll in terms of compromised quality of life and lifelong disability. Additionally, these require special education, psychological and medical support services that drain resources and contribute to further stress on the families and communities. While it is generally accepted that the cause for these disabilities is likely to include genetic and environmental factors, for a vast majority of these disabilities, the cause remains unknown.

Many factors contribute in complex ways to brain development. These include gene expression, heredity, socioeconomic factors, stress, drugs, nutrition and chemical contaminants. Brain development is a long, complicated process involving cell proliferation, migration, differentiation and cell death (apoptosis). There are multiple ways by which chemicals can disrupt neurological development such as influencing gene expression, protein pathways<sup>(1)</sup> and hypothyroidism<sup>(2)</sup>. It is a well established fact that a child's nervous system is more sensitive to chemical exposures compared to an adult nervous system. This is evident from incidence of permanent brain damage in fetus of pregnant mothers who consumed alcohol during their pregnancy resulting in fetal alcohol spectrum disorder<sup>(3)</sup>. Similarly, pregnant women involved in methylmercury disasters showed minimal signs of toxicity compared to their children who displayed effects ranging from cerebral palsy to delayed development<sup>(4)</sup>.

In the 1950s, Thalidomide was introduced into the market to treat morning sickness and as a sedative. It created an epidemic of 15,000 babies worldwide with missing limbs and other developmental disabilities including mental retardation and autism<sup>(5)</sup>. Today, it is a widely accepted fact that chemicals in the environment can cause developmental disabilities in children. Even more intriguing is the fact that certain environmental agents can cause long-lasting damage to the developing brain at exposure levels that have no lasting effect in the adult.

A wide range of toxic chemicals in the environment have been associated with neurodevelopmental disabilities which affect an estimated 3-8% of the 4 million babies born each year in the United States. In a recent study published in *The Lancet*, researchers from Harvard School of Public Health and the Mount Sinai School of Medicine examined publicly available data on chemical toxicity to identify the industrial chemicals likely to damage the developing brain. The researchers compiled a list of 202 industrial chemicals that are known to be toxic to the human brain using the Hazardous Substance Data Bank of the National Library of Medicine and other data sources<sup>(6)</sup>. The exposure to these chemicals came from industrial accidents, occupational exposure, suicide attempts and accidental poisonings. The authors noted that the list was not comprehensive since the number of chemicals that can cause neurotoxicity in laboratory animal test exceeds 1000. A key point highlighted in the study was the fact that even though moderate amounts of chemicals, such as lead and mercury, were needed to cause neurological damage in most adults, only small amounts might be needed to damage the developing brains in babies, infants and young children.

It is a well known fact that certain chemicals, such as lead, mercury, PCBs, dioxins, arsenic and toluene can cause clinical and sub-clinical deficits in neurobehavioral development through injury to the fetal brain. The developing brain is extremely vulnerable to these environmental agents at doses much lower than those that affect adult brain function. Studies have shown that prenatal exposure to even relatively low levels of lead result in lifelong reductions of intellectual functions and disorders of behavior <sup>(7)</sup>. Polychlorinated biphenyls (PCBs) cross the placental barrier and can cause injury to the developing brain <sup>(8)</sup>. Organic mercury compounds such as methyl mercury are among the most potent neurotoxins causing severe developmental problems <sup>(9)</sup>. In view of this fact, it seems disconcerting that there is little information available on possible toxic potential for the 80,000 chemicals registered with the Environmental Protection Agency (EPA). Of the 3000 chemicals produced or imported at over 1 million pounds a year, a mere 23% have been tested for their potential to cause developmental damage <sup>(10)</sup>.

Autism is a neurodevelopmental disorder characterized by impaired social interaction as well as verbal and non-verbal communication. There are various degrees of severity involved in this disorder. Therefore, this condition is commonly referred to as "autism spectrum disorders" or ASD which include autism, Asperger's syndrome, pervasive developmental disorders not otherwise specified (PDD-NOS) and high-functioning autism. Statistics based on data gathered in 2002 indicates that more than 550,000 children are affected by varying degrees of autism spectrum disorders (ASD). In fact, it has been reported that autism is the fastest growing developmental disability, increasing at a rate of 10 to 17 percent annually according to the Autism Society of America. While improved diagnostic measures may contribute to the perceived increase in the number of cases, it is becoming increasingly apparent that environmental neurotoxins in combination with genetic predispositions could also create adverse gene-environment interactions.

Surveys conducted in California indicate an almost 210% increase in the number of cases of autism in children over the past 10 years. There is increasing concern that certain chemicals (such as mercury, halogenated aromatics and pesticides) and biotic factors (such as vaccine antigens) may act synergistically to alter certain susceptibility or genetic risk factors to result in ASD. The UC Davis Center for Children's Environmental Health has established the first large scale epidemiological study to investigate the underlying causes of autism. The UC Davis researchers at the Children's center have suggested an association between thimerosal (ethyl mercury) and immune system dysfunction in mice. In a recent study, Windham et. al. (2006) explored the possible association between ASD and environmental exposures to hazardous air pollutants in the San Francisco Bay area <sup>(11)</sup>. Based on the data from the study, the authors suggested that living in areas with higher ambient levels of HAPs, especially metals and chlorinated solvents, during pregnancy or early childhood could be associated with a moderately increased risk of autism. This study highlighted the need for more complex etiologic studies combining exposure to multiple compounds by various pathways with genetic information to further understand the contribution of environmental exposures to the development of autism.

Another developmental disorder that affect the areas of social skills, behavior and communication is Attention Deficit Hyperactivity Disorder (ADHD). Presently, some researchers believe that there is a correlation between ASD and ADHD. It is estimated that ADHD affects approximately 4.5 million children in the US. The main characteristics that define ADHD include inattention, hyperactivity and impulsivity. Though almost everyone at some point in their life blurts out something inappropriate or has difficulty focusing on a task or could become forgetful, experts say that such behavior must be demonstrated to a degree that is inappropriate for that age, for a diagnosis to be made. There is insufficient evidence that suggests that ADHD could be a result of simply social factors or child-rearing factors. Other factors such as environmental agents like heavy metals and organohalides, traumatic brain injury, food additives and sugar, neurobiology and genetics have been implicated in the etiology of this condition.

Medications that seem to be most effective in treating ADHD are a class of drugs known as stimulants such as Ritalin (methylphenidate). However, there is mounting controversy over the widespread use of methylphenidate and possible life-threatening effects from its long-term use. This makes it imperative that alternative modalities be implemented for ADHD management. Nutrient deficiencies are common in ADHD; supplementation with minerals, the B vitamins (added in singly), omega-3 and omega-6 essential fatty acids, flavonoids, and the essential phospholipid phosphatidylserine (PS) can improve ADHD symptoms <sup>(12)</sup>. In a first of its kind study, Dr. Sarina Grosswald, an educator and expert in cognitive learning and clinical neuropsychologist, William Stixrud investigated the effect of meditation in kids with ADHD in the school setting. For the study, kids with ADHD meditated 10 minutes, twice a day. This study revealed that kids who meditated showed a 45 to 50 percent reduction in stress, anxiety and depression. These kids also showed significant improvements in organizational skills, memory, strategizing, mental flexibility, attention and impulsivity. According to Stixrud, teaching a child to regulate his own body and mind in response to anxiety should be the first response rather than putting them on medication.

Neurodevelopmental disorders have increased over the past 30 years and are at least partly attributed to exposure to environmental contaminants. Therefore, it becomes imperative to mitigate environmental factors that may influence disease. The impact of environmental toxins on children's health has become a major focus in the federal government resulting in establishment of eight new research centers in children's environmental health with joint funding from EPA and the National Institute of Environmental Health Sciences (NIEHS). "The brains of our children are our most precious economic resource, and we haven't recognized how vulnerable they are," says Philippe Grandjean, adjunct professor at Harvard School of Public Health and the lead author of the study published in *The Lancet*. "We must make protection of the young brain a paramount goal of public health protection. You have only one chance to develop a brain."

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**While the generally accepted causes of neurodevelopmental disorders like Autism and ADHD include genetic and environmental factors, a wide range of toxic chemicals in the environment have also been associated with these disorders.**

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