Autism and the Environment
Science Brief 7

Identifying Environmental Contributions to Autism: Provocative Clues and False Leads, Mental Retardation and Developmental Disabilities Research Reviews, November 2004

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In the past twenty years the number of children diagnosed with autism spectrum disorders (ASD) (also called the prevalence of ASD) has increased significantly. Autism researchers have hypothesized that this might be because many doctors and other professionals have received training on recognizing signs of autism. This training has helped doctors diagnose patients they may have missed earlier (did not recognize). The training also helped doctors diagnose autism earlier in new patients. Some researchers also think that the number of autism cases went up because of more chemicals and biological agents pregnant women and young children are exposed to. For example, there was a lot of concern about the Measles-Mumps-Rubella (MMR) vaccination causing some young children to develop autism. Researchers who studied this felt there wasn’t good evidence that the MMR vaccine causes autism. Most researchers agree that we do not know enough about how environmental factors might lead to the development of ASD in some children.

The purpose of this study was to review published articles which have studied the effects of exposure to toxic (harmful) substances and the development of ASD in children.

Research Design
(What did the Researchers do?)

The authors reviewed selected articles on environmental factors which might be related to ASD. Environmental factors are things that people are exposed to that may cause a negative reaction in their body. Many environmental
studies have tried to connect environmental factors to some ASD behaviors or changes in the brain of people with ASD. The authors provided a framework for understanding environmental influences in autism. The framework looked at the interaction of genetic and environmental influences. The authors then presented the following four guiding principles. The principles help to identify and understand how environmental factors might be harmful to the human nervous system and/or related to ASD. This is called “neurotoxicology.” “Neuro” means “nervous system” (the brain and spinal cord, but the brain in particular). “Toxicology” is the study of chemicals that are poisonous or harmful to the body.

1. **Dose-effect relationship**
   “Dose” refers to how strong the environmental toxin is that a child with ASD is exposed to. If it is a medication, then the dose of the medication is carefully measured and you know how much a child takes every day and how often. If the environmental toxin is air pollution or exposure to radiation (near the house where the child lives), the dose is hard to measure.

   Figure 1 has a graph of hypothetical (not real) data that shows what might be the dose-effect relationship between an environmental toxin and brain development. The vertical axis in the graph represents the dose or exposure to the toxin, which goes from 0 (no exposure) to 100 (a lot of exposure). “Effect” refers to whether there is a measurable effect on the person who has been exposed. In this hypothetical (not real) case of ASD, the “effect” is abnormalities in the brain of a subject with ASD. As you can see, if a toxin contributes to changes in the brains of people with ASD, the more exposure to the toxin, we would see more severe the changes in the brain.

2. **Toxicant disposition**
   A second key concept is finding out what the body does with the toxin (called toxicant disposition). When an environmental toxin is studied, it is important to understand how the toxin is absorbed into the body. We also want to know where it is sent in the body, whether it is changed into some other substance, and how it is excreted (goes out of the body). Researchers look at the pathway into the body. They identify when and if the toxin goes to the brain and if the body can “neutralize” it, or get rid of it quickly before it does harm. How quickly the toxin
passes through the body is also important to know because this can affect whether the toxin reaches a dose that can harm the child.

3. **Cellular Differentiation**

Researchers have identified critical periods in brain development where neurons (nerve cells) develop, duplicate, and differentiate. Cellular differentiation is the process where a less specialized cell becomes a more specialized cell type and then becomes a specific part of the body. See Figure 2 for a picture of how this happen. Differentiation occurs many times during the development of a complex organ such as the brain and nervous system. The brain also goes through other stages of development including formation of synapses, which are junctions between neurons. At the synapse the nervous system signals travel from cell to cell. The signals are sent from the brain and nervous system to other organs like the muscles or GI system. Another important time is when the brain gets rid of extra neurons. The brain trims the synaptic “trees” so they are more efficient. An environmental toxin can occur at any of these critical periods. The toxins effect will depend on the dose of exposure and what critical period of development was interrupted. In general, the earlier the insult, the more catastrophic the effect. For example, researchers have found the period between 20-25 days after a woman becomes pregnant is a critical period when taking a drug like Thalidomide. This drug is taken for nausea and can lead to significant changes in the brain of the child, and possible development of ASD. Researchers found that when pregnant women took the drug later it did not have the same effect.
4. Neuro-pathological clues
Researchers believe it is very important to study environmental causes of ASD. Their studies are important because ultimately the potential environmental cause should be linked to changes in the brain which we see in people with ASD. The authors note that research has found abnormalities in a number of brain regions, including the cerebral cortex, brainstem, cerebellum, amygdala, and other sites. They agree with other researchers that there is no “single” brain lesion for ASD. They hypothesize that ASD is likely to be caused by a “dysregulation” of systems or networks that stimulate or engage various parts of the brain.

Results
(What did the Researchers find?)

Researchers think that environmental agents alone probably cannot cause autism. But those agents can combine and act together with other factors such as genetics. There are several ways in which environmental factors and genetics may interact. One idea is that environmental exposures may work together with genetics to cause autism. Another is that while the genes may trigger autism, the environmental factors may act to alter phenotypic expression. For instance, all children with autism have difficulties with social interactions; however, the degree of difficulty varies from child to child. It can be that the environmental exposures during pregnancy or early childhood are partly responsible for the differences in how autism shows itself in different children.

Why do children react differently when exposed to certain chemicals? This may have something to do with their genes. The review of studies suggested that some people are more sensitive and respond more strongly to
environmental exposure because they are genetically more susceptible. It might be that our genes can either protect us or make us more vulnerable when it comes to chemical exposure. Researchers now want to use this information to look for genes to understand pathways to ASD. Researchers think that if they find the gene segments that control the way we respond to environmental factors such as chemicals and other biological agents; this will help to identify some of the genes involved in ASD for some sub-groups of children.

Although researchers are finding some environmental factors that may be harmful, we still do not know how much exposure is harmful and in which groups of children. We don’t know if there is a critical period (for example, very early in pregnancy) when the exposure to toxins is especially harmful. Until we have answers to these questions, it is hard to make a connection between an environmental toxin and the development of ASD.

There is some evidence that some chemicals interfere with proper brain development in embryos. The brain starts to grow early in the development of the fetus. Growth of the brain continues throughout the entire pregnancy and continues after birth. A potentially harmful substance can disrupt the development and result in abnormalities in some brain regions. Because multiple brain structures usually develop at the same time there may be a problem in children with ASD with the chemicals that regulate or control how various regions of the brain develop. This may also explain why certain brain areas are associated with certain sub-types of ASD.

In their review of published articles, the authors said there are around 50 substances and chemicals that are known to be toxic during human development. They include alcohol, cocaine, pesticides, and certain medications. Also, some studies showed that imbalance of chemicals produced by the brain itself may also lead to ASD. Researchers hypothesize that environmental agents may interfere with the proper release of these chemicals and then contribute to the development of ASD.

Another group of researchers are also trying to find out if some abnormalities associated with the immune system may be related to ASD. The immune system consists of biological structures and processes within the body that protects us from disease. The immune system does this by finding and killing pathogens and tumor cells. To work properly, the immune system must be able to detect harmful agents like bacteria, viruses and parasitic
Researchers think that an overly active or poorly working immune response during critical stages in fetal brain development may disrupt the normal development of the brain. The job of the immune system is to respond to toxic substances present in the body. If the immune system turns on when there is no toxin present then chemicals that the developing brain. This may lead to changes in brain development in the fetus. The child may then develop characteristics of ASD. Environmental exposures can affect the brain 3 ways:

1. By being absorbed into the body and directly harming the brain
2. By interfering with brain development or
3. By altering the fetus or child’s immune system.

Substances such as lead (found in old paint), mercury (found in some fish), and PAH chemicals (found in coal, produced during fuel burning) have been known to cause an immune system response in people. It is very important to do more studies of the possible relationship between the immune system and brain development. This information may help future researchers develop ways to prevent the immune system from harming brain development in at-risk fetuses.

What does this mean for my child and my family?

We are beginning to learn more about possible environmental causes of ASD. But the environment alone probably doesn’t cause autism. We still need more research. Below are some things that might be helpful to you and your family.

1. Some people might be more genetically susceptible to environmental exposures or toxins than others.
2. Environmental agents may contribute to how ASD is expressed in the child, how severe their symptoms are, or when the first signs of ASD are observed.
3. Some substances might be toxic to fetuses and young children even at very low doses.
4. Environmental factors may act directly on the brain, by disrupting brain development or by triggering the immune system to release chemicals that interfere with brain development.
If you are able to attend conferences about environmental causes of ASD you will learn about new discoveries which are happening all the time.

If you are worried that you or the child you are carrying might be exposed to something harmful in the environment, talk to your doctor.

Glossary of Terms

**Hypothesis** – refers to a proposed explanation for something that has been observed. Most hypotheses come from theories related to what has been observed or from previous research. Researchers “test” hypotheses when they do their studies.

**Prevalence** – number of people in a population affected by a disease at certain time.

**Incidence** – the number of “new” cases of a disease in a population.

**Environmental exposure** – things like chemicals, pollutants and other substances that people are exposed to that may cause sickness and other health problems.

**Toxic** – materials or chemicals which are harmful or poisonous.

**Neurotoxicology** – Neuro” means “nervous system” (the brain and spinal cord, but the brain in particular). “Toxicology” is the study of things that are poisonous or harmful to the body.

**Neuron** – Refers to a cell of the nervous system.

**Cellular differentiation** – the process in which a less specialized cell becomes a more specialized cell. Differentiation occurs numerous times during the development of an individual, resulting in a complex system of tissues and cell types.

**Synapses** – specialized chemical junctions between neurons which allow nerve signals to move from cell to cell and then from the nervous cell to other cells (such as the muscle or GI system).

**Neutralize** – the process of making a toxin less harmful.

**Simultaneously** – at the same time.

**Immune system** – A system of biological structures and processes in the human body that protects against disease. Cells of the immune system identify and kill pathogens—things that have entered the body and might hurt it, such as a bacteria.

**Pathogens** – an infectious agent, or more commonly a germ or a biological agent that causes disease in its host.

**Nervous system** – A system of structures and processes that contain a network of specialized cells called neurons that coordinate the actions of the human body. It does this by sending and receiving signals to and from different parts of the body.

**Phenotypic expression** – what we see, observable characteristics.

**Susceptible** – to be affected, to be sensitive to.
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