2008

Biological versus Environmental Factors: Determining the Cause of Pervasive Developmental Disorders in Children

Jami Zaretsky

Follow this and additional works at: http://preserve.lehigh.edu/cas-lehighreview-vol-16

Recommended Citation

http://preserve.lehigh.edu/cas-lehighreview-vol-16/6

This Article is brought to you for free and open access by the Lehigh Review at Lehigh Preserve. It has been accepted for inclusion in Volume 16 - 2008 by an authorized administrator of Lehigh Preserve. For more information, please contact preserve@lehigh.edu.
Biological versus Environmental Factors: Determining the Cause of Pervasive Developmental Disorders in Children

by Jami Zaretsky
Being diagnosed with a pervasive developmental disorder can mean that a patient may have mild to severe impairments. Four classic disorders have been identified within the spectrum – Asperger’s Syndrome, Autism, Rett Syndrome, and Childhood Disintegrative Disorder – with Asperger’s Syndrome showing the lowest level of impairment. When a child’s symptoms are not typical of these specific diagnoses, he or she is placed in the category PDD-NOS (not otherwise specified). Characteristic of all these disorders is delayed development in communication and social skills along with affects on cognitive and behavioral functioning. The severity of impairment differs between disorders and even more between individual patients. Because the differences between the levels of impairment can be so extreme, it is imperative that research is given to each individual disorder alone, instead of trying to treat the entire continuum. The possibility exists that each syndrome is caused by similar, but not identical factors. If this is the case, the factors contributing to each specific syndrome must be individually examined in order to find the appropriate cures.

Aside from having their own levels of impairment, each of the pervasive developmental disorders has a unique rate of incidence. The most well-known is autism, which is diagnosed in approximately 3.4 of every 1000 children ages 3-10. Asperger’s Syndrome follows with a diagnosis rate of approximately 2 in 10,000. The rarest and most severe disorders, Rett Syndrome and Childhood Disintegrative Disorder are much less prevalent. Rett Syndrome affects approximately one of every 10,000 to 15,000 girls. Similarly, Childhood Disintegrative Disorder affects less than two out of every 100,000 children, with the majority of cases being reported in males. There are many children with significant developmental delays, but with symptoms that do not warrant a diagnosis of a specific disorder. In these cases, children are diagnosed as PDD-NOS, which is the most commonly diagnosed pervasive developmental disorder (National Institute of Mental Health Online, 2007). To be diagnosed with any pervasive developmental disorder, a child must display specific characteristics, which are outlined in Appendix A.

Diagnosis usually occurs as early as age two, although symptoms can present themselves much earlier or later than this. Depending on the type of syndrome and the severity of impairment, children can follow different sequences in terms of early development. Generally, children that fall under the autism diagnosis will follow a typical pattern of development for up to 18 months, at which point signs of autism may become apparent (Sicile-Kira, 14). These children are usually withdrawn, lack the skills necessary to imitate others, and have irregular speech patterns, if any at all. Children with autism can be regarded
as having “very significant difficulty in social interaction, in language, in nonverbal communication, and in pretend play” (Levine, 1996, pg 1). These children also demonstrate a very narrow set of interests and up to 75% are mentally impaired. Children with Asperger’s Syndrome have very similar symptoms as those present in autism, with the exception being that they have normal or near-normal speech and cognitive development (Levine, 1996, pg 1). Children diagnosed with PDD-NOS may present some, but not all, of the symptoms indicative of autism. The rarest disorders, Rett Syndrome and Childhood Disintegrative Disorder have a different range of symptoms than found in the other pervasive developmental disorders. Rett Syndrome affects only girls and those affected follow a typical pattern of development until 5 to 30 months, when the child begins to lose skills she has previously mastered (Levine, 1996, pg 1). These girls typically lose all gross and fine motor coordination, and may subsequently develop heart and lung problems. Similarly, the quality of life for those with Rett Syndrome or Childhood Disintegrative Disorder is severely diminished.
With such a broad range of symptoms and an increasingly large number of children being diagnosed, the underlying causes of pervasive developmental disorders must be examined. Various factors ranging from genetics to food allergies have been said to be at the root of these disorders. Some of the most frequently investigated factors include immunizations, neurological brain abnormalities, genetics, environmental toxins, and food allergies. The possibility exists that any of these factors could work as a single agent or together with one another to cause the symptoms associated with pervasive developmental disorders. Further research must be performed in order to rule out or provide evidence toward which factor(s) are contributing to these devastating disorders.

Food allergies have been said to contribute to pervasive developmental disorders. Celiac disease, a disorder in which the body cannot process the protein gluten found in wheat, may be linked to the disorders (Center for Disease Control and Prevention Online). Evidence supporting this claim is found in some children with pervasive developmental disorders, as removing wheat as pesticides, household cleaners, and lead may have something to do with these disorders.

A specific study was performed in California to test the relationship between autism and pesticides. Spanning a two year birth period from 1996-1998, 465 autism diagnoses were made within nineteen counties in the Sacramento and San Joaquin Valleys. Nineteen pesticide varieties were tested and only one –organochlorines- seemed to pose a potential threat. Twenty-nine mothers living near agricultural fields where organochlorines were used in their first trimesters of pregnancy produced 8 children later diagnosed with autism. This rate was 6 times higher than found in a control group (News10 Online). While this information is certainly shocking and warrants further research, it does not tell us that pesticides are a definitive cause of autistic disorders.

Despite the aforementioned claims, the most apparent cause for these disorders is a genetic defect. It has been noted that children with autism spectrum impairments are likely to have a parent, sibling, or other close relative who also has the syndrome or another pervasive developmental disorder (Constantino, 2006). Additionally, children falling within the autism spectrum often have family members with other genetic abnormalities, which could contribute to the development of a PDD. With this being the case, it is evident that genetics plays at least a partial role in causing pervasive developmental disorders.

**The Case for Genetics**

There is roughly a 10% chance of sibling recurrence involved when at least one child in a family is affected with a pervasive developmental disorder (Constantino, 2006). This statistic alone provides evidence toward the
existence of a genetic component being present. The problem with identifying genetics as the cause for pervasive developmental disorders is that the gene or genes responsible have not yet been determined. Recent research has isolated some of the potential genes believed to be involved in autism, located on chromosomes 7 and 15 (Waltz, 2003, pg 8). Additionally, the first gene involved in speech disorders was identified on chromosome 7, within close proximity to the gene mutation site believed to cause autism (Waltz, 2003, pg 9). This is a significant finding, as speech defects are present in almost all cases of pervasive developmental disorders. Due to the defects to their children, there has to be a reason why some children express the disorder in the first place, especially when they are conceived from two non-affected parents. One explanation is the possibility that pervasive developmental disorders are recessive genetic disorders. In a recessive disorder not phenotypically expressed by either parent, both parents must be carriers of the defect in order for the child to be affected. Assuming recessive inheritance, there is a 50% chance that a child could inherit a PDD when one parent shows signs of having the disorder. Autism and Asperger’s Syndrome may be more prevalent than Rett Syndrome due to the per-

Girls have two X chromosomes, but only need the genetic equivalent of the information on one of the two chromosomes. Because of this, one X chromosome (from the mother or father) is inactivated and becomes a Barr body. If the X chromosome carrying the mutation is inactivated, the child may express milder or fewer symptoms of Rett Syndrome. In cases where the active X chromosome is the one carrying the mutation, the child will experience full blown Rett Syndrome (RSRF Online).

There are two possible ways to inherit a mutated MECP2 gene from the maternal set of chromosomes when the mother appears to be unaffected by the disorder. The first is known as germline mosaicism, where the mother has the mutation in her eggs, but in none of her somatic (body) tissues. Secondly, the mother may have the mutation, but be asymptomatic due to X-inactivation of the mutated X chromosome. It is also possible to inherit the mutated gene from the father; however, since MECP2 mutation causes mental retardation in males, it would be previously known that the father carries some genetic mutation (RSRF Online).

With this knowledge, it is possible that the majority of pervasive developmental disorders are caused by multiple genetic mutations, while Rett Syndrome is caused by a single

Because the differences between the levels of impairment can be so extreme, it is imperative that research is given to each individual disorder alone, instead of trying to treat the entire continuum.

uncertainty as to which genes are directly involved with the disorders, it is impossible to perform genetic testing at this time.

Assuming the claim that pervasive developmental disorders are caused by genetics can be substantiated, it is interesting to examine the incidence of occurrence of both Rett Syndrome and Childhood Disintegrative Disorder. If genetics is the only contributing factor in pervasive developmental disorders, then what makes some disorders more prevalent than others? While it is true that children with Rett Syndrome and Childhood Disintegrative Disorder rarely live long enough to reproduce and transmit any genetic percentage of the population carrying the affected genes. The assumed recessive pattern of inheritance for most pervasive developmental disorders can be observed in Appendix B.

While the causes of autism and Asperger’s Syndrome still remain unknown, studies have revealed that Rett Syndrome is caused by a mutation of the MECP2 gene on the X chromosome during pregnancy. In boys, this type of mutation causes mental retardation, while in girls it causes Rett Syndrome to occur. Girls with Rett Syndrome can have varying levels of impairment, which may be due to which X chromosome is carrying the defective gene. Girls have two X chromosomes, but only need the genetic equivalent of the information on one of the two chromosomes. Because of this, one X chromosome (from the mother or father) is inactivated and becomes a Barr body. If the X chromosome carrying the mutation is inactivated, the child may express milder or fewer symptoms of Rett Syndrome. In cases where the active X chromosome is the one carrying the mutation, the child will experience full blown Rett Syndrome (RSRF Online).

There are two possible ways to inherit a mutated MECP2 gene from the maternal set of chromosomes when the mother appears to be unaffected by the disorder. The first is known as germline mosaicism, where the mother has the mutation in her eggs, but in none of her somatic (body) tissues. Secondly, the mother may have the mutation, but be asymptomatic due to X-inactivation of the mutated X chromosome. It is also possible to inherit the mutated gene from the father; however, since MECP2 mutation causes mental retardation in males, it would be previously known that the father carries some genetic mutation (RSRF Online).

With this knowledge, it is possible that the majority of pervasive developmental disorders are caused by multiple genetic mutations, while Rett Syndrome is caused by a single
mutation, making it less common than the other disorders. Although the mutation for Childhood Disintegrative Disorder has not yet been identified, it is likely that it is caused by a single mutation as well. When there are more mutations or combinations of mutations involved, the likelihood of expressing the disorder becomes much greater. This would explain why autism and Asperger’s Syndrome occur in much greater frequency than Rett Syndrome and Childhood Disintegrative Disorder.

The Case for Immunizations

Besides genetics, the second most commonly scrutinized factor in determining the cause of pervasive developmental disorders is immunizations, particularly the Measles, Mumps, Rubella vaccine. The first vaccine of its type was licensed for use in the United States in 1963 as a single dose, and administration of the vaccine began in the 1970s. In 1989, the American Academy of Family Physicians, the American Academy of Pediatrics, and the Center for Disease Control recommended that two doses of the vaccine be administered to all children residing in the United States, instead of the one dose which was being used up until that point. Using only one dose, 95% of children would be protected against the disease triad, while after a second dose, 99.7% of children nationwide would be protected. Because the second dose offered such a high protection rate, the diseases would be nearly eradicated in the United States if all children were given the vaccination. The first dosage is recommended to be administered when a child reaches 12-15 months of age and the second dosage between 4-6 years of age (Immunization Info Online).

The MMR vaccine is a combination of live attenuated viruses used to prevent children from developing measles, mumps, or rubella (Center for Disease Control and Prevention Online, 2007). Until recently, the vaccine has contained Thimerosal, a mercury containing organic compound. Thimerosal has been used in various vaccinations since the 1930s and there is no significant evidence supporting the claim that it poses a threat to vaccinated individuals (Center for Disease Control and Prevention Online, 2007). In 1999, Thimerosal was removed from many vaccinations as a precautionary measure, including the MMR vaccinations as claims were made that the chemical compound may have exposed children to unnecessary, excessive amounts of mercury (Madsen, 2002).

Many parents believe that their child’s pervasive developmental disorder was caused by the MMR vaccination. Because the early warning signs of these disorders begin to surface at approximately 18 months age and the vaccination is given just a few months prior, the MMR vaccine makes for a good scapegoat in this controversy. In 1998 a study by Wakefield, et al. was used to test this theory. The experiment had a great deal of limitations, including that the sample size was only 12 children. This study indicated a correlation between autism and the MMR vaccination, but due to the small sample size it cannot be viewed as a comprehensive analysis of the issue (Center for Disease Control and
When attempting to determine the cause of any disease or disorder, it is imperative to take into consideration the many factors that could contribute to the problem, no matter how significant or trivial the contribution may seem. One of the biggest obstacles incurred in determining the cause of pervasive developmental disorders is that we are dealing with children who often cannot appropriately express themselves, if at all. In these cases, researchers must rely on parents, many of whom are quick to try to blame anything they can for their child’s disorder. This poses a great risk, as unsupported theories can begin to circulate and cause much scientific and public debate, such as the case with the MMR vaccination. Additionally, because there are five types of pervasive developmental disorders, researchers must carefully examine the possibility that each one may be caused by a different factor. Taking into account all of the knowledge and insight we presently have in respect to these disorders, it seems that there is a single probable cause for pervasive developmental disorders.

Each human has a unique set of genetic material. While family members share similar genomes, no two people have identical genomes (aside from identical twins). In the case of identical twins, when one twin suffers from a pervasive developmental disorder, there is an 85% chance that the other twin will have some degree of impairment as well (Constantino, 2005). This alarming statistic shows us that autism spectrum disorders must have a definitive biological nature, and that a group of genetic anomalies shared amongst family members are contributing to the disorders. As previously discussed, patterns of inheritance dictate that not all members of a family will actively express the genes related to pervasive developmental disorders; however, these phenotypically normal family members may be carrying the detrimental genes and passing them on to their children. While the exact genetic material involved in these disorders has not yet been determined, we can be sure that a genetic component does exist based on the statistics involving identical twins and sibling recurrence rates.

The genetic basis of pervasive developmental disorders alone is not enough to explain why different children express the disorders to varying degrees. Additionally, at this time there is no explanation for why diet and other lifestyle alterations have miraculously cured some children of their disorders and not others. The best way to describe this phenomenon is to understand that all people process stimuli differently. Just as some people have a higher threshold for pain or loud noises; children have different mechanisms for reacting to other environmental stimuli. Many cases have been documented where children have been cured from autism upon removing wheat products from their diets, while this does not help other children in the slightest. In these cases, it is likely that both sets of children have the genetic makeup related to autism, yet the onset of symptoms could have been triggered by an environmental factor, in this case the addition of the protein gluten into the diet. In these cases, the protein found in wheat could have activated the genes responsible for expressing autism. When the stimulus is removed, the child’s body no longer needs to react to it, and the characteristics of autism may be significantly reduced or entirely disappear.

The case for the Measles, Mumps, Rubella vaccination having anything to do with the onset of autism is very weak. While the timeframe for the initial dosage of the vaccination and the typical onset of autism symptoms do seem to coincide, the vast majority of medical research explains that this is a coincidental finding and that the
vaccination has no meaningful effect on whether or not a child will develop a pervasive developmental disorder. Even if the MMR vaccine was found to play a role in the development of an autism spectrum disorder, the vaccine itself would be acting as an environmental agent and not as the underlying cause for the disorder. If the MMR vaccine was the real problem, every child who has been vaccinated would have developed a pervasive developmental disorder. In the unlikely event that the vaccine has anything to do with these disorders, children would be expressing the disorders due to their genes being activated by a stimulus, in this case the MMR vaccine.

The idea that genes react to environmental stimuli can be further explained when examining the case study regarding the rise of autism in select areas of California. The study found that when mothers were exposed to harmful organochlorines during their first trimesters of pregnancy, their children were 6 times more likely to develop a pervasive developmental disorder than the control group. It is very likely that prenatal exposure to these pesticides could have activated the genes involved in autism, or could have triggered genetic mutations which in turn caused the children to express autism spectrum disorders.

The most necessary component in solving the autism puzzle is determining which genes are responsible for causing autism spectrum impairments. Medical research has already made great strides in attempting to isolate these genes, and have recently found the first of these genes on chromosomes 7 and 15, which are also the sites of many other genetic disorders. Determining the location of the other genes responsible for pervasive developmental disorders will enable doctors and scientists to figure out how to better understand, explain, and eventually treat children diagnosed with these devastating illnesses. After isolating these genes, it will be possible to perform genetic testing on individuals trying to conceive children, so parents will know if their child is at risk for developing an autism spectrum disorder. Additionally, gene therapy may be useful in treating and correcting the problems that pervasive developmental disorders can cause. Lastly, greater knowledge of the biological basis of these disorders will lead to a further understanding of how environmental agents work to alter or intensify the phenotypic expression of these genes.

Although pervasive developmental disorders are on the rise in the United States and throughout the world, it is important to recognize that diagnoses are on the rise and not necessarily the disorder itself. With advances in modern medicine and technology, as well as increased public awareness about disease and disease prevention, it seems natural that more and more children are being diagnosed with a pervasive developmental disorder. In terms of the medical world, autism is a relatively new frontier and was not well studied in the past. The disorder was only discovered in 1943 and Asperger's Syndrome was only introduced as a viable medical diagnosis in America in 1994. With this being true, it makes sense that diagnoses are on the rise, as more and more parents are learning about PDDs and physicians are able to understand and recognize the signs and symptoms. In years past, children presenting classic signs of autism may have been labeled mentally retarded instead of receiving what we know now to be the proper diagnosis. It may be that the labels have changed, but the frequency of the disorders has always been the same. This is something that we will never be able to know, as we cannot go back in time and re-diagnose patients. Fortunately, there are many physicians and scientists who understand the magnitude of the problem with pervasive developmental disorders, who are dedicated to researching and finding a cure for tomorrow’s children.