

Prenatal and perinatal factors in autism

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Autism is a neuro-developmental disorder that remains largely mysterious. The incidence of autism is on the rise, not just in Puerto Rico, but globally. Local research institutes, like the University of Puerto Rico's, FILIUS Institute of Disability and Rehabilitation, have contributed greatly to both research and its practical application, helping a great number of people with autism and their families. However funding is scarce and governmental bureaucracy is often complex and slow-moving, often times cutting short the potential of those involved in investigation. Fortunately, a new law to combat Autism was passed in December 2006, which allots 217 million dollars to the Federal government for additional research in autism, providing hope that new insights can be gained into the complex nature of autism. Current investigations into prenatal and perinatal factors of autism are taking place at both the genetic and non-genetic levels. However, much of the research is contradictory. This is partly due to the fact that methodologies are varied. Researchers are beginning to see that if headway is to be made in uncovering the causes of autism, research must begin to reflect the complex nature of the disorder itself, as until now the analysis and compilation of data is often isolated within the confines of one particular discipline to the exclusion of others, which might also have relevant contributions to study results. Therefore, investigators are calling for research to be done on an interdisciplinary level. Discipline specialists are still learning how to work together as a single unit, because each for so long has been intensely specialized and focused on their respective fields.

Current research investigates whether or not there exists a genetic predisposition to autism and attempts to uncover the ways in which an embryo affected genetically in the prenatal stage. A gene is a basic unit wherein information is encoded which, in turn, determines the particular characteristics of an organism. Any change that occurs within the information encoded in the gene (denoted by a letter) will have an effect on the function specified, the protein produced and the metabolism of the cell. Certain changes on the gene level can occur such as, the elimination of a letter or the exchange of one genetic letter for another, resulting in genetic information being copied erroneously during cell growth. Any of these changes will affect the information that this genetic base receives. Recent studies are bringing to light that, not only are there internal modifications taking place, but that there exists the possibility for external modifications to also take place. These modifications affect the way genetic information is transmitted. The genetic

base can receive external codification, which might affect the way the information is encoded within the cells. Although genes are very vulnerable, cells are well equipped with an enormous capacity to repair a certain level of genetic modification; however, if the modifications supercede the capacity of the cell to regenerate the information a genetic mutation will occur and changes in cellular function will be evident.

The effect of the time at which the gene mutation occurs is also an important factor currently under investigation. It appears that cells are particularly vulnerable to these changes in the genetic structure early in gestation. The impact of infections or other immunological factors, of a gene can effect a change in the gene, which in turn will affect the behavior of the transmission of information and eventually affect the information contained in the chromosome as a whole and, thereby, the fetus. The first two weeks to the second or third month after conception is a very sensitive time. Disturbances which occur early in the gestational period are more likely to cause a more severe genetic mutation. If the gene does, in fact, continue to be normal, there is still the possibility that cell production will be modified.

Overall, it is very difficult at this time and with the technology we have, to measure the impact and to study these phenomena as they relate to autism because the variables are too many and too diverse. There are no genes which specifically cause autism. Rather, autism is a condition attributed to polygenetic factors. Genetic inheritance by the mother or father may cause an increased susceptibility and predisposition to certain conditions which may, in turn, be associated with autism. Studies have found that in families where there is an instance of autism, there is an increased chance, approximately 2 in every 100, of recurrence. This is ten times the norm in the general population. But much investigation still needs to be done because much of the research in this area has, again, contradictory results.

One important area of intense research into prenatal factors contributing to autism is the investigation of genetic linkage, the phenomenon whereby alleles, minor variations of the same gene, at loci close together on the same chromosome will tend to be inherited together. In terms of determination of a genetic predisposition to autism, it is important to mention that, although much focus is given to the mother, the father is also under investigation. That is not to say that the genes of both mother and father must be investigated. If both parents share a genetic predisposition, the offspring's genetic disposition to certain illnesses will be increased. But at this point it is still very difficult to measure to what degree.

The significant increase in the number of children diagnosed with autism in recent years, has also led scientists and researchers to explore non-genetic prenatal factors in the environment, which may be at least partially responsible. The prenatal environment remains an area still under intense investigation. The mother's state of health will affect the environment of the fetus. Conditions such as obesity, anorexia, and diabetes have shown to have an effect on a fetus' immune system. In the same light, the consumption of caffeine, alcohol, and drugs (prescription or illegal), especially in the first two weeks of gestation, can be extremely dangerous. Often during this time a woman might not know she is pregnant. One area of recent interest to researchers has been the investigation into disturbances during the process of neural tube closure, which takes place between days 20–34 of gestation. At this time, disturbances related to drugs, such as thalidomide and certain retinoids, have been hypothesized as a possible cause of autism (Duggan & Schmie, 2006)

Perhaps one of the greatest dangers that women face today is the duration and intensity of stress levels that have been steadily on the rise. The effect of stress on women and other conditions such as depression, especially during the time of pregnancy, is currently being investigated. Stress often causes an imbalance in hormone levels and may have an impact on the development of the fetus' brain. Studies show that pregnant women under high levels of stress were found to have higher levels of testosterone, cortisone and serotonin, hormones which can be activated under stress. High levels of these hormones were also found in the baby. Studies show that babies with autism have been found to have high levels of serotonin. Autism and high levels of cortisone and serotonin have been shown to be related, but there is a large amount of statistical error in these studies so research and testing need to be redone.

In trying to determine prenatal factors in autism, the disorder must be looked at through a socioeconomic lens as well. Neurological and metabolic processes for the mother and the effect they have on the fetus have proven contradictory. Unplanned pregnancy is a great concern and Puerto Rico in particular, has a high rate of unplanned and adolescent pregnancy. To complicate this matter even more, a large portion of the population uses governmental medical plans. The process of getting into prenatal care is bureaucratic and often times delayed. By the time the woman applies for the medical plan, especially government plans, one and a half months has usually passed- a critical developmental time for the fetus, in light of the fact that the neural tube closes after 20-34 days. Thus, if this time is passed without the care of an obstetrician, the results

can be devastating, since a woman, unaware in the first weeks that she is pregnant may continue to make uninformed health choices such as, the use anti-depressants, tobacco, alcohol and low-fat dieting.

There are many factors which can arise shortly before, during, or shortly after the time of birth, which may provide clues to our better understanding autism. Many studies have been done on perinatal risk factors; however the results have largely been contradictory. Analysis and compilation of data has been very difficult and sample sizes and methodologies have varied greatly. There also exists the additional problem of mothers and fathers, failing to disclose certain conditions from their doctor such as, use of toxins and sexually transmitted diseases (STD's), for reasons of shame and embarrassment, not understanding the potential effect these secrets can have on the baby.

New research is looking for clues to autism in the placenta. The development of the placenta plays an important part in the birthing process, and the synchronization between mother and baby can be traced in the placenta. This relationship between the placenta and the baby is an important one which should not be overlooked. If the baby has been born with genetic defects, the placenta has been found to also contain genetic abnormalities. Thirty percent of mothers bleed during pregnancy. The blood comes from the placenta and can affect the environment in which the baby develops. If there is an increase in hormones in the mother, the baby will also experience it. The impact of this is especially important if it occurs during the development of the baby's central nervous system. However, the placental environment, though it provides important clues, is also extremely difficult to measure.

Recent studies have detected the presence of trophoblast inclusions, which are abnormal folding of microscopic layers in the placenta and appear to result from altered cell growth. Studies found that placentas for children later determined to be autistic were three times more likely to have the inclusions (n.d.) Widespread recognition of this fact among healthcare workers in the delivery room would allow for a tentative diagnosis at the time of birth rather than at two years of age.

There are other risk factors which have statistically been correlated to an increased risk of autism in obstetric events. The birthing process itself gives rise to many factors which might contribute to autism. One commonality found in babies later diagnosed as autistic is the experience of a prolonged labor. The reasons for this are still unknown and are not a matter of

cause and effect. The situation is largely circumstantial. Stress during labor can be a factor, and how this stress manifests, is yet another factor. Induced labor has resulted in a greater incidence of autism, and the fear of medical malpractice on the part of both patient and doctor.

There have also been many studies focusing on single perinatal factors. Autistic children have been found to have low APGAR test scores. APGAR is an acronym for a newborn test assessing: activity, pulse, grimace, appearance, and respiration. This test is administered at the first and fifth minutes after birth to assess the overall health of a baby. It is reliable up until the eighth minute and not to be done after the tenth minute. In addition to low APGAR scores, low birth weight, premature birth, breech births, cesarean section and congenital abnormalities trauma have all been associated with autism.

These factors must also be looked at in combination with other circumstances surrounding the pregnancy, such as the age of parents. Women greater than 30 and men greater than 35 have been found to be statistically related to an increased risk of autism. Other factors include use of contraceptives such as the pill, use of medicines during pregnancy, uterine bleeding, vaginal infection, auto-immune disorders in the mother and muscle tone of mother which can either facilitate or hinder the birthing process. Factors can also be psychological in nature, such as a mother's hesitance and resistance to pass through something like labor or fear of doctors.

Conclusions

Determining the cause of autism is an extremely difficult task largely because of the sheer individuality and number of factors involved. Both genetic and non-genetic environments must be examined. Methodological differences, changes in diagnostic criteria, data compilation, analysis and reporting errors, misclassification and misdiagnosis of the disorder, reproductive risk factors, and socioeconomic factors all have been associated with autism. Moreover, there has been little research as to whether there exists ethnic variation in terms of predisposition to autism and how this might apply specifically to Puerto Rico. Right now, the interaction among all of these variables can appear to differ in each situation and case of autism, and elude the scope of current research. This explains why the results of many studies have been contradictory. However certain things can be done.

Education is very important for the prevention of potential genetic and non-genetic disturbances. Getting prenatal health from the very beginning of pregnancy is crucial to the detection of potential risks and damage to the fetus. Education can also contribute to lowering

the rates of unplanned pregnancies and benefit the mother's physical, psychological, and emotional health, all of which have been shown to affect the fetus. However, education alone cannot solve the problem.

As it stands, profound changes need to be made in the way research is undertaken. Investigators must broaden their research horizons. Research must be done, not only in terms of how it relates to an isolated field of scientific interest, but rather on an interdisciplinary level so that a larger picture of the interactions which contribute to autism may emerge. Many specialists have great knowledge of their field but are limited in their perception of how it relates to autism studies occurring in other fields. Therefore, experts in the study of autism from the fields of medicine, biology, technology and behavior sciences, have the responsibility to share their information, and design studies which explore and treat this disorder from an interdisciplinary perspective.

But while there may be a consensus regarding the necessity of interdisciplinary investigations, there is uncertainty as to what this research looks like. Many experts are looking to patient databases as the key to providing important data which can be accessed and analyzed by different disciplines. Currently the law allows for such databases; however, access is, for the most part, denied for research purposes. Databases would provide a middle ground for different fields. Certain steps are being taken toward this goal. For example, the VA Caribbean Health care system in Puerto Rico currently has such a system, which allows patients and medical professionals access to data, and clinical results, both of which can be viewed locally and remotely. Many experts from all disciplines want to expand this idea and apply it on an international level. International databases, set to international standards and which provide access to patient data, would be a key component for researchers from all disciplines opening up a world of information. It is the most logical beginning step for interdisciplinary union.

If underlying complexities contributing to a disorder such as autism are to be revealed and understood, sufficient resources must be assigned. In this way, research can begin to encompass the many fields addressed above, both in isolation and in combination, in order to get a better understanding of all the factors involved.

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