Autism: Recent Research and a Brief Personal Story

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Since the 1970s, the United States has officially recognized April as "Autism Awareness Month."[1] I hope that this paper will provide you with both "awareness" and a greater understanding of autism, as seen through the eyes of a parent of an autistic son.

I have divided this talk into three parts: first, the definition, diagnosis, prevalence and causes of autism; second, a summary of the treatments of autism; third and finally, the story of my autistic son, Joseph, now in his mid-twenties.

Definition of autism

The Autism Society of America defines autism as "a complex developmental disability that typically appears during the first three years of life and is the result of a neurological disorder that affects the normal functioning of the brain, impacting development in the areas of social interaction and communication skills. Both children and adults with autism typically show difficulties in verbal and non-verbal communication, social interactions, and leisure or play activities."

Diagnosis

According to the website of the American Academy of Pediatrics (www.AAP.org), the common symptoms of autism are:

1. The child does not coo by 12 months.
2. The child does not point or gesture by 12 months.
3. The child does not say single words by 16 months.
4. The child does not say 2 or more words by 24 months.
5. The child has lost some of his / her social skills and/or language ability. (This symptom is especially baffling and frustrating for the parents, who see their child begin to develop these skills, then lose them).

About a dozen less common characteristics may be present, among them:

1. No fear of danger. For this reason alone, most moderately to severely autistic children require constant supervision.
2. Over or under sensitivity to pain.
3. Difficulty expressing what he or she wants or needs.

In addition, autistic children may insist on routines always being the same, break into tantrums for no apparent reason, avoid cuddling, and injure themselves when upset, biting themselves or banging their heads.

A commonly used diagnostic tool is the Childhood Autism Rating Scale (CARS).[2] Assigning numeric values in fifteen categories of autistic symptomology, such as "relating to

people," "emotional response," and "verbal communication," a professional can rate a child as non-autistic, mildly-moderately autistic, or severely autistic.

Prevalence

Estimates of frequency, or prevalence, vary widely. In the United States, the CDC recently updated the estimate from one child in 110 to one in 88.[i]

Drawing from all countries where data are recorded, the figure most commonly cited is that one out of 150 children has "autism." However, this figure is based on all five of categories of Pervasive Developmental Disorders (PDD); not just autism *per se*, but also Autistic Disorder, Asperger's Disorder, Rett's Disorder, Childhood Disintegrative Disorder, and PDD-Not Otherwise Specified. (Recently *The Diagnostic and Statistical Manual of Mental Disorders–5* reorganized the categories of autism, and "Asperger's Disorder" is no longer recognized as a diagnosis.) Considering autism by itself, distinct from other PPDs, the figure for all countries is 0.5 - 1 case per 1,000 children.

Is there an autism epidemic? Most experts would say no. However, a broadening of diagnostic criteria, as well as inclusion of all PPD categories, has meant that children who would have been labeled "mentally retarded" or "learning disabled" fifteen or twenty years ago now fall under the all-encompassing umbrella of PDD.

Autism is four times more likely to occur in boys than in girls. Simon Baron-Cohen and his group at Cambridge have long studied the sex differences between female and male brains in the general population and in autistic individuals, concluding that the female brain is better at empathizing (the capacity to predict and to respond to the behavior of agents by inferring their mental states and responding with appropriate emotion) while the male brain is better at systemizing (the capacity to predict and to respond to the behavior by analyzing input-operation-output relations and inferring the rules that govern such systems). Autism represents an extreme of the male pattern—impaired empathizing and enhanced systemizing. Baron-Cohen calls this the Extreme Male Brain model.[ii]

Recent research conducted at Cold Spring Harbor Laboratory (CSHL) in New York discovered that girls actually have *more* genome regions linked to autism than boys do: girls have a median "genetic disruption" of 15.5 genes; the figure for boys is only two genes.[iii] These data show that girls are somehow—the mechanism is not yet known—more resistant to these particular genes that cause autism than boys are. According to Michael Wigler of CSHL, "Overall, it does look like a girl can have the same genetic insult as a boy, but not be diagnosed with autism" (quoted in Sanders).[iv]

Causes

The various genome regions associated with autism affect the neuroanatomy of a developing brain, including gray matter (neurons), white matter (myelinated axons), synapses, and chemicals at the synapses (neurotransmitters). Pathological and fMRI studies have

consistently discovered specific widespread or regional neuropathologies in the autistic brain (Bauman and Kemper; Esciencenews.com; Eurekaalert.org).

New data have uncovered huge numbers of genetic aberrations that cause autism. Typically, rather than a single genetic culprit, a jumble of genetic and perhaps environmental triggers occur for each individual's autism.

Many of these new findings come from Wigler's group at CSHL and a group at Yale led by Matthew State. State's team examined the DNA of 1,124 family cohorts for copy number variations (CNVs), each cohort consisting of two unaffected parents, one child with "high functioning autism spectrum disorder," and (when possible) one unaffected sibling. The number of genome regions in these families with CNVs linked to autism was between 130 and 234. Wigler's group conducted similar research on 887 family cohorts consisting of the same categories; between 250 - 300 genome regions were found with CNVs linked to autism (Sanders, Muthra, Gupta, *et al*.). (The difference in the results is likely due to individual patients' genetic variations and thus not significant.)

In these family cohort studies, unaffected parents have a child with autism, but their other children are not autistic. This is typically the case. So, how do unaffected parents wind up with an autistic child? The answer is that each parent carries a mutation that is not severe enough to scramble or eliminate a gene's function, but the autistic child of two such parents will have a dysfunctional gene or genes. It is more complex than most other genetic conditions that involve parents as carriers, but the idea is similar. This research, according to Huda Zoghbi of Baylor University, "really speaks to the immense heterogeneity of autism. We suspected it, but these data show it clearly" (Sanders).

Treatments: the good, the bad, and the ugly

Since the symptoms and behaviors of autism combine in many ways and vary in severity, good treatment strategies are those tailored to meet individual needs and family resources. In general, the earlier a child is diagnosed as autistic and treatment begun, the better; in general, autistic children respond best to highly structured and specialized treatment.

The AAP recommends these four treatment strategies:

1. *Behavioral training and management.* In this technique, any desired behavior that is the focus of the treatment is rewarded with positive reinforcement. One such program is Treatment and Education of Autistic and Related Communication Handicaps, or TEACCH, developed in the mid-1960s by Eric Schopler, one of the truly great pioneers in autism treatment.
2. *Specialized therapies***,** such as speech, physical and occupational therapy.
3. *Medicines*. No single medicine or class of medications available treats all of autism's wide variety of symptoms, but commonly used medicines include anti-depressants , anxiolytics, and medications for hyperactivity and obsessive-compulsive behaviors.

4. *Community support and parent training***.** Support and advocacy groups for autism are available at the local level in most areas.

Unfortunately, the history of treatments for autism includes not just the good, but the bad and the ugly as well—from well intentioned but questionable alternate therapies without documented efficacy to out-and-out scams. "Accounts of individual success are not sufficient evidence to support a treatment. Look for large, controlled studies to validate claims," cautions the AAP. This is excellent advice, and not just for autism.

I place the following treatments in the "bad and ugly" category not necessarily because they are harmful, but because their effectiveness in ameliorating autistic symptoms and behaviors has not been verified by rigorous scientific testing. Many of these methods are in continued use today because of anecdotal accounts of their success and emotional, rather than logical, persuasiveness of their defenders.

A.I.T. Auditory Integrated Training, or AIT, was founded in France in the 1970s by Guy Berard as a cure for autism, depression, and suicidal tendencies—even dyslexia (Wikipedia). Therapy typically consists of twenty half-hour sessions over ten days listening to specially filtered and modulated music through headphones. Every scientific study of AIT has failed to demonstrate its efficacy. The FDA has banned the importation of the "Audiokinetron," or any other AIT device, due to lack of evidence of medical benefit.

Gluten-Free, Casein-Free Diet (GFCF). Many families claim that their autistic child showed marked improvement by following a GFCF diet, which eliminates wheat (gluten is a protein found in wheat) and casein, a protein found in dairy products. Scientifically rigorous studies show no significant improvement in autistic symptoms for children following the diet. Susan Hyman, who studies GFCF diets and autism, concluded "It would have been wonderful for children with autism and their families if we found that the GFCF diet could really help, but this study didn't show significant benefits" (ABC News, "A gluten-free…").

Secretin therapy. Secretin is a hormone released by the small intestine to stimulate pancreatic digestive enzymes. In 1998, a study reported an improvement in the social and language skills of patients with autism spectrum disorders after secretin administration (Horvath *et al*.). The study was uncontrolled and consisted of only three subjects, but a link between secretin and behavior was somewhat plausible, as release of the hormone is modulated by the vagus nerve, a cranial nerve that has actions on the autonomic nervous system, including responses to social situations. So, despite the paucity of data, secretin therapy became widely used.

In further research, secretin as a therapy for autism has been proven ineffective. In a 2005 review of 15 double-blind, random, placebo controlled trials of secretin therapy, almost none reported any significant effects, and none concluded that secretin was effective (Sturmey).

*Facilitated communication***,** or FC, uses a small, portable keyboard device so that autistic individuals can type out their responses to questions asked of them. They cannot do it by

themselves—a "facilitator" supports their arm at the wrist, and using gentle pressure, helps them guide their fingers to the letters on the keyboard. In the early 1990s a Syracuse University professor, Douglas Biklen, extolled FC's virtues as a way to communicate with non-verbal autistic children (Biklen), and the technique caught on, due in large part to extensive media coverage.

Benign though treatment seems, ugly accusations began to surface. Some therapists, mostly speech pathologists, reported their clients typing out graphically detailed allegations of sexual abuse. In many cases, the accused person was arrested and charged. The charges eventually would be dismissed, with questions raised whether the facilitators were, in fact, guiding their young clients to make the unthinkable accusations.

In 1994, the APA deemed FC "an unproved communicative procedure with no scientifically demonstrated support for its efficacy." Their position has not changed (ABC News, "Not just the Wendrows").

Anti-vaccine panic. Although it is not a treatment, the anti-vaccine panic that linked the measles-mumps-rubella (MMR) vaccine with autism also goes to show the damage that rumor and flawed research can inflict on easily frightened parents. Andrew Wakefield's 1998 paper linking the vaccine to autism appeared in a distinguished medical journal, *The Lancet*, and set off a wave of newspaper articles and talk-show discussions.

However, in 2010, *The Lancet* retracted the paper, and in 2011 the *British Medical Journal* called the paper an outright fraud, having found clear evidence of falsification of data and further claiming that Wakefield sought to exploit the ensuing MMR scare for financial gain. He had taken more than 674,000 dollars from lawyers who had intended to sue vaccine manufacturers.[v]

Even though numerous scientific studies have failed to show any link between autism and the MMR vaccine, many parents still avoid having their children immunized, putting not only their own children but also others in the community at risk of developing serious diseases.

My autistic son, Joseph

Our son Joe had a traumatic, premature birth at twenty-nine weeks gestation, and spent the first six weeks of his life in a neonatal intensive care unit. He weighed a little over three pounds at birth.

As an infant, he seemed fine, and my wife and I felt fortunate that he had survived and avoided all of the major medical complications associated with preemies. By the time he turned one, however, we knew aspects of his development were delayed, and he began to have unusual behaviors in the ensuing couple of years. He was diagnosed with autism at age four.[vi]

After his diagnosis in 1990, Joe attended a pre-K program for autistic children at the University of South Florida in Tampa. The idea was that the children could receive "state of the art" treatments and education techniques for autism. The teacher was certified in the TEACCH program mentioned above. I don't know whether the class helped Joe or not; I did have concerns

that exposure to only other autistic children might cause him to emulate inappropriate behaviors, but who knows?

The next year, we flew with Joe from our home in Florida to Chapel Hill for him to be evaluated by Dr. Schopler's TEACCH team at the University of North Carolina, intending to move there for Joe to participate in the TEACCH program, which was not available in Florida. He was extensively tested over two days, and his autism diagnosis was confirmed, at a "severe" level. However, Dr. Schopler advised that uprooting an entire family for the benefit of just one member was not a good idea, and we decided not to move.

Thus, Joe entered the Special Education system in Florida, and I have nothing but good things to say about the professionalism and commitment of the faculty, principal, and various therapists that provided Joe's public schooling in special education.

We tried several of the "bad" therapies I mentioned earlier. Despite my skepticism, Joe received A.I.T. at about age eight. The sessions did not appear to cause him any harm, but he showed no signs of improvement. Working with a gastro-enterologist, we tried the GFCF diet on Joe when he was twelve, but gave up after three days because it was causing him rampant diarrhea. (One study reported the diet caused diarrhea seven times more often in an autistic group than in controls.) I was also skeptical of Facilitated Communication because the technique reminded me of an Ouija board, but fighting down my skepticism, I found a speech pathologist that did FC and took Joe to see her. She allowed me to witness the sessions, and mostly he typed out gibberish without looking at the keyboard. Words or phrases occasionally emerged, but it seemed to me the therapist was putting words in Joe's fingers, so to speak, though perhaps unconsciously.

Joe was given the CARS test at age 14. His score put him in the "severely autistic" category, but at the higher end of the range for functionality. It took many years before the optimal classes and dosages of medications for him were discovered, but in 2007, at the age of twenty, Joe graduated from Carson High School in Rowan County, North Carolina, with a degree in Special Education.

Today, Joe has an excellent day-care worker three days a week, and each year we enter him in the lottery for the week-long summer camp provided by the North Carolina Autism Society. Joe has been selected randomly from the lottery pool about 50% of the time, each time he has gone, he has seemed to thrive and blossom.

Life is seldom easy for autistic persons or their families, but thanks to legitimate research, things are slowly getting better and the old stereotypes are being overcome.

Notes

[i] www.cdc.gov/ncbddd/autism/data.html; A detailed analysis of the CDC findings is presented by Baio (see bibliography).

[ii] Many of Simon Baron-Cohen's publications are presented in vol. 43(1) of *Mensa Research Journal*, 2012. He is the recipient of the 2010 International Lifetime Achievement Award presented by Mensa Education & Research Foundation.

[iii] These findings refer only to *copy number variations* (CNV), which are alterations of the DNA of a genome that results in the cell having an abnormal number of copies of one or more sections of the DNA. Copy number variations correspond to relatively large regions of the genome that have been deleted (thus, fewer than the normal number of copies) or duplicated (more than the normal number) on certain chromosomes. For example, the chromosome that normally has sections in order as A-B-C-D might instead have sections A-B-C-C-D (a duplication of "C") or A-B-D (a deletion of "C). See http://en.wikipedia.org/wiki/Copy_number_variations.

[iv] For publications by Wigler, see www.cshl.edu/Faculty/wigler-michael-professor.html

[v] The James Randi Educational Foundation's annual *Refusal to Face Reality* "Pigasus Award" went to Wakefield. See "The 5 worst promoters of nonsense," 01 April 2011, *JREF News*. (http://randi.org/site/index.php/jref-news/1260-pigasus-2011.html)

[vi] I wondered at the time of Joe's diagnosis whether the birth trauma he had endured was associated with his autism. Recently, the journal *Pediatrics* published the results of a major study finding that babies born before thirty-seven weeks gestation were five times more likely to have autism than those born on time with normal weights. Pinto-Martin, the lead author, postulates that brain hemorrhage, a common complication of premature birth, could be a factor in the high incidence of autism that she discovered. See the article, "Premature babies 'have higher risk of autism' as scientists discover link between the condition and low birth rate." (http://www.dailymail.co.uk/health/article-2049875).

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*Biographical Note

After obtaining a B.A. and M.A. in Zoology at Miami University in Oxford, Ohio, Randy Martin received a Ph.D. in Biology at Florida State University, Tallahassee, Florida. His primary field of study was animal behavior; specifically, he studied sexual and aggressive behavior in fishes.

After completing Post Doctoral studies at the University of Florida, he was an Assistant Professor in Biology at North Carolina A & T State University, Greensboro, NC, where, in addition to teaching, he continued his research into fish behavior.

When his wife, Sharon D. Martin, M.D., began her practice in Cardiology, Dr. Martin left academia to be a stay-at-home father, eventually raising three children. As the children grew, he held various part-time positions, including Adjunct Professor at various community colleges in Florida and North Carolina, Environmental Specialist at an engineering firm, and Assistant Director at an Archaeological Research Institute.

Dr. Martin and his wife, both retired, live in Maggie Valley, NC, with their autistic son, their daughter and son-in-law, and a menagerie of dogs and other pets, including fish, snakes, and spiders.