A New Look At the Vaccines and Autism Debate

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On February 28th, 1998 an article in *the Lancet* set off a media firestorm, which launched a major social movement, spreading a rumor which continues to reverberate around PTA meetings, parents' magazines, and pediatrician's offices to this day. Andrew Wakefield, a British transplant surgeon, published findings from twelve children with autism, a developmental disorder characterized by emotional, social, and language processing difficulties. This study claimed to find evidence for an autoimmune problem in autistic children that could cause their own bodies to attack the brain. These children all had experienced a severe regression in development at the time of onset of their behavioral symptoms, and their immune system and behavioral symptoms had begun at the same time. Wakefield noted that this regression in eight out of the twelve cases coincided with the administration of the measles, mumps, and rubella (MMR) vaccine, suggestive to Wakefield, of some sort of immune reaction. Though the study had only 12 participants, was very preliminary, and lacked statistical evidence to establish any sort of clear relationship between autism and the MMR vaccine, the paper's authors felt the need to hold a press conference to announce their results[1]. While the paper itself said explicitly that the authors had not proven any link between autism and vaccines, Wakefield strongly advised against the administration of the MMR vaccine to children, as he felt their immune systems might become overwhelmed, leading to autistic behavior and pathology[2].

Given the increasing public interest in the issue, and the obvious implications, scientists across the globe began to study a possible relationship between autism and the MMR. Epidemiological studies failed to find any relationship at all between the two[3], or between autism and any other type of vaccine. Do vaccines cause autism? For many scientists the answer to this question is an unequivocal no.

Autism is a spectral disorder, which means that autistic children have many different behaviors and neural changes, with differing degrees of severity and still fall under the umbrella term "autistic". Most individuals with autism have mutations that affect genes that regulate processes in neural development—potentially leading to these adverse changes in their brains[4]. These genes are "environmentally sensitive", that is, many individuals with mutations can be perfectly normal. Only when an individual has these genes and comes into contact with some sort of environmental stimulus (for example, exposure to some sort of toxin) does this person become autistic. People with autism have genes that give them an inherent weakness for developing autism, and were then exposed to some sort of "trigger" that made them autistic.

For many anti-vaccine advocates, the reason behind why epidemiological studies have failed, again and again, to find a link between autism and vaccines, is due to this spectral nature of autism. There are thousands, if not millions of different combinations of possible gene mutations found in autism, which may be triggered to cause an autistic phenotype by a vast variety of different environmental stimuli. A stimulus that triggers autism for one type of underlying genetic weakness might not cause autism in another. Thus, an epidemiological study of autistic people in general could easily, theoretically, fail to show a connection between autism and vaccines, because vaccines might be implicated in only a very small subset of autistic cases.

The trouble is, anti-vaccine advocates have never been able to establish that a particular set of symptoms, or a particular set of gene mutations are related to their proposed vaccine-induced autism. Instead, anti-vaccine advocates claim to find connections between vaccines and pretty much all types of autism, and developmental disorders in general. Evaluating proposed theories for how vaccines could cause autism becomes difficult, because neural changes in autism are extremely diverse, with a great deal of variability in what an "autistic brain" looks like. However, there are certain, general features common to most (but certainly not all) autistic cases that given the reported pervasiveness of vaccines causing autism, anti-vaccine advocates' theories would have to account for.

The stereotype of an autistic person is someone off in their own little world, talking only to themselves. Studies find that autistic individuals have increased local connectivity, and drastic decreases in long-distance connections[4], so each part of the brain is spending too much time talking t itself, and has trouble communicating with other parts of the brain. Essentially, the different parts of the autistic brain are autistic. The inputs from the different brain regions are having trouble coming together to form "big picture" ideas, which may be why individuals with autism seem to have difficulty grasping more complex, nuanced concepts like emotions, or social dynamics.

The autistic brain grows much faster than normal brains during the first 2-3 years of life[4], not because their development is somehow speeding up, but because autistic children, for whatever reason, seem to have many more neurons (brain cells) than normal[4], so normal size increases become amplified. Because the brain has to take up a finite amount of space in the skull, having extra cells makes it difficult for the brain to grow normally, as the cells end up squishing each other, and aren't able to grow and develop properly[4]. There is some debate as to why autistic children have so many more neurons, but it appears to be due to a defect in either controlling the numbers of neurons produced or the numbers, which die over the course of early neural development[4].

Infants are born with virtually all the neurons they will ever have. During fetal development, neurons in the cerebral cortex, whether they are destined to be involved in visual processing, or solving math problems, are made in a special area near the center of the brain, and then packaged and shipped to their particular specialized brain region. The cerebellum has a separate, but similar system. After all the cells are in place, they start linking up and creating the connections that allow the brain to function. By birth, most of the major information pathways are there, and throughout the first several years of life, the brain continues to develop them. The brain continues to fine-tune these connections, but the major hook-ups happen either before birth or during the first few years of life. Because these information pathways are so critically important, and because the brain cannot create any new neurons after birth (at least not in the cerebral cortex), the brain errs on the side of caution actually makes many more neurons than actually needed. While the connections in the brain are being established, the cells that end up not being needed are killed off to make room so that the brain can continue to grow and fully develop.

Having too many neurons is a serious problem, not just because of space concerns, but because of the way information is processed in the brain. In normal brains, which cells live and which cells get killed off appears to be decided based on how good their connections are—cells that found their way to the correct part of the brain, and

established the right connections get to live, cells that messed up, somehow during the course of development and either ended up in the wrong area, or failed to make the correct connections are killed off, preventing bad connections and aberrant signals from disrupting the normal flow of information. The brain is, in a way, sculpted, so that only the cells that are capable of correct brain function survive.

In autism, while it is debated as to whether or not too many neurons are produced in the first place, it is clear that not enough neurons are being killed off[4]. Too many cells that formed bad connections are surviving, preventing information from being processed properly because there are too many aberrant, disruptive signals. Neurons are so cramped that many are unable to establish connections outside their immediate surroundings, leading to too many local connections, and not nearly enough connections between brain regions. Cells that failed to migrate properly to their correct brain regions are retained in autistic brains[4,5,6], their abnormal placement and activity further disrupts brain function.

Over time, as autistic children age into adulthood, these unwanted neurons begin to die in increasing numbers, but it seems to be a matter of "too little, too late." The neurons that would have been ordinary, and healthy, had apoptosis lead to the death of neighboring cells, are crowded out—unable to grow properly, or form correct synapses[4]. Much of the brain's connections have to be formed by a certain period of time—language, for example, is developed largely in the first decade of life—thus, autistic brains finally begin to become ready to develop much later in life, but by then it's too late for the right connections to be made. It's like showing up to run a marathon the day after it was held—you can't run the full course anymore, because the city has reinstated the usual traffic patterns, and you'll never be able to run the race in quite the same way.

As to how vaccines could be disrupting this neural sculpting, two theories have been put forward. The first suggests that the immune systems of children who develop autism get over-activated in response to the vaccine, and end up attacking not only the inactive virus from the vaccine, but also proteins in the brain[7]. The second claims that the mercury-containing preservative thimerosal induces an autoimmune response[7]. Thimerosal is broken down by the body into ethyl mercury[7], which anti-vaccine activists confuse with methyl mercury, a similar but not identical substance common environmental contamination that has been found to suppress immune system[7]. Anti-vaccine enthusiasts give no clear explanation as to how immune system suppression leads to over activation. Thimerosal, as a preservative, is being gradually phased-out of most vaccines to assuage these concerns[8], however, the numbers of reported cases of autism still continue to increase[9]. However this spontaneous autoimmunity is generated, this proposed assault by the immune system on the brain at around 2-3 years of age is purported to be causing normal brains to become autistic ones.

Scientists have been unraveling the mysteries of neural development for decades, and it is here that anti-vaccine proponents' theories are on the very thinnest ice. By 2-3 years of age, autistic brains are already 10% larger, than normal[4]. Thus, if vaccines are somehow preventing the normal killing off of extra, unwanted neurons, in order for autistic children's brains to increase by 10% relative to normal children within a period of less than a year from vaccination to brain scan, then over the course of normal development, cell death would have to increase in normal, healthy children such that their brains would shrink 10% in a matter of months—a fairly dramatic change. As many studies can attest, humans do not, generally, undergo a routine, sudden brain shrinkage at

around 2-3 years of age, making the possibility that vaccination is able to prevent this cell death unlikely, to say the least. Even if this immune system over-activation were a chronic, rather than acute response (thus with every inoculation the problem gets increasingly worse), many more neurons would have to be dying in normal children than appears to be the case[14].

Undaunted, many anti-vaccine advocates suggest that over-activation of the immune system triggers a temporary re-activation of the parts of the brain which produced neurons during fetal development, leading to an overall increase in the numbers of cells in autistic brains[4], over a period of *8-22 days* from vaccination to the beginning of symptoms[10]. Some suggest even earlier—within *24 hours* following inoculation[15]. Apart from there being no evidence for continued creation of new neurons in the cortex after the end of fetal development[11,12], it takes new neurons an estimated *28-56 days* to migrate to their proper position and form mature, active connections[13]. There just isn't enough time between vaccination and the beginning of autistic symptoms for enough new neurons to be born and form connections to even remotely resemble an autistic brain. There is also the obvious problem that in order to have the 10% increase in brain size reported for autistic children at that age, the child's brain would have to be increasing by that much in *1-3 weeks*. If the "sudden head shrinkage" over a matter of months was ridiculous, this goes far beyond that.

If this proposed temporary re-activation of neuron-production were to occur in response to chronic immune over-activation due to successive inoculations, there still is the problem as to why anti-vaccine advocates are suggesting that autistic behaviors appear so suddenly they can establish a time course between a particular vaccination and the beginnings of symptoms. While many absent behaviors associated with autism do not develop in normal children until 2-3 years of age, and thus are noticeable in their absence, a number of other autistic behaviors are observable earlier, and would be expected to change if vaccination really did cause autism. Many reported cases of "vaccine-triggered autism" occur in children older than 2-3 years of age, when behaviors that classically distinguish autistic children from non-autistic children have almost certainly been fully developed. If the reason for why gradually increasingly autistic behaviors weren't being observed prior to the last inoculation is that at a certain point, the neural problems become so great that the autistic behavior develops—that still doesn't explain why this tipping point would occur so soon following vaccination, when any neurons born from a reinstatement of neurogenesis would not have had enough time to migrate and mature to cause that kind of damage.

There simply isn't any evidence, or any logic in the claims that autism is caused by vaccines. Even if the epidemiological studies were too broad to find a narrow subset of autistic cases that could actually be caused by vaccines, the proposed mechanisms for how vaccines could cause autism fail to account for any of our current understanding of how neural development works. Anti-vaccine advocates are suggesting things about the brain that not only do they have no evidence for, they don't appear to fully understand. The brain is an amazingly complex, powerful organ, capable of immense change and structural reorganization, but such extreme changes, as seen in autism, take time. Massive changes in neural architecture can't happen overnight. There simply aren't any logical mechanisms as to how vaccines would be able to cause autism. Yet every year children in the United States die from diseases that are fully preventable with vaccination, because so

many people believe that vaccines are dangerous. This is the danger in not thinking an idea fully through. There is absolutely no reason on earth why there should be sudden re-emergences of diseases like measles, mumps, or whooping cough. So please don't wait, vaccinate.

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