MERCOLA
Take Control of Your Health

Discoveries May Unlock the Link Between Vitamin D Deficiency and Autism

Analysis by Dr. Joseph Mercola | March 03, 2024

STORY AT-A-GLANCE

- Vitamin D gets converted into a steroid hormone that regulates over 1,000 different physiological processes, and controls around 5% of the human genome
- Vitamin D regulates a gene responsible for the conversion of tryptophan into serotonin. Serotonin is crucial during fetal brain development. When vitamin D is lacking, so is serotonin, which can produce neurological defects
- Vitamin D insufficiency may heighten maternal autoimmune responses by hindering tryptophan from being metabolized (by a second pathway) into kynurenine, which forms autoimmune-fighting T regulatory cells

Editor's Note: This article is a reprint. It was originally published February 14, 2016.

When I was in medical school more than 32 years ago, the incidence of autism was 1 in 10,000. Today, the incidence has climbed to less than 1 in 50, according to CDC statistics.[1]

Projections from reputable experts suggest that within 10 to 20 years, HALF of all children will have some form of autistic disorder. While there's a strong component of increased awareness, which means more children are being diagnosed, this still cannot account for the exponential increase in autism incidence.

How can a culture continue to thrive if every other child has a dysfunctional brain? It can't. It's a prescription for social breakdown. Clearly something needs to be done to

curb this avalanching trend. But just what can a parent do to reduce the risk to their child?

Biological scientist Rhonda Patrick, Ph.D. has published two papers[2,3] that expand on some very exciting, simple, but powerful lifestyle interventions that could have profound influence not only on autism but a variety of other developmental disorders in childhood.

We've heard about the influence of vitamin D on autism before, but only from a superficial point of view. In her studies, Patrick has dug deep, arriving at a really brilliant hypothesis.

Vitamin D Is an Important Gene Regulator

To understand why vitamin D plays such an important role in brain function (and dysfunction), it's important to understand what vitamin D actually is. Despite being named a "vitamin," vitamin D actually gets converted into a steroid hormone (other steroid hormones include estrogen and testosterone).

As a steroid hormone, it regulates over 1,000 different physiological processes, and controls around 5% of the human genome. Dr. Michael Holick, who's a leader in vitamin D research, thinks it may even control twice that amount of genes.

When you have enough vitamin D in your body, it binds to vitamin D receptors located throughout your body, thereby acting like a key that opens the proverbial door.

The vitamin D receptor complex can go deep inside the DNA, where it recognizes the tell-tale sequence of code that instructs the vitamin D receptor complex to either turn the gene on (making it active), or off (making it inactive).

Emerging evidence suggests those little tell-tale sequences are present in as much as 10% of all genes, but according to Patrick, it hasn't been empirically proven that vitamin D has the ability to activate or deactivate all of those genes.

She agrees it's quite likely that this might be the case though, which gives vitamin D a truly profound influence.

Autism Has Risen in Tandem With Vitamin D Deficiency

While autism is not likely caused by any one factor, it's worth noting that as autism incidence has gone up, so has vitamin D deficiency.

> *"There's that correlation between autism incidence rising and vitamin D deficiency rising, largely as a consequence of people wearing sunscreens, and staying indoors more ... UVB radiation is very important to make vitamin D in the skin,"* Patrick notes.
>
> *"What my research identified when I was at Children's Hospital Oakland Research Institute (CHORI) with* [biochemist] *Dr. Bruce Ames, is that one of the genes vitamin D regulates encodes a for an enzyme called tryptophan hydroxylase (TPH).*
>
> *TPH is responsible for converting tryptophan (which is a rare amino acid you get from the protein that you eat) into serotonin.*
>
> *Most people associate serotonin with being a neurotransmitter in the brain that regulates your mood. It's important for feeling good. But actually it does so much more in the brain during brain development and also throughout the rest of the body."*

Gut Versus Brain Serotonin

You have two different tryptophan hydroxylase genes in your body — one in your brain (TPH2), and one in your gut (TPH1).

The one in your brain makes serotonin in the brain, and the one in your gut converts tryptophan into serotonin in the gut, and, contrary to popular opinion, the latter CANNOT cross the blood-brain barrier to get into your brain.

This is an important point, because while many understand that the majority (about 90%) of the serotonin in your body is produced in the gut and not the brain, the thinking has been that the gut serotonin will automatically influence serotonin in the brain.

Since it's unable to cross the blood-brain barrier, this is not the case. The two serotonin systems are completely separate.

Your gut serotonin does serve an important function, though, as it plays a role in the ability of a specific type of blood cell called platelets to respond to tissue injury. On the other hand, it can also cause trouble, by promoting inflammation. As explained by Patrick:

> *"The serotonin made in the gut gets taken up by your platelets. Platelets can't make their own serotonin, so they need to get it from the serotonin that's made in the gut.*
>
> *It plays a very important role in causing platelets to aggregate together, which is important when you injure yourself. If you cut yourself you want to have that coagulation ... to form a clot, so that you don't bleed out. Serotonin plays an important role in making sure that platelets do that.*
>
> *You need to make serotonin in your gut. But on the other hand, it's a double-edged sword, because too much serotonin in the gut actually causes gut inflammation. The reason it does that is it also activates immune cells in your gut called T-cells, causing them to proliferate.*
>
> *They can start firing away pro-inflammatory cytokines ... It's been shown that if you stop mice from producing serotonin in the gut, it completely takes away their gut inflammation. It resolves very robustly."*

Vitamin D Keeps Gut Serotonin in Check

What Patrick discovered is that, in the gut, vitamin D turns off, or dampens the activity of the gene responsible for making the enzyme that converts tryptophan into serotonin. In

this way, vitamin D helps combat inflammation in your gut caused by excessive serotonin levels.

In the brain, the tryptophan hydroxylase gene has a sequence that causes the opposite reaction. Here vitamin D activates the gene, thereby increasing serotonin production! Needless to say, when you have sufficient amounts of vitamin D, two things then happen simultaneously:

1. Gut inflammation is reduced, courtesy of deactivating the gene associated with serotonin production
2. Serotonin levels in the brain are increased by gene activation, and in the brain, serotonin plays an important role in mood, impulse control, long-term planning, long-term behavior, anxiety, memory, and many other cognitive functions and behaviors, including sensory gating — the ability to filter out extraneous or unimportant stimuli

Since the publication of Patrick's first paper[4] in 2014, an independent group at the University of Arizona has biochemically validated her findings,[5] confirming that vitamin D does activate the tryptophan hydroxylase 2 (TPH2) gene in a variety of neuronal cell types.

Prior to the publication of that paper, this simply wasn't known, and it's a significant finding that can help shed a great deal of light on vitamin D's influence in autism, as a majority of autistic kids have not only brain dysfunction, but also gut inflammation. Her research shows quite clearly how important it is to have enough vitamin D to prevent and treat both of these problems.

The Role of Serotonin During Early Brain Development

During the fetal brain development phase, serotonin plays an important role in brain morphogenesis. Simply put, serotonin is an ingredient required for the development of the brain's shape, structure, and internal wiring. Serotonin basically tells the neurons where to position themselves in the brain, and what type of neurons they should

become. If you don't have sufficient amounts of serotonin, abnormal brain structure and brain wiring will result.

> *"In mouse models, it's been shown to lead to the mouse equivalent of autistic behaviors,"* Dr. Patrick notes. *"Serotonin plays a very important role in brain development. What's really interesting is that the developing fetus depends entirely on the mother's levels of vitamin D.*
>
> *The vitamin D from the mother crosses over the placenta, gets into the blood-brain barrier, gets into the fetal brain, and activates all those fetal genes.*
>
> *If a mother is deficient in vitamin D, this may have severe consequences in the developing fetal brain of her child, because maybe that gene that needs vitamin D to get activated is not getting activated. As a consequence, there's not enough serotonin being made in the fetal brain, which possibly could affect the way that brain develops ...*
>
> *Vitamin D and low serotonin have been linked to autism by many different researchers. But no one has put the two together as a mechanism going, 'Look, maybe the low vitamin D leads to low serotonin in the developing brain. This may be part of the reason why there's an increase in autism, and maybe part of the way why low vitamin D leads to autism.'"*

Maternal Autoimmunity and Autism

Maternal autoimmunity has also been linked to autism. Mothers of autistic children are four times more likely to have autoantibodies against fetal brain proteins in their blood. It's not normal to have antibodies against brain proteins in your blood, but mothers of autistic children often do.

Studies have also shown that when you cause monkeys to have a very strong autoimmune response during pregnancy, it causes abnormal brain development in their offspring. In short, having an autoimmune response is not beneficial for anyone, but it can be truly devastating when it occurs in a pregnant woman.

"For people that don't really understand what that means, an autoimmune response means your immune system is so activated that it starts to recognize its own tissue as something foreign, like a bacteria or a virus, when it's not foreign; this is your own organ, this is your own tissue," Patrick explains.

"Your immune cells, for a variety of different reasons, can't recognize that so they start attacking it and damaging the tissue. In the case of pregnancy, there's an embryo that starts growing into this little developing fetus. Your body can recognize that as foreign. It's like, 'Whoa, what's this? This isn't supposed to be here. Attack! Get rid of it.' That can lead to a very severe autoimmune response.

But our bodies have a wonderful protective mechanism to prevent that from happening. We can make a type of immune cell called T regulatory cells (Tregs). T regulatory cells are very important because ... [they] keep your immune system in check, making sure that your immune system knows what's really foreign and what's your own self ..."

Vitamin D Deficiency Can Fuel Autoimmune Response During Pregnancy

As mentioned earlier, you have an enzyme in your gut that converts tryptophan into serotonin. In pregnant women, that same enzyme is also found in the placenta; so, tryptophan can be converted into serotonin in the placenta as well, during pregnancy.

Tryptophan also gets metabolized by a second pathway into something called kynurenine, which in turn forms those important T regulatory cells that help combat autoimmune responses. When the tryptophan is prevented from forming kynurenine, your T regulatory cell count will plummet and your body's autoimmune response will heighten.

In animal studies, pregnant mice in which the enzyme that produces kynurenine has been deleted have such a strong autoimmune response toward the fetus that they end up aborting it.

"Thus you want to make sure that not all the tryptophan is being converted into serotonin in the placenta," Patrick says, *"because you also want it to be converted into this other pathway; into T regulatory cells ...*

Now, back to vitamin D. If you don't have enough vitamin D, you may be making way more of this enzyme that binds tryptophan and it may act like sink, where tryptophan is being sucked into that pathway producing serotonin in the placenta.

The tryptophan then doesn't have a chance to be converted to that other pathway that forms kynurenine and T regulatory cells. This may have a negative effect, particularly during pregnancy, because you're not making enough T regulatory cells and therefore you start to have a heightened autoimmune response."

Vitamin D has been connected to autoimmunity via a variety of different mechanisms, and Patrick believes this may be yet another mechanism by which vitamin D can regulate autoimmunity. In short, it helps suppress the enzyme that binds so tightly to tryptophan that it traps and prevents it from forming kynurenine and T regulatory cells. With sufficient amounts of vitamin D, the tryptophan can go into both pathways, forming:

- Serotonin in the gut and in the placenta
- Kynurenine and T regulatory cells, which help keep autoimmune responses in check

If You're Pregnant or Have an Autoimmune Disorder, Be Sure to Optimize Your Vitamin D

Optimizing your vitamin D is of particular importance during pregnancy. In fact, optimizing vitamin D levels before and during pregnancy may be one of the most important actions a pregnant mother can take to have a healthy baby.

"I think there's a simple solution for OB-GYN practitioners, normal family practitioners, or for any female that wants to get pregnant or is pregnant, and

that is 1) get your vitamin D levels measured and 2) supplement. Make sure you're getting enough vitamin D; high enough to make sure that you have optimal levels, so you're not deficient," Patrick says.

"I think that's a simple solution to possibly help prevent diseases like autism. This is relevant for other diseases as well — ADHD, schizophrenia, and a variety of different brain dysfunctions. As I mentioned, serotonin plays an important role for a variety of behaviors."

The mechanism described in the section above also likely plays a role in the regulation of autoimmune responses in general, by promoting the production of T regulatory cells. Hence it's highly advisable for anyone suffering from any autoimmune disorder to optimize your vitamin D level. Ditto for those with any kind of neurological dysfunction.

As for the optimal vitamin D level, the bulk of the research now suggests the ideal range is between 40 and 70 nanograms per milliliter (ng/ml). You definitely don't want to be below 40 — that much we know. The sweet spot might be right around 50. The ideal way to optimize your levels is to expose significant amounts of bare skin to sunlight. If you cannot get enough sun exposure, then you're going to have to take a vitamin D3 supplement.

Keep in mind that if you opt for a vitamin D supplement, you also need to take **vitamin K2**. The biological role of vitamin K2 is to help move calcium into the proper areas in your body, such as your bones and teeth. It also helps remove calcium from areas where it shouldn't be, such as in your arteries and soft tissues.

Vitamin K2 deficiency actually produces the symptoms of vitamin D toxicity, which includes inappropriate calcification that can lead to hardening of your arteries.

Common Gene Polymorphism Predisposes Many to Low Vitamin D Levels

It's worth noting that a fairly significant portion of the population have a gene polymorphism called CYP2R1, a genetic aberration that prevents your liver from hydroxylating the vitamin D3 into 25-hydroxy vitamin D, which is the major circulating form of vitamin D in your body. In this case, the amount of vitamin D you'd need to take could be extraordinarily high.

> *"This polymorphism in the gene ... [means] vitamin D3 is not getting converted into 25-hydroxyvitamin D very well. As a consequence, people with this gene polymorphism, in some cases, have to take very high doses of vitamin D3 orally to achieve normal levels of 25-hydroxy vitamin D — levels that people like you and I would never take, because it could induce some negative effects.*
>
> *But you wouldn't know that [you have this polymorphism] if you never got your vitamin D levels measured. I actually know some people in my close friend network that have this gene polymorphism, and they have to take very, very high levels of vitamin D ... I don't know what the incidence is ... [but] in order for anything to be considered a gene polymorphism, it has to be over 1% of the population.*
>
> *The difference between a mutation and a gene polymorphism is that a mutation is thought to occur randomly. For whatever reason, your mitochondria metabolism isn't working properly, and it's dumping all sorts of toxic things that may possibly cause a mutation ...*
>
> *A gene polymorphism is thought to be because of a certain reason ... It's largely thought, at least in the scientific community, that gene polymorphisms occur based on nutrition [and] environment ...*
>
> *If, for example, we live in a part of the world where the selenium in the soil is very, very high, as a population, we could have gotten a gene polymorphism in the gene that lowers our selenium absorption, because we don't need as much in one dose since we are continually getting it."*

More Information

To learn more about Patrick's work, please visit her website, FoundMyFitness.com. She also has a podcast where she interviews health professionals and scientists on a variety of topics related to health. On her website, you can find videos in which she summarizes key information in clear and easy to understand layman's terms. You can also sign up for her newsletter, in which she publishes longer, heavily referenced articles.

Click here for the free report, "Vitamin D Regulates Serotonin: Role in Autism," which includes helpful illustrations and covers some of the topics discussed in this interview, including: how vitamin D is involved in serotonin production in the gut vs. the brain, how vitamin D deficiency can lead to autoimmunity, why autism may be more common in males. (Hint: It has to do with estrogen, and more.)

Sources and References

- [1] CDC.gov, National Health Statistics Report, Number 65, March 20, 2013 (PDF)
- [2, 4] FASEB Journal 2014 Jun;28(6):2398-413
- [3] FASEB Journal 2015 Jun;29(6):2207-22
- [5] FASEB Journal 2015 Sep;29(9):4023-35