Nightshades and Anesthesia

BChE Gene Variants

Genetic Lifehacks
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Nightshade sensitivity, Anesthesia risk – Genetic Lifehacks

Are you sensitive to nightshades? Your genetic variants may hold the key to the cause.

Butyrylcholinesterase (BChE) is a cholinergic system enzyme that acts on the autonomic nervous system, which regulates processes such as blood pressure and breathing. But the BChE story is more than just autonomic function, and this ancient enzyme has some fascinating links to modern health issues.

This ebook explains what BChE does and how genetic variants can cause a deficiency. Best known for negative reactions to anesthesia, BChE deficiency can also lead to seemingly unconnected consequences, such as an increased risk for Parkinson's or food sensitivity to potatoes.

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What is butyrylcholinesterase (BChE)?

Butyrylcholinesterase (BChE) is an enzyme with several unique functions. Many studies refer to it as a kind of backup for *acetylcholine esterase*, which is a neurotransmitter that causes cholinergic neurons to fire.

However, recent research points to several important roles of BChE in addition to being a backup for acetylcholine esterase.

Let me diverge for just a moment to explain cholinergic nerves...

Cholinergic neurons are important in autonomic nervous system function as well as in the brain for circadian rhythm, time and spatial memory, and olfactory function.

Acetylcholinesterase (AChE) is the enzyme responsible for breaking down the acetylcholine in the synapses of nerves. Think of it as the 'off switch' for stopping a neuron from firing repeatedly. For example, in the synapse of a neuron, acetylcholine causes it to fire, contracting a muscle. AChE breaks down the acetylcholine, stopping the neuron from firing and letting the muscle relax. It all happens instantly and relies on having the right amount of acetylcholine and acetylcholine esterase (AChE). Too much inhibition of AChE results in death. Muscles need to relax – especially those controlling respiration – and excessive inhibition of AChE causes asphyxiation. AChE is essential for life, and there are very few genetic mutations that impact the ACHE gene.[ref]

Getting back on topic here...

What does BChE do? BChE can break down acetylcholine, similarly to acetylcholinesterase. However, it doesn't usually act within neurons like acetylcholinesterase (AChE). In other words, it isn't the main way the body breaks down acetylcholine, at least under normal circumstances. [ref]

Interestingly, we have about 10-times more BChE in the body than AChE. So it must be important for something!

Not only can BChE bind to acetylcholine, but it can also bind to other substances that inhibit AChE. In this way, **BChE is considered a bio-scavenger,** protecting the body from certain toxicants or poisons.[ref] Inhibiting AChE at higher levels is deadly, so BChE plays an important role in protecting the function of AChE.

When is BChE important?

While the functionality of the BChE enzyme used to be in question, recent research shines a lot of light on this molecule. BChE is essential for:

1. Inactivating certain compounds in **nightshades**
2. Recovery from certain types of **anesthesia**
3. Inactivating **immune response**
4. Protecting against nerve agents, **snake toxins**, and other AChE inhibitors
5. Modulating the hunger hormone **ghrelin**

Let's dig into all of these topics further...

1) Decreased BChE as a possible cause of Nightshade Sensitivity

The edible nightshade vegetables include potatoes, tomatoes, eggplant, and peppers.

All of the nightshade family produce varying amounts of **glycoalkaloids**, which are AChE and BChE inhibitors. The plants produce these compounds to repel insects.[ref][ref][ref]

Getting more specific: One component of potatoes is a glycoalkaloid compound called α-solanine. The compound is found in the leaves, stems, and tuber we eat. When potatoes are exposed to light, they turn green due to increased α-solanine. (Green potatoes are toxic.)[ref]

The amount of glycoalkaloids in plants also depends on exposure to light, mechanical damage to the plant, and ripeness or spoiling of the plant. Glycoalkaloid levels do not become altered by cooking.[ref]

It is theorized that BChE variants interact with the alkaloid compounds in nightshades. For some people, having problems with nightshades depends on:[ref]

- the amount of nightshades eaten
- growing conditions (damage to the plant, ripeness)
- possibly a combination with pesticides (AChE inhibitors)

It has led some clinicians to theorize that people who carry genetic variants that significantly reduce BChE function may have food sensitivities to nightshade vegetables.

What are the symptoms of nightshade intolerance?

Nightshade vegetables have associations with increased **joint pain**, especially in people with rheumatoid arthritis.[article]

Potatoes, especially fried potatoes, are thought to increase the risk of **inflammatory bowel diseases** due to their glycoalkaloid content.[ref]

Additionally, people with **psoriasis** may be more prone to nightshade sensitivity. A survey from the National Psoriasis Foundation found eliminating nightshades was beneficial for about half of psoriasis patients who had tried it.[ref]

In addition to the nightshade vegetables we eat, other plants that people could consume are also in this family.

- Popular supplements such as **ashwagandha and goji berries** also fall into the nightshade category.
- Belladonna is also known as 'deadly nightshade' due to its effect on AChE.
- **Cocaine** is another plant product that BChE breaks down. In fact, researchers are working on ways to utilize BChE to reverse cocaine overdoses.[ref]

2) BChE and recovery from anesthesia (succinylcholine)

More important but less common is the problem with anesthesia in people with more severe BChE deficiency.

BChE levels become important when exposed to certain types of anesthesia. The BChE enzyme controls the breakdown rate of succinylcholine, which is a muscle relaxant used during surgery. People with genetic variants that significantly decrease the amount of BChE (listed below in the genetics section) can have problems coming out of anesthesia and returning to breathing on their own. It is important to talk with your doctor before surgery if you have certain BChE variants so that anesthesia can be adjusted.

I'll go into more detail on this in the genetic variants section below. Coming out of anesthesia and being able to breathe... it comes up at the top of my "important' list.

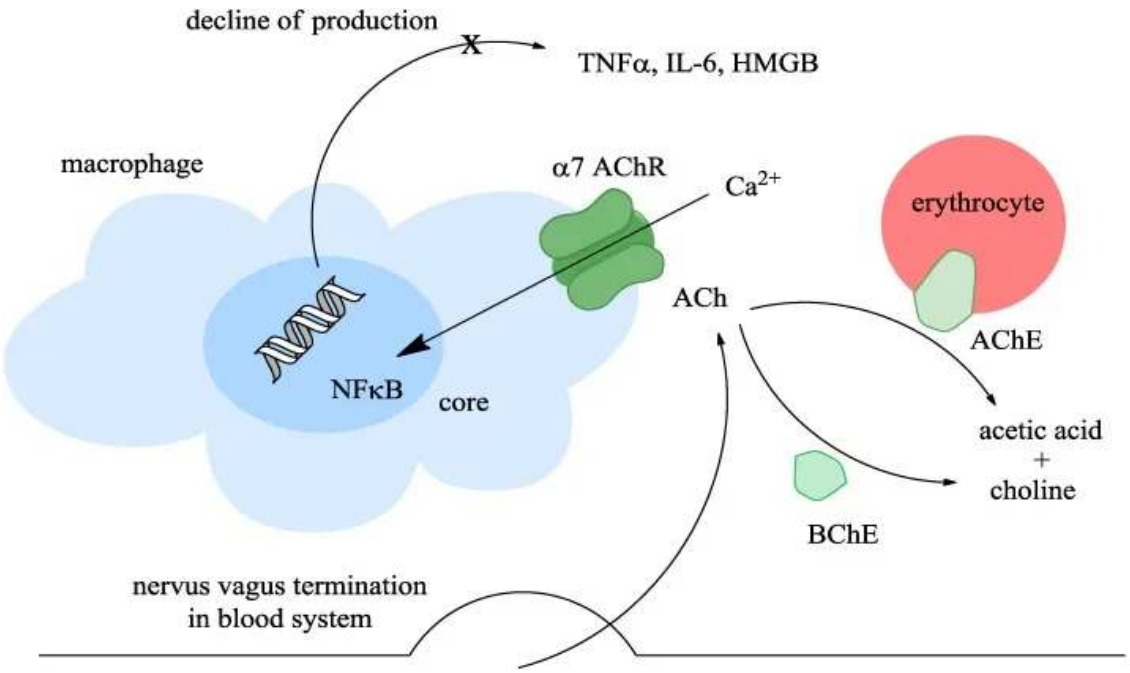
3) Immune function, Macrophages, and the Vagus nerve

BChE also plays a role in the cholinergic anti-inflammatory system.

The cholinergic anti-inflammatory system is a one-way system by which the brain can signal and control the immune response through the **vagus nerve**.

Macrophages, a type of white blood cell, have acetylcholine receptors on their surface, and acetylcholine can then trigger a part of the immune response. AChE and BChE can turn off the immune activation when it is no longer needed.[ref] BChE can be especially important in the immune response – more so than AChE – since it circulates in the bloodstream.

Below: *AChE and BChE inactivating acetylcholine, released from the vagus nerve and acted on a macrophage.*[Ref-CC license]



4) BChE as a bio-scavenger:

Inhibiting AChE is generally bad and often deadly. Thus, researchers think this is one reason why we have a built-in system in which BChE can break down toxins to protect AChE.

AChE inhibitors include:

- Some natural toxins, such as snake venom
- Sarin and VX nerve gas
- Pesticides such as organophosphates and carbamates

BChE may act as a bio-scavenger in the plasma, breaking down these molecules before they can interfere with nerve transmission and AChE.

Nerve Gas Tests: In the past (1940s-'60s), tests on military volunteers determined the effects of low levels of the nerve agents that targeted AChE. These human tests demonstrated the vast differences between individuals' responses to nerve gas, and the differences showed ties to genetic variants in the BChE gene. Modern animal and cell studies have confirmed this since we thankfully no longer test nerve gas on people![ref]

Interestingly, researchers are working on creating bacteria that produce the human BChE enzyme as a bioremediation method for combating environmental pesticides.[ref]

Pesticides: Organophosphates, Carbamates, and BChE

Organophosphates are a class of insecticides commonly used in agriculture, veterinarian use, home pest control, and mosquito control. They are the most widely used type of pesticide.

First developed in the 1930s in Germany as a new insecticide, organophosphates were also used in biological warfare in WWII.[ref]

Organophosphate pesticides include:[ref][ref][ref][ref]

- malathion (lice, mosquitoes)
- chlorpyrifos (worms, termites)
- parathion (banned in a lot of countries),
- diazinon (agricultural insecticide)
- fenitrothion (chewing and sucking insects)
- dichlorvos,
- ethion

Carbamates are another prevalent insecticide. Carbamyl (**Sevin**), a carbamate, is extensively used as an insecticide in home and agricultural.

Organophosphates and carbamates work to kill insects by inhibiting AChE. Organophosphates are irreversible AChE inhibitors, meaning that large exposure to organophosphates can't be counteracted. Carbamates, on the other hand, are a little less toxic and reversible inhibitors of AChE.

BChE possibly acts as a bio-scavenger, protecting AChE from being impacted by organophosphates and other substances.[ref] People with BChE genetic variants may be more prone to detrimental effects from exposure to organophosphates.[ref]

BChE, organophosphates, and Parkinson's risk:

Pesticide exposure has been linked to Parkinson's disease for a long time. Chlorpyrifos and other organophosphates increase the risk of Parkinson's disease, depending on the amount of exposure and the genetic variants the person carries.[ref][ref][ref]

More importantly, one of the genetic variants that increase the risk of Parkinson's due to pesticide exposure is in the BChE gene. (below)

5) BChE and Ghrelin:

Recently, researchers have found that there may be another physiological role for BChE in humans. It has been shown that BChE also inactivates ghrelin, the 'hunger hormone'. The cells of the stomach release ghrelin, thus causing the stimulation of muscle cells in the stomach that gives us 'hunger pains'. Ghrelin also activates certain regions in the brain, causing us to seek out food and helps drive food cravings. Finally, ghrelin is also active in fat storage.[ref][ref]

Both humans and animals with a lack of BChE have higher than normal ghrelin levels. When researchers altered the BChE gene in mice to overexpress BChE, the mice had significantly lower ghrelin levels. Researchers have also found that increasing BChE levels keep formerly obese mice from rebounding and gaining back weight.[ref]

Related article: Ghrelin Genes

When is cholinesterase inhibition a good thing?

While too much of a cholinesterase inhibitor is obviously bad (death is never a good side-effect), a minor inhibition of cholinesterases can be beneficial in some circumstances.

Extending the time a neuron has exposure to acetylcholine can be beneficial in some cases of Alzheimer's disease. It also can increase REM sleep, which could be beneficial at times in relation to learning and memory. Also, cholinesterase inhibitors are sometimes prescribed for schizophrenia.[ref][ref]

In fact, a recent study in mice looked at a couple of traditional African medicines made from the leaves of plants in the nightshade family. The study found that the leaves of the African eggplant and Black nightshade may help with cognitive impairment in mice.[ref]

The dose makes the poison is a well-known saying, and the right amount of cholinesterase inhibition can be beneficial in specific medical circumstances, including myasthenia gravis and certain types of glaucoma. Carrying a genetic variant that decreases BChE could be beneficial in some ways – and thus explains why a BChE variant that mildly decreases enzyme function is common in the human population.

BChE and Sudden Infant Death Syndrome (SIDS):

A recent study examined blood samples of infants who had died of SIDS (sudden infant death syndrome) and found that they had low levels of BChE. The researcher thought that the low BChE could be responsible for SIDS.[ref]

While an interesting finding, the research study raised questions since they could also not test for acetylcholine esterase levels. Hopefully, this study will be followed up with more research to replicate the findings on this important topic.

BCHE Genotype Report

The variants below reduce the function of the BChE enzyme. Researchers think that the effect is additive, so if you have two variants (e.g., the A variant and the K variant), the effect is stronger than if you have one variant.[ref]

BChE A-Variant:

The A-variant is a more severe change in the BChE enzyme function. About 2% – 5% of certain population groups carry one copy of the A-variant. It causes a decrease in the enzyme's function and an alteration to the way it functions.

Check your genetic data for **rs1799807** (23andMe v4, v5; AncestryDNA):

- T/T: typical
- C/T: one copy of A-variant, may have delayed recovery from succinylcholine, increased risk of leprosy (talk with your doctor before surgery)[ref][ref][ref][ref]
- C/C: two copies of A-variant (very rare), severe BChE deficiency (talk with your doctor before surgery)

BChE K-variant:

The K-variant decreases BChE enzyme production by 33%. It is a more common variant, with around 20% of some ancestry groups having one copy of the K-variant.

Check your genetic data for **rs1803274** (23andMe v4, v5):

- C/C: typical
- C/T: one copy of the K-variant, decreased BChE, possibly more sensitive to nightshades; increased risk of Parkinson's with organophosphate exposure, slightly impacts anesthesia[ref], possibly increased risk of breast cancer
- TT: two copies of the K-variant, 30% decrease in BChE, possibly sensitive to nightshades; increased risk of Parkinson's with organophosphate exposure; possibly increased risk of breast cancer[ref][ref][ref][ref][ref]

BChE F-variants:

These last two are rare mutations, known as F1 and F2, which can cause delayed recovery from succinylcholine anesthesia. They are fairly rare. You should tell your doctor about these variants if you are having surgery.

Check your genetic data for **rs28933389** (23andMe v4, v5; AncestryDNA):

- A/A: increased risk of post-anesthesia (succinylcholine) apnea[ref][ref]
- A/G: increased risk of post-anesthesia apnea
- G/G: typical

Check your genetic data for **rs28933390** (23andMe v4, v5; AncestryDNA):

- A/A:increased risk of post-anesthesia (succinylcholine) apnea[ref][ref]
- A/C: increased risk of post-anesthesia apnea
- C/C: typical

Minor reductions in BChE:

The variants below in the BChE gene cause minor reductions in enzyme function. These may become important if combined with the above variants.

Check your genetic data for **rs2668207** (23andMe v4):

- T/T: typical
- C/T: slightly lower BChE (4-9% lower)[ref]
- C/C: lower BChE (>4-9%)

Check your genetic data for **rs1126680** (AncestryDNA):

- C/C: typical
- C/T: lower BChE activity, increased risk of hyperhidrosis when combined with K-variant
- T/T: lower BChE activity, significantly increased risk of hyperhidrosis when combined with K-variant[ref][ref][ref]

Lifehacks

Everyone should avoid exposure to nerve gas, but people who have a BChE variant may be even more at risk...

If you've been exposed to organophosphates or nerve agents in the first Gulf War, you may be interested in the genetic connections between the BChE variants and Gulf War Syndrome.

Avoiding Organophosphates:

The risk of Parkinson's Disease is increased in people with the BChE K-variant with exposure to organophosphates. It is particularly important for people in agricultural industries. Eating organic, watching your exposure to pesticides (e.g., agricultural spraying), and avoiding using pesticides in your home can reduce your exposure to organophosphates.

- If you are interested in knowing which pesticides are commonly detected on foods in the US by the FDA, check out the What's On My Food website.
- The Environmental Working Group puts out a list each year called the "Dirty Dozen" of the fruits and vegetables tested which have the most pesticide residue.

Anesthesia complications:

People carrying the BChE K-variant have a somewhat delayed recovery from succinylcholine, which is a muscle relaxant used when intubating patients under anesthesia. It can cause a delay in returning to normal function (a problem when that normal function involves breathing). While the response is delayed, it isn't by much in people who are heterozygous for the K-variant (less than a minute on average). It may be no problem at all for you, but since you know about it, you should mention it to the doctor before surgery.[ref]

The **A-variant** is associated with longer delays in returning to normal when succinylcholine is used. This delay can be more serious, and you should tell your doctor if you carry the A-variant and are going to have surgery. The combo of the K-variant and the A variant can lead to more serious complications with succinylcholine.[ref][ref][ref]

Alzheimer's:

The risk of Alzheimer's may be increased in people carrying the BChE K-variant. And people who are homozygous for the K-variant may have a negative response to AChE inhibitors for Alzheimer's disease. In fact, BChE k-variant carriers had worsening symptoms with the medication donepezil.[ref][ref]

Don't take cocaine:

Cocaine is also metabolized using BChE. Combined with BChE mutations, cocaine could have deadly effects via overdose.

How to do a Nightshade Elimination Diet:

The alkaloids in nightshades are theorized to cause some people to have aching joints, skin symptoms, muscle stiffness, or autoimmune disease flare-ups.

A nightshade elimination diet is just what it sounds like: avoiding foods and supplements that contain nightshades for a period of time. Usually, people do the elimination diet for more than three days (sometimes more than a week) and then add back in nightshade vegetables to see if they notice a resumption of symptoms. Nightshades belong to a family of plants called Solanaceae, which includes thousands of different plants.

Edible nightshades include:

- tomatoes (all varieties, plus tomato products like ketchup, salsa, pizza sauce, marinara)
- tomatillos (often found in green salsas)
- potatoes (but not sweet potatoes)
- eggplant
- peppers (Bell peppers, hot chili peppers, jalapenos, etc.)
- pepper-based spices (chili powder, cayenne powder, red pepper flakes, paprika)
- pimentos
- tobacco (cigarettes, chewing)
- goji berries
- ground cherries or Cape gooseberry (not the same as the cherries you eat as fruit from the tree)
- ashwagandha

If you are going to try a nightshade elimination diet, you will need to plan your meals ahead. Tomatoes, potatoes, and peppers are some of the most common foods eaten in a Western diet.

Eliminating nightshades long-term can really limit your food choices, and it may not be ideal for optimal nutrition. Instead, you may want to experiment with different ways of preparing nightshade vegetables and/or watching the amount you eat in one meal.

For example:

- Removing the skins of potatoes (and especially the eyes) cuts down on the alkaloid content.
- Ripe tomatoes have significantly less alkaloid content (alpha-tomatine) than green tomatoes.[ref]
- Theoretically, organic vegetables should have less pesticide residue and may be less likely to cause problems.

Supplements to watch out for:

You may find that your supplements also contain nightshades.

- **Ashwagandha** is commonly used as a supplement for modulating the HPA axis. It may be a stand-alone capsule or included in supplements for 'stress relief', so check the labels.
- **Goji berries** are sometimes included **in antioxidant supplements**. Check the label.

Conclusion:

Your genes make you unique - including in your reactions to foods and medications!

Nightshade sensitivity may not be caused by BChE variants for everyone, but it is something to be aware of, if you carry these genetic variants. Experimenting briefly with a nightshade elimination diet may show you if you have any side effects from these plant foods.

The most important take away from this ebook is:
If you carry the BChE A-variant or F-variant, talk with your doctor about it before having surgery or anesthesia.

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