

The Connection Between Iron Overload and Alzheimer's

Analysis by [Dr. Joseph Mercola](#)

March 17, 2025

STORY AT-A-GLANCE

- › Iron plays essential roles in brain function, helping transport oxygen and create neurotransmitters, but if excess iron accumulates in brain tissue, it disrupts normal cellular processes
- › Research shows higher iron levels in Alzheimer's patients' brains correlate with cognitive decline severity, suggesting iron buildup directly contributes to disease progression
- › Scientists have revealed that malfunctioning amyloid precursor protein and tau proteins in Alzheimer's disease contribute to iron accumulation, creating a harmful feedback loop that accelerates neuronal damage
- › Through advanced imaging, researchers found an imbalance favoring Fe³⁺ (ferric iron) over Fe²⁺ (ferrous iron) in Alzheimer's-affected brains, particularly around amyloid plaques
- › Regular blood donation and monitoring ferritin levels (ideally 20 to 40 ng/mL) help manage iron levels, while adequate copper intake is important for proper iron metabolism

Iron is essential for your energy levels – it plays a role in helping to carry oxygen throughout your body. But did you know iron also plays a complex, and somewhat surprising, role in your brain? Just like so many other factors in health, balance is key. Too little iron leaves you feeling tired and sluggish, but too much iron, especially in your brain, isn't a good thing either.

As you get older, iron tends to accumulate gradually in your brain. Scientists have revealed that this “brain rust,” as some researchers are starting to call it, is linked to significant brain health issues that become more common as we age. For instance, research has found a strong connection between iron buildup in the brain and Alzheimer's disease, a condition that causes memory loss and cognitive problems.

Iron Is Your Brain's Ally – but Also a Foe

Iron plays a number of essential roles, starting with helping to carry oxygen from your lungs to your brain.

- **Not just an oxygen transporter** – Iron is also involved in creating important chemical messengers called neurotransmitters, which allow your billions of brain cells to talk to each other and form the complex networks that underlie your thoughts and actions. Think of iron as a delivery service and a sophisticated communication network all rolled into one for your brain.
- **Your brain needs iron to function** – The brain is a remarkably hungry organ, constantly working and demanding a lot of energy and resources. It needs a steady and reliable supply of iron to function at its best. Like the rest of your body, your brain gets iron from the food you eat, from sources like red meat and leafy green vegetables.

This dietary iron is then carefully transported through your bloodstream to your brain, crossing a specialized barrier called the blood-brain barrier, and is then used in various processes inside your brain cells.

- **Your body has natural systems to regulate iron levels** – However, these systems can become less efficient over time. As you age, your brain's ability to manage iron declines. Instead of being efficiently used and recycled, excess iron can accumulate in certain areas of the brain, as the body has no natural way to eliminate it except through blood loss.

Having too much iron, or “iron overload,” is a significant concern for your brain health. Imagine your delicate brain cells slowly getting “clogged” or overwhelmed with iron particles. This overload actively interferes with how your brain cells function, disrupting their communication and even damaging them over time.

How Iron Is Linked to Alzheimer's Disease

Alzheimer's disease is a progressive neurodegenerative disorder and the most common cause of dementia. It is characterized by a gradual decline of memory, thinking ability, and cognitive function.

- **Iron buildup causes neurodegeneration** — Past research has found higher levels of iron present in the brains of people with Alzheimer's compared to the brains of healthy individuals of the same age. In fact, some studies began to suggest a direct link — the more iron buildup observed in the brain tissue, the more severe the cognitive decline in those with Alzheimer's.¹
- **The link between misfolded proteins and iron** — To investigate this iron connection further, researchers studied specific proteins within the brain that are already known to be involved in Alzheimer's disease, particularly amyloid precursor protein (APP) and tau protein.

Think of APP and tau proteins as workers inside your brain cells, normally performing important jobs that keep your brain healthy. However, in Alzheimer's disease, these essential workers create tangles and plaques associated with disrupted brain function.

In a study published in *Frontiers in Aging Neuroscience*, researchers found that these malfunctioning APP and tau proteins are also closely linked to how the brain manages and processes iron.² It appears the accumulation of abnormal APP and tau proteins actively contributes to unwanted iron buildup in the brain.

- **Accumulated iron worsens neurodegeneration further** — Adding to the problem, the increased iron that accumulates further worsens neuronal loss, creating a harmful

feedback loop. It's like a snowball effect rolling downhill – each problem makes the other one progressively worse, driving the disease further and faster along its course.

Understanding How Iron Harms Your Brain Cells

So, how exactly does this iron overload, this "brain rust," damage delicate brain cells? Scientists are increasingly focusing their attention on a specific cellular process called ferroptosis to understand this mechanism.³

- **The mechanism of ferroptosis** – It is a type of cellular “rusting” process, specifically driven by the presence and reactivity of iron. It's similar to what happens when metal rusts due to iron reacting with oxygen in the environment – a somewhat analogous process occurs inside your brain cells when there's too much iron present and available to react.
- **Brain cells are susceptible to rusting** – Your brain cells, and especially specialized brain cells called neurons, are incredibly active, energy-demanding cells. Neurons also have a naturally high content of fats. Polyunsaturated fats (PUFs) such as docosahexaenoic acid (DHA) and arachidonic acid (AA), are essential components of neuronal membranes and play key roles in maintaining membrane fluidity, synaptic plasticity, and neuronal signaling.

However, these fats are also particularly vulnerable to damage from this cellular “rusting” process of ferroptosis.

- **Neuronal rusting erodes brain function** – The destructive ferroptosis process leads to neurons becoming damaged and, eventually, they die. When large numbers of neurons begin to die, as seen in Alzheimer's and other neurodegenerative diseases, it leads to a range of debilitating symptoms, including memory loss, cognitive decline, and difficulties with movement and coordination.

It's important to understand that this link between iron, ferroptosis and brain cell damage isn't just relevant to Alzheimer's disease. Iron dysregulation and ferroptosis also

play a significant role in the development and progression of other serious brain diseases that affect people as they age, including Parkinson's and Huntington's disease.⁴

Advanced Imaging Reveals Iron Imbalance in Alzheimer's

Research published in Science Advances provides new insight into how iron behaves in the brain affected by Alzheimer's disease. Scientists have developed innovative tools that allow them to literally "see" different forms of iron within living cells and, remarkably, even in brain tissue.⁵

- **Detecting cellular iron in real time** – The technology uses special sensors, crafted from DNA, that selectively light up and reveal the presence of two key forms of iron: Fe²⁺ (ferrous iron) and Fe³⁺ (ferric iron).

It's like having microscopic spotlights that can distinguish between two subtly different types of iron, mapping their exact locations within the complex landscape of the brain. Using these advanced iron sensors, researchers made some striking discoveries in mouse models of Alzheimer's disease. They found, confirming previous research, that overall iron levels are indeed elevated in Alzheimer's-affected brains compared to healthy brains.

- **There is a more oxidized form of iron** – The researchers went much further, showing that a significant imbalance in the types of iron present. Specifically, they observed a much greater buildup of Fe³⁺, the more oxidized form of iron, compared to Fe²⁺, especially in areas of the brain where amyloid plaques are known to accumulate.⁶

This is an important distinction because Fe³⁺ is more strongly linked to oxidative stress and the damaging "rusting" process discussed earlier.

- **Iron imbalance among Alzheimer's patients** – Interestingly, when the researchers studied ferroptosis, the iron-driven cell death process, they saw the opposite trend – the ratio of Fe³⁺ to Fe²⁺ actually decreased.⁷ This contrast highlights that different iron redox dynamics are at play in various brain processes, and that in

Alzheimer's, the imbalance leans toward a buildup of the more reactive, oxidation-promoting Fe³⁺ form of iron.

The imaging findings provide visual confirmation of the “brain rust” concept, showing us, in detail, how iron distribution is altered in Alzheimer's. They also point to the role of iron redox imbalance, not just total iron, in the disease process. Finally, they suggest that targeting the specific forms of iron, particularly reducing the harmful Fe³⁺ buildup, could be a more effective therapeutic strategy than simply trying to remove all iron from the brain.

Iron Overload Leads to Body-Wide Health Risks

It's not just your brain that suffers from an iron surplus; **excess iron** also poses other serious health.

- **Risk of cancer increases** — Research indicates a significant correlation between elevated ferritin — the carrier molecule of iron — and cancer.⁸ Excess iron has also been implicated in Type 2 diabetes⁹ and osteoarthritis.¹⁰
- **Bone strength is affected** — Elevated iron levels adversely affect your **bone microarchitecture**, compromising bone strength and increasing fracture susceptibility.
- **Mitochondrial function is compromised** — Iron causes significant harm primarily by catalyzing a reaction within the inner mitochondrial membrane. When iron reacts with hydrogen peroxide, hydroxyl free radicals are formed.

These are among the most damaging free radicals known, causing severe **mitochondrial dysfunction**, which in turn is at the heart of most chronic degenerative diseases. The hydroxyl free radicals are an oxidative stress that will also damage your cell membranes, stem cells, protein and DNA.

Test Your Iron Levels Regularly

Maintaining optimal iron levels starts with awareness. A straightforward blood test, known as a **serum ferritin test**, provides valuable insights into your iron status. Regularly including this test in your preventive health screenings is a prudent step toward proactive health management. Low ferritin levels are indicative of iron deficiency, while elevated levels signal an iron surplus.

- **The ideal iron range** – You want your ferritin level below 100 ng/mL; the ideal range is 20 to 40 ng/mL. Below 20 ng/mL is an indicator that you are iron deficient, while a level above 100 ng/mL indicates inflammation, high iron, or both. A gamma-glutamyl transpeptidase (GGT) test is another screening marker for excess free iron and is a great indicator of your risk for sudden cardiac death, insulin resistance and cardiometabolic disease.
- **Contributors to iron accumulation** – While genetic predispositions, such as hereditary hemochromatosis, play a role, most adult men and menopausal women face a general risk of iron accumulation simply because they lack a routine mechanism for blood loss, which is the body's primary means of reducing excess iron.
- **Poor habits and other factors exacerbate iron overload** – Consuming processed foods enriched with iron, using iron supplements or cooking with cast iron cookware all elevate your iron intake. Drinking well water with high iron content is another source, emphasizing the importance of water filtration systems like iron precipitators or reverse osmosis filters. Regular alcohol consumption also contributes, as it enhances iron absorption from food.

A Simple Strategy to Lower Your Iron Levels

Managing iron overload is relatively straightforward. Regular blood donation, two to four times annually, is a highly effective method for lowering iron levels. Alternatively, smaller, monthly blood withdrawals are also beneficial.

- **Safety reminders when donating blood** – Individuals with congestive heart failure or severe chronic obstructive pulmonary disease (COPD) should consult their physician before donating blood, but for most others, it is generally a safe and appropriate recommendation. If blood donation is not feasible due to center restrictions, therapeutic phlebotomy can be prescribed by your doctor.

Men	150 ml
Postmenopausal Women	100 ml
Premenopausal Women	50 ml

- **Balance copper and iron** – Iron reduction is only one aspect of iron balance. It's also important to recognize the interplay between iron and copper. **Iron overload coupled with copper deficiency** presents a particularly risky scenario. **Copper deficiency** is widespread, and many individuals require increased copper intake to support proper iron metabolism.
- **Consider supplementing with copper** – If your copper status is low, supplementing with 3 milligrams (mg) to 4 mg of copper bisglycinate daily is beneficial. Alternatively, incorporate copper-rich foods like bee pollen, grass fed beef liver and acerola cherries into your diet. Retinol, found in beef liver and organ meats, also enhances copper bioavailability and is important for overall iron regulation.

Adequate calcium intake also reduces your risk of iron overload naturally. Focus on getting calcium from whole food sources, like raw grass fed dairy products and **eggshells**, rather than supplements. When calcium levels are low, your body releases more parathyroid hormone (PTH), which increases iron storage. Breaking this cycle through proper calcium nutrition helps protect both your bones and overall health.

Frequently Asked Questions (FAQs) About Iron Overload and Brain Health

Q: Why is iron important for brain health?

A: Iron plays a crucial role in brain function by transporting oxygen, creating neurotransmitters and supporting brain cell activity. A balanced iron level is essential for cognitive health and energy production.

Q: How does excess iron negatively affect the brain?

A: As people age, iron accumulates in the brain, leading to oxidative stress and damage to neurons. This buildup, often called "brain rust," is linked to neurodegenerative diseases like Alzheimer's.

Q: What is the connection between iron and Alzheimer's disease?

A: Research shows that excessive iron contributes to the formation of amyloid plaques and tau tangles, which disrupt brain function. Iron imbalance also accelerates neuron loss through a damaging process called ferroptosis.

Q: How can you test and manage your iron levels?

A: A serum ferritin test measures iron levels, with an optimal range of 20 to 40 ng/mL. To reduce excess iron, you can donate blood, limit iron-rich processed foods and balance iron intake with nutrients like copper.

Q: Does excess iron pose health risks beyond the brain?

A: Yes, iron overload is linked to cancer, diabetes, osteoporosis and mitochondrial dysfunction. It also increases oxidative stress, which damages cells throughout the

body.

Sources and References

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- ^{5, 6, 7} [Science Advances April 19, 2023](#)
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- ⁹ [J Am Heart Assoc. 2024 Mar 16;13\(6\):e031732](#)
- ¹⁰ [Front Cell Dev Biol. 2022 Jan 14;9:817104](#)