Lithium and Alzheimer's
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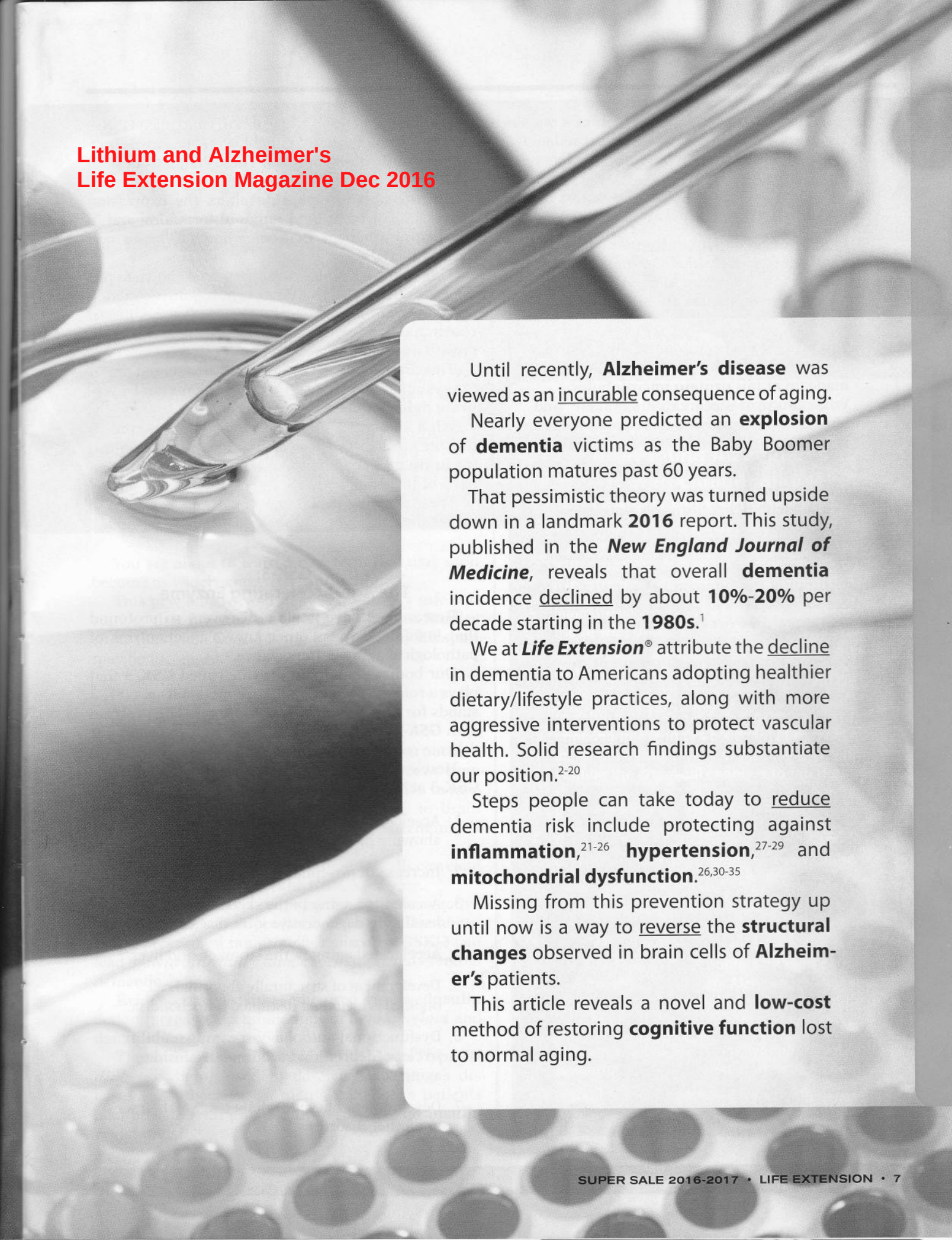


Until recently, **Alzheimer's disease** was viewed as an incurable consequence of aging.

Nearly everyone predicted an **explosion** of **dementia** victims as the Baby Boomer population matures past 60 years.

That pessimistic theory was turned upside down in a landmark **2016** report. This study, published in the ***New England Journal of Medicine***, reveals that overall **dementia** incidence declined by about **10%-20%** per decade starting in the **1980s**.[1]

We at ***Life Extension***® attribute the decline in dementia to Americans adopting healthier dietary/lifestyle practices, along with more aggressive interventions to protect vascular health. Solid research findings substantiate our position.[2-20]

Steps people can take today to reduce dementia risk include protecting against **inflammation**,[21-26] **hypertension**,[27-29] and **mitochondrial dysfunction**.[26,30-35]

Missing from this prevention strategy up until now is a way to reverse the **structural changes** observed in brain cells of **Alzheimer's** patients.

This article reveals a novel and **low-cost** method of restoring **cognitive function** lost to normal aging.

In order to understand how **Alzheimer's** dementia develops, you should know the **structural** damage that occurs in your **brain** as a part of normal aging.

The major structural defects are:

- ***Beta amyloid* accumulation**: Amyloid plaques are senile protein "clumps" that damage areas involved in memory consolidation. These **plaques** are highly toxic to neurons (brain cells).
- ***Tau protein* dysfunction**: Healthy neurons are held together by a cellular skeleton made up of **tau protein** microtubules. When **tau proteins** are dysfunctional[36] and abnormally accumulate,[37] the consequence is cellular death.
- **Neurofibrillary tangles**: As damaged ***tau proteins*** accumulate, neurons become clogged with ***neurofibrillary tangles***.[38] This renders neurons dysfunctional.

In a stunning development, two natural factors have been discovered that protect against ***structural*** brain cell alterations observed in the elderly. These new neuro-protectors are microdose **lithium** and a colostrum-derived **proline-rich polypeptide**.

Published studies reveal how these two nutrients can stabilize cognitive function, slow Alzheimer's progression and possibly reverse it. These discoveries provide an easy way to protect against senile changes that up until now were thought to be unavoidable.

Lithium acts by inhibiting an ***enzyme*** called **GSK-3** that causes the formation of abnormal **tau proteins**[39] and **neurofibrillary tangles**. These "tangles" destroy brain cells and impair memory.[40,41]

Proline-rich polypeptide alters the expression of genes involved in **beta amyloid** formation and in **tau protein** damage that contributes to **brain cell** destruction.[42,43]

This "mother's milk" extract has been shown to produce meaningful **improvements** in cognitive function and daily living activities in **human** studies. Additional research demonstrates an increase in new nerve cell growth and connectivity.[43,44]

This article will focus on an unprecedented opportunity for aging humans to halt certain mechanisms of **brain aging** using very **low-cost** nutrients.

What should excite ***Life Extension*** supporters is that the mechanisms by which these nutrients protect the **brain** may confer similar benefits to cells in other parts of the aging body.

These discoveries open new fields of innovation to **target** the underlying causes of degenerative aging.

GSK-3: The Age-Accelerating Enzyme

Researchers have made a discovery so profound that it might surpass other known mechanisms of pathological aging in importance.

Our bodies contain an enzyme called **GSK-3** that plays a role in regulating **glucose** metabolism. GSK-3 stands for ***glycogen synthase kinase-3***. The problem with ***GSK-3*** as we age is that it severely damages our delicate cellular structures.

Here's a description of what scientists find when **GSK-3** activity is increased:

1. Accelerated aging in heart and muscle, showing profound dysfunction.[45]
2. Increase in pro-inflammatory cytokines.[45]
3. Accelerated aging in the skeletal system, leading to degenerative joint disease.[45]
4. Accelerated aging in the stomach and liver.[45]
5. Development of structurally abnormal cell organelles including disrupted mitochondria.[45]
6. Dysfunctional autophagy, meaning inability to clear "debris" that accumulates inside aging cells.[45]
7. Development of type II diabetes,[46] Alzheimer's and other disorders.[47]

You are about to learn a new term that may soon become as widely known as "**antioxidant**."

This new longevity strategy is to identify safe substances that function as **GSK-3 inhibitors**. Studies show that when **GSK-3** is inhibited, healthy **lifespan** may be increased.[48]

Note: Boron also inhibits GSK-3

How GSK-3 Contributes to Alzheimer's disease

Alzheimer's disease brains undergo **structural** changes that result in accumulations of ***beta amyloid*** plaque and damaged ***tau proteins***.[49] This in turn creates ***neurofibrillary tangles*** that lead to brain ***shrinkage*** and cell death associated with **Alzheimer's** dementia.[50]

These **structural** alterations in brain cells correlate with increased activity of the **GSK-3** enzyme.

GSK-3 converts ***tau proteins*** into destructive tangled clumps that poison brain cells. The abnormal expression of tau proteins caused by **GSK-3** can lead to ***neurofibrillary tangle*** formation and eventual dementia.[39,50,51]

Evidence suggests that impaired **glucose/insulin** action increases accumulations of ***beta amyloid*** and damaged ***tau proteins***.[50]

These observations have led to the term ***"type III diabetes"*** being used to describe Alzheimer's disease. That's because so many Alzheimer's patients also present with **glucose impairment** and **insulin resistance**.[52,53]

What You Need to Know

Preventing Alzheimer's with Lithium and Proline-Rich Polypeptide

- Alzheimer's disease threatens aging Americans with progressive erasure of memories, cognitive function, and normal social interactions.
- Mainstream medicine offers little hope for those with or at risk for Alzheimer's, providing only temporary symptomatic relief with no ability to reverse the disease's progress.
- Lithium, an element used as a drug for decades to achieve brain changes in psychiatry, is now showing tremendous promise, at microdoses, in inhibiting the GSK-3 enzyme, thereby preventing the chemical changes to tau proteins that cause them to aggregate into neurofibrillary tangles.
- Colostrum-derived proline-rich polypeptide can modify gene expression to reduce the amount of beta amyloid precursor production and damage to tau proteins.
- Lithium and proline-rich polypeptide have been shown in recent human studies to stabilize cognitive decline in people with mild cognitive impairment or early Alzheimer's disease. Colostrum-derived proline-rich polypeptide is capable of reversing cognitive decline.
- Lithium and proline-rich polypeptide work more powerfully in the earliest stages of Alzheimer's.

Studies have shown that by inhibiting **GSK-3** activity, one can effectively lower blood **glucose** in diabetic animals, while increasing **insulin sensitivity**.[54,55]

Since Alzheimer's patients frequently suffer from abnormal sugar and insulin action in their brains, this has led to the idea that ***GSK-3 inhibition*** might be a useful approach in **Alzheimer's disease**.[51] In fact, the title of a comprehensive scientific report on this topic is:

"GSK-3 is essential in the pathogenesis of Alzheimer's disease"[39]

Lithium: A GSK-3 Inhibitor

You don't have to wait for pharmaceutical research to resolve the devastating impact inflicted by excess **GSK-3**. That's because a **GSK-3 inhibitor** already exists and holds tremendous promise in the fight against Alzheimer's. This **GSK-3 inhibitor** is the trace element ***lithium***.

Lithium has a long history in medicine as a psychoactive drug.[56] It has also been shown to be an important component for cognitive and mental health.[57-59]

Epidemiologic studies show a strong association between low lithium levels in drinking water and *high rates* of suicide and homicide, suggesting that insufficient lithium contributes to mental destabilization.[60] Because lithium intake from natural sources varies widely, this has led to speculation that many of us are failing to consume the element in quantities large enough to provide natural neuroprotection.[5]

And that, in turn, means that there may be real benefits in increasing our regular consumption of lithium by ***tiny*** amounts, on a regular basis. We now have persuasive evidence on how microdose **lithium** exerts robust brain-protective effects.

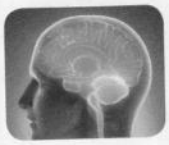
Lithium Reduces Brain Plaque Accumulation

The **GSK-3 enzyme** causes ***neurofibrillary tangles*** to aggregate, which is a **structural** defect observed in **Alzheimer's disease**.[40]

At much lower doses than used in psychiatric treatment, **lithium** inhibits **GSK-3**.[41]

Just as humans do, fruit flies accumulate ***beta amyloid*** as they age and demonstrate progressive brain cell dysfunction. They therefore serve as a surrogate model to ascertain structural changes that occur in aged human brains. In fruit fly models of Alzheimer's, **lithium** was shown to inhibit action of the **GSK-3** enzyme, resulting in a reduction of ***beta amyloid*** toxicity to brain cells.[40,41]

Lithium and Longevity



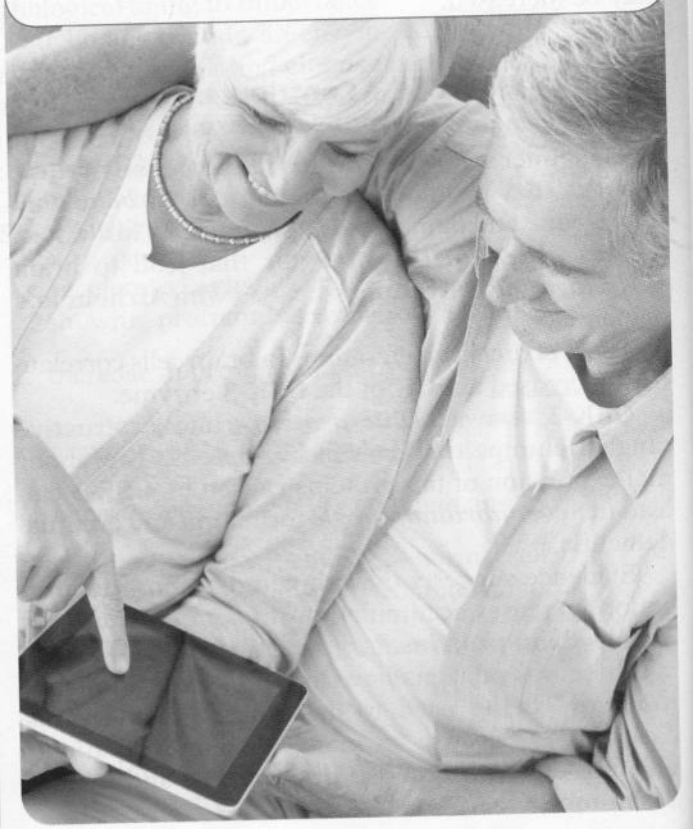
Long known as a medication used to treat bipolar disorder, depression, and other illnesses, the element **lithium** has lately been found to possibly hold the key to extending lifespan.

Researchers at University College London have found that fruit flies live a median **16%** longer when given microdoses of lithium.[48] The scientists say lithium inhibits the enzyme **glycogen synthase kinase-3 (GSK-3)** while activating a transcription factor, **NRF-2**,[48] which plays an important role in fortifying cells against damage.

Interestingly, lithium's longevity benefits for fruit flies–which included stress reduction and reduced fat production for flies on a high-sugar diet–only occurred with low doses. Higher doses reduced lifespan.

Lead researcher Dr. Jorge Iván Castillo-Quan of **Harvard Medical School** believes that by targeting **GSK-3**:

"We could discover new ways of controlling the aging process in mammals, including humans."[62]

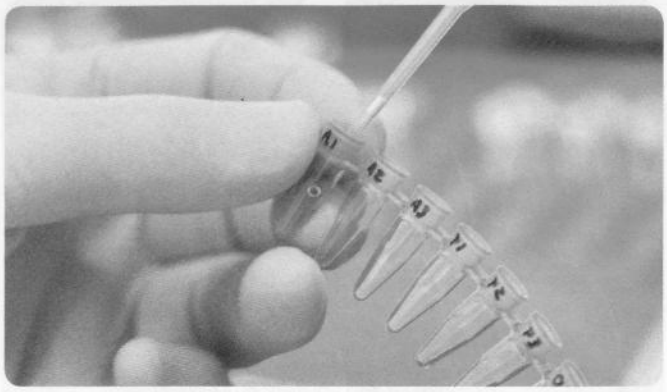


In a separate study of fruit flies, lithium administered either throughout adulthood or only later in life extended lifespan, in part by means of **GSK-3 inhibition**.[48] This study showed the profound impacts of **GSK-3**, an effect that is now being seen in higher vertebrates as well.

In a mouse model of Alzheimer's disease, researchers studied the effects of **microdose** lithium, in amounts **1,000-fold** smaller than those used in human psychiatry.[61] These mice were supplied with **lithium** carbonate in drinking water, beginning in early and middle adulthood, while treating control animals with water alone.

By the end of treatment, there was no memory disruption seen in any of the Alzheimer's or normal mice who were ingesting the **lithium** water. The Alzheimer's-prone mice that drank water without lithium had significant **disruption** of **memory** during tasks.

In other words, the **Alzheimer's-model mice** that were treated with **lithium** in their drinking water retained the **memory** and **cognitive performance** of normal mice.



Mice treated with lithium from early adulthood onward also showed a decrease in ***beta amyloid*** plaques in their brains, had no loss of neurons in memory centers of the brain, and had higher levels of protective **brain-derived neurotrophic factor** compared with non-treated animals.[61] This would be an astonishing finding if replicated in humans.

Indeed, there is now growing evidence for just such an effect on **human memory** and behavioral characteristics.

Only "Tiny" Doses of Lithium

Lithium is a naturally occurring element present in drinking water in various quantities based on geographic location.

Even tiny amounts of lithium in drinking water appear to have a beneficial effect in improving brain health and mood.

One published analysis looked at 27 counties in Texas with a variety of lithium levels in people's water from 1978-1987.[60] The findings showed that people whose water had the least amount of lithium had significantly greater levels of suicides, homicides, and rapes compared to areas where drinking water had the ***higher*** levels of lithium.[60] Those who consumed water with the highest lithium level (but still tiny) had nearly **40%** fewer suicides than those with the lowest lithium level.[60]

These findings were corroborated in separate studies of Japan,[64] Greece,[65] and Austria.[66,67]

A review of epidemiological studies of the **lithium content** of drinking water showed that 9 out of 11 studies found an association with higher lithium levels in local drinking water and better behavioral and medical outcomes.[68]

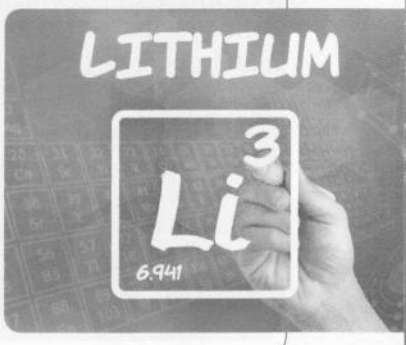
Some scientists are suggesting lithium in tiny doses be added to beverages as a way to reduce psychiatric disorders and prevent dementia.[69]

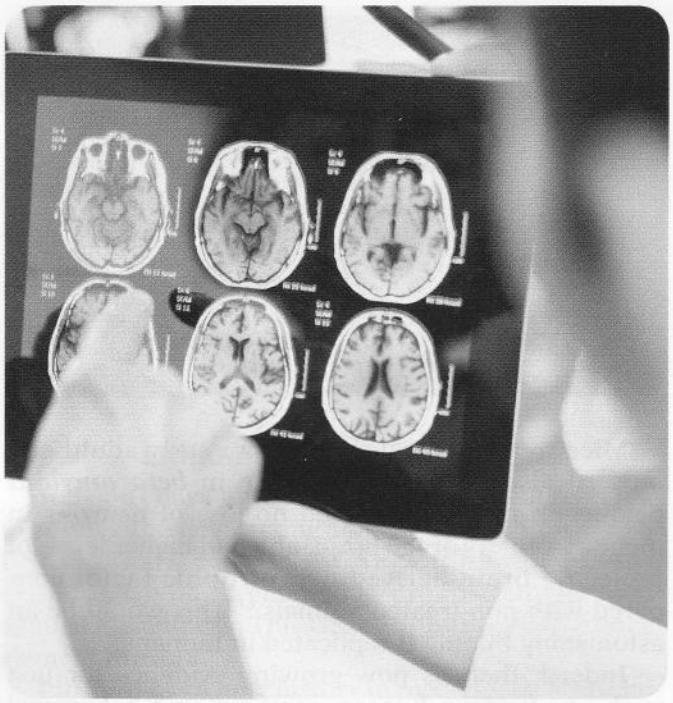
Holding back this advance are side effects that occur in response to massive doses of ingested lithium. Like any mineral, high doses of lithium induce toxicity.

Psychiatric patients with **bipolar disorder** are typically prescribed lithium doses **3,000-4,000 times** higher than the microdoses (**300 mcg**) given to Alzheimer's patients over a 15-month study period. This tiny dose of lithium did not produce any of the side effects that psychiatric patients endure, nor would any side effects be expected.

Lithium is considered a trace micronutrient with a suggested daily requirement of about **1,000 mcg**.[57] The problem is most people are not getting anything near this amount in their drinking water, especially if it is heavily filtered or distilled, which can remove all natural minerals.

Based on the results of a 15-month Alzheimer's clinical trial where **dementia progression** was halted and no side effects observed, the daily microdose used in this study (**300 mcg** per day) is a rational starting supplemental dose to suppress excess **GSK-3 activity** in our aging brains.





Human Study Shows that Lithium Preserves Cognition

Lithium at microdoses in humans shows **cognition-preserving** effects.

A study involving **Alzheimer's** patients was conducted using **microdose lithium**, administered at **300 mcg** per day for 15 months.[59] Cognitive impairment was evaluated by scores on the **Mini-Mental State Examination**.[63]

At the outset of the study there were no significant differences in Mini-Mental State Examination scores between treated and control Alzheimer's subjects. The maximum Mini-Mental State Examination score is 30 points. A score of 20 to 24 suggests mild dementia, 13 to 20 suggests moderate dementia, and less than 12 indicates severe dementia.

By **90 days**, statistical analysis revealed that Alzheimer's subjects treated with **microdose lithium** had cognitive performance scores that remained **stable**, while patients taking the placebo experienced a decrease in cognitive performance scores. The **placebo** group of **Alzheimer's** patients was approximately 3 points below the lithium-treated group (17.37 vs. 20.60) during the initial study period, and by the end of the study, placebo controls were approximately 5 points below the lithium-treated Alzheimer's group (14 vs. 19.82).[59]

Astonishingly, this study demonstrated that there was virtually no further **cognitive decline** during the study period in **Alzheimer's** patients supplemented with **microdose lithium**.

Proline-Rich Polypeptide Reverses Neurologic Decline

Derived from mother's milk, **colostrum**,[43] a **proline-rich polypeptide**, has been shown to influence **gene expression** in the immune system and brain.

Colostrum-derived **proline-rich polypeptide** is being studied for its ability to beneficially affect ***beta amyloid*** and damaged ***tau proteins***.[43]

The ability of **proline-rich polypeptide** to favorably modulate neuronal structure is being translated into positive clinical findings when studied in Alzheimer's patients.

Proline-Rich Polypeptide Lowers Beta Amyloid and Abnormal Tau Levels

In a lab study, **proline-rich polypeptide** altered the expression of genes involved in ***beta amyloid*** protein production and in the changes to ***tau proteins*** that trigger formation of ***neurofibrillary tangles***.

At the same time, **proline-rich polypeptide** altered the expression of genes to increase the production of ***enzymes*** that break down and eliminate ***beta amyloid*** as part of the natural clearance process.[42]

This study demonstrated additional protective effects of **proline-rich polypeptide**, including enhanced defenses against chemical stresses and decreased expression of cytokines that promote **inflammation**, a process long implicated in Alzheimer's disease.[42]

Together, these properties of **proline-rich polypeptide** change the expression of molecular networks that lead to **beta amyloid** formation and **tau alterations**. This **mother's milk**-derived compound thus has the potential to prevent some of the fundamental **structural** causes of Alzheimer's disease!

Proline-Rich Polypeptide Improves Cognitive Performance

Compelling laboratory studies demonstrate that **proline-rich polypeptide**, when applied to **nerve cells** growing in culture, triggers a cascade of events very similar to that produced by natural ***nerve growth factor***.

These structural effects include important brain benefits such as enhanced ***differentiation*** of premature cells into functioning adult neurons, and increased outgrowth of ***neurites***, the tiny projections on nerve cells where cell-to-cell communication takes place.[43,44]

A study was done on senescence-accelerated mice, which age at a much higher rate than do normal mice.

They were fed either **colostrum-derived proline-rich polypeptide**, colostrum, or a mixture of cow-derived proteins.[71] The mice were then subjected to a battery of behavioral tests to study spatial learning and memory.

In the group fed **colostrum-derived proline-rich polypeptide**, but not the others, learning and memory capabilities were found to be significantly improved as the animals aged, and the median lifespan was extended by **26%**.

Reversal of Cognitive Decline in Human Alzheimer's Patients

Studies of anti-Alzheimer's drugs are considered successful when they show a slowing or stabilization of cognitive decline.

Human studies of **colostrum-derived proline-rich polypeptide** are showing not only stabilization, but also ***reversal*** of brain dysfunction in those with early-stage disease.

In one study, 46 patients with **Alzheimer's** were randomly assigned to receive, every second day, either **100 mcg** of colostrum-derived **proline-rich polypeptide**, 100 mcg of selenium, or placebo tablets.[72] Subjects took the supplements for three weeks, followed by 2 weeks of no treatment, and repeated this cycle 10 times over the one-year trial. This dosing regimen was designed to maximize the impact of colostrum-derived **proline-rich polypeptide**, which can lose effectiveness when taken continuously without a regular time-out interval.[72]

Subjects were then assessed by psychiatrists blinded to the treatment assignment of each patient, using the standard **Mini-Mental State Examination** score.

In the **proline-rich polypeptide** group, **54%** of Alzheimer's patients showed improved scores (average improvement **25%**). In the other **46%** of Alzheimer's patients receiving **proline-rich polypeptide**, the dementia progression stabilized (did not worsen). Patients with milder Alzheimer's at the beginning of the study showed greater improvement than those who had more advanced disease, demonstrating the value of early intervention.

In the selenium-treated group, **7%** of the patients saw improvement and **87%** stabilized.

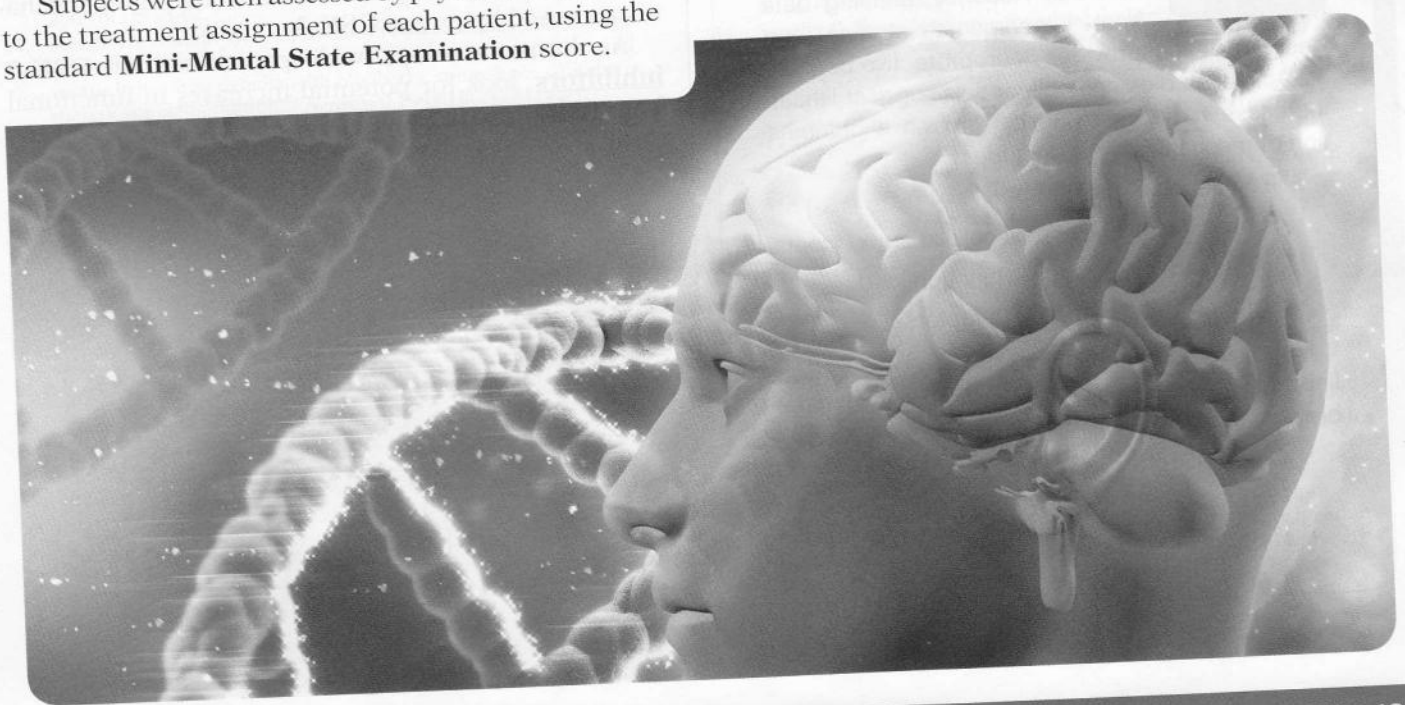
In the unfortunate **placebo** group, Alzheimer's patients with mild and moderate disease saw their mental test scores decrease by **36%** and **55%**, respectively. Scores of placebo patients with the most severe Alzheimer's decreased by **31%**.[72]

A second study by the same group of researchers, and using the same dose and dosing schedule, was performed to evaluate longer-term effects of treatment.[73] In this study, however, no placebo group or selenium group was included.

Treatment continued for 16 months, but included a group (1/3 of the whole) who had participated in the ***earlier*** study, and so were in fact treated for a total of **28** months.

By the end of the study, significant improvements in **Mini-Mental State Examination** scores were seen at each interval, compared with baseline values.

The **mental test score** improvements of the Alzheimer's patients who received **proline-rich polypeptide** are substantial and translate into an exciting new direction for future clinical studies.



Unprecedented Findings

A very low dose of the element **lithium**, along with natural colostrum-derived **proline-rich polypeptide**, has been shown in both animal and human studies to halt Alzheimer's progression.

In the case of **proline-rich polypeptide**, **54%** of Alzheimer's patients were able to reverse the **cognitive decline** produced by the disease.

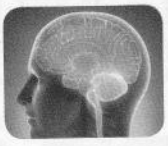
Lithium acts by inhibiting the destructive **GSK-3** enzyme. GSK-3 is implicated in the chemical changes that cause abnormal **tau proteins** to form toxic ***neurofibrillary tangles***, which destroy brain cells and impair memory.

Proline-rich polypeptide inhibits expression of genes involved in the production of **beta amyloid** and the abnormal expression of **tau proteins**, both of which contribute to neuronal destruction.

While no truly effective medication for Alzheimer's exists,[74,75] **lithium** and **proline-rich polypeptide** contribute to potential prevention of the ***structural*** changes that contribute to Alzheimer's. They are safe enough for regular use over the long term, and should be included in a supplement regimen aimed at decelerating destructive aging processes.

Lithium and Alzheimer's

Multiple Mechanisms of Cellular Protection



Lithium has an established role in the treatment of major psychiatric problems, especially bipolar disorder. Recently, enticing data from experimental studies suggest that lithium provides neuroprotective benefits.

Animal studies and cell models suggest lithium increases nerve cell viability through a combination of mechanisms that includes:[70]

- Regulation of cell lifespan,
- Removal of dysfunctional cellular components,
- Increased mitochondrial function, and
- Synthesis of nerve growth factors.

In clinical studies, lithium treatment has been linked to markers of cellular neuroprotection in the brain, such as:[70]

- Cerebral cortex thickening,
- Increased gray matter density, and
- Hippocampal enlargement.

As described at the beginning of this article, **GSK-3** inhibitors not only confer protection against neuronal **structural** changes, but may protect other cells in the body against age-associated deterioration.

Based on the data uncovered in this article, if a pharmaceutical were developed that produced anywhere near these same clinical benefits, it would become a multibillion-dollar blockbuster drug that would cost consumers hundreds if not thousands of dollars per bottle.

The cost of these two nutrients, on the other hand, is remarkably low.

Summary

Alzheimer's disease remains a looming threat for the aging population. Its consequences are devastating, not only for patients, but also for their families and caregivers.

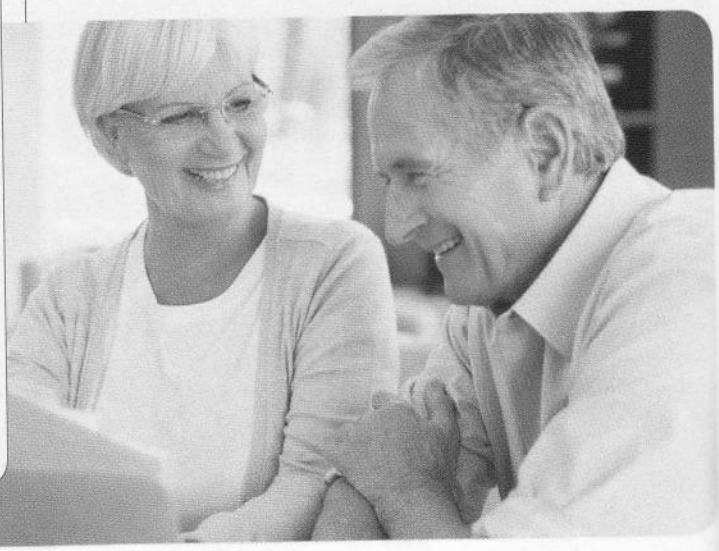
The availability of a pharmaceutical that protects against damaging ***structural*** alterations of **brain cells** would represent a game-changing advance in medicine.

If this same pharmaceutical was able to halt and partially reverse age-associated cognitive decline in older individuals, it would likely become the most ubiquitously-prescribed drug in medical history.

The incredible news for consumers is that these kinds of cellular protective benefits can be found in the novel use of **nutrients** that cost less than **50 cents** a day.

The findings about microdose **lithium** alone represent a new weapon against a destructive aging mechanism caused by excess **GSK-3** activity.

As humans adopt widespread use of **GSK-3 inhibitors**, look for potential increases in functional **human longevity**. ●



If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

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