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 and abnormally accumulate, the consequence is cellular death.

- **Neurofibrillary tangles**: As damaged tau proteins accumulate, neurons become clogged with neurofibrillary tangles. 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 and neurofibrillary tangles. These “tangles” destroy brain cells and impair memory.

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

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.

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.
2. Increase in pro-inflammatory cytokines.
3. Accelerated aging in the skeletal system, leading to degenerative joint disease.
4. Accelerated aging in the stomach and liver.
5. Development of structurally abnormal cell organelles including disrupted mitochondria.
6. Dysfunctional autophagy, meaning inability to clear “debris” that accumulates inside aging cells.
NEW METHOD TO SLOW BRAIN AGING

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.

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.

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. This in turn creates neurofibrillary tangles that lead to brain shrinkage and cell death associated with Alzheimer's dementia.

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.

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

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.

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Studies have shown that by inhibiting GSK-3 activity, one can effectively lower blood glucose in diabetic animals, while increasing insulin sensitivity. 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. In fact, the title of a comprehensive scientific report on this topic is:

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

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. It has also been shown to be an important component for cognitive and mental health.

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. 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.

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

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.
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. 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. 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. 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. 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. Those who consumed water with the highest lithium level (but still tiny) had nearly 40% fewer suicides than those with the lowest lithium level.

These findings were corroborated in separate studies of Japan, Greece, and Austria.

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.

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

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. 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. Cognitive impairment was evaluated by scores on the Mini-Mental State Examination.

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).

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, 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.

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.

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.

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.

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. 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. 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. 

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%.

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. 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.

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. •
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References


