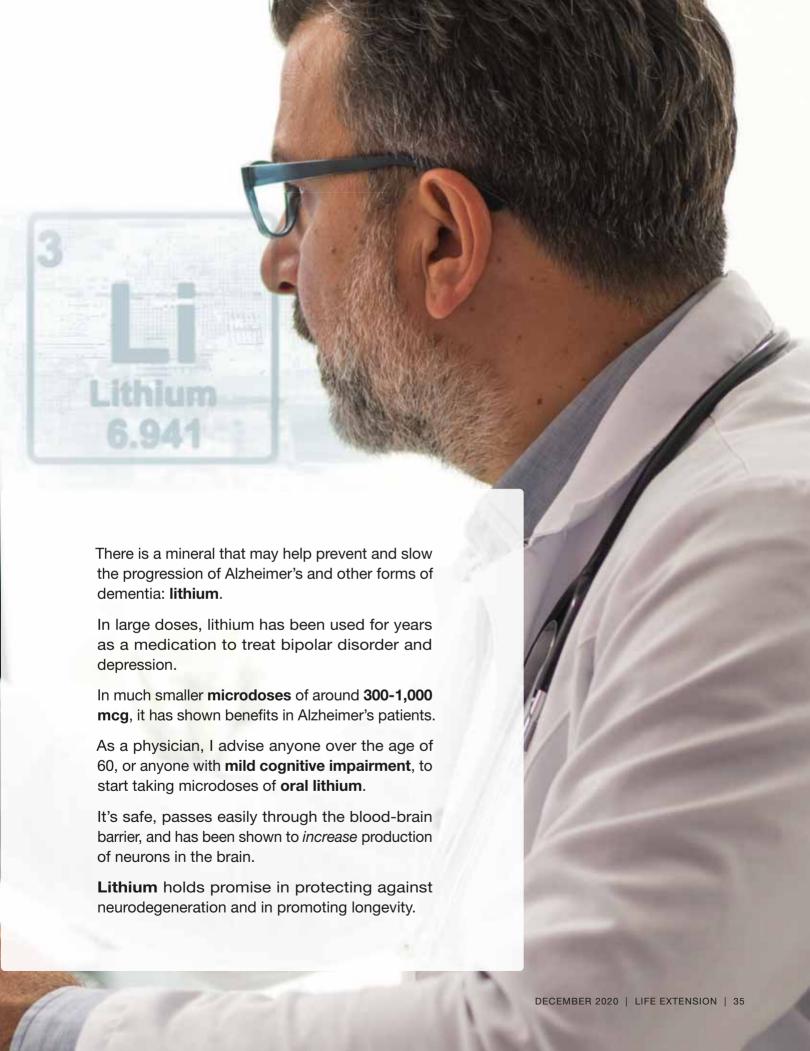
# LITHIUM, ALZHEIMER'S, and Other Dementias

BY T.R. SHANTHA, MD, PHD, FACA



#### Where Lithium Comes From

**Lithium** is a mineral present in nearly all rocks and natural water sources.

Today, people get small amounts from natural spring water, grains, vegetables, eggs, and milk.

The World Health Organization considers lithium a nutritionally essential trace element, alongside zinc, iodine, and others.

#### **Lower Rates of Dementia**

Doctors have long used high doses of lithium to treat bipolar disorder and depression.

Scientists noticed that bipolar patients receiving lithium had *lower* rates of **cognitive decline** than patients on other medications.1 That got them interested in whether lithium could be used to treat neurodegenerative disorders.

To test this observation, researchers compared the rates of **Alzheimer's disease** in 66 elderly bipolar patients using chronic lithium therapy with 48 similar patients who were *not* prescribed this mineral.

In patients receiving lithium, just 5% had Alzheimer's, compared with 33% in the non-lithium group.2

Two studies in Denmark confirmed similar results. Investigators surveyed the records of over 21,000

patients who had received lithium treatment and found that it was associated with a reduced rate of Alzheimer's and other forms of dementia.3,4

And in 2018, researchers studying lithium levels in different regions of Texas discovered that rates of death from **Alzheimer's** disease were *higher* in areas with *low* levels of lithium in the water.5

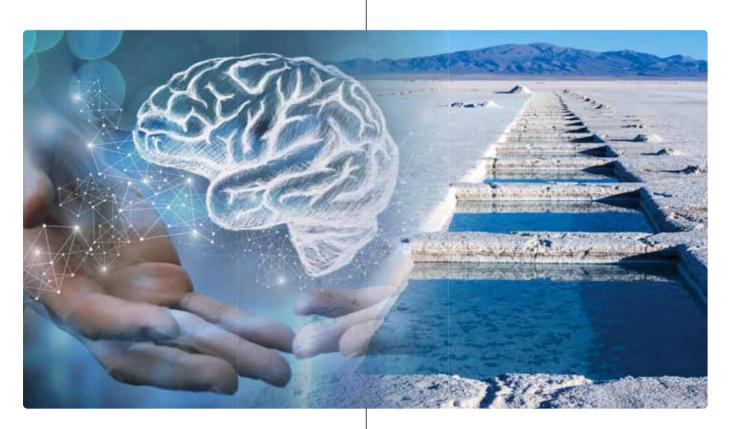
This finding indicates that high lithium drug doses may not be needed to confer neuroprotection.

Based on findings from a 2020 study of Alzheimer's disease in rats, scientists from McGill University have suggested that microdoses of lithium could slow the progression of Alzheimer's in its initial stages and even improve cognition.6

## **How Lithium Protects the Brain**

Experimental and clinical studies offer evidence of the many ways that lithium exerts neuroprotective effects.

Microdoses of lithium may help maintain the length of telomeres, protective caps on the ends of chromosomes.7,8 Telomere length has been linked to increased longevity and to warding off diseases, including Alzheimer's.





Research shows that lithium promotes the synthesis and release of two vital proteins, brain-derived neurotrophic factor (BDNF) and neurotrophin-3.9

These are both **neurotrophic** factors, which means they stimulate the growth, development, and repair of brain cells. 9,10 This may explain why patients on lithium have a significantly higher volume of gray matter, the layer of the brain containing nerve cell bodies. 11,12

One study directly demonstrated that damaged nerve cells exposed to lithium respond with increases in the number and length of **dendrites**, the parts of neurons that receive signals from other neurons.<sup>13</sup>

Lithium reduces levels of an enzyme called glycogen synthase kinase-3 (GSK-3). This enzyme is involved in the production of neurofibrillary tangles, which lead to the damaging plaques found in the brains of patients with Alzheimer's. 14-16

Lithium also reduces oxidative stress and inflammation, providing additional neuroprotection.1

## **Human Studies**

A placebo-controlled trial was conducted on people with a form of mild cognitive impairment that made it difficult to learn or recall new information. The study found that low-dose lithium was associated with lower concentrations of abnormal tau proteins in cerebrospinal fluid.17

Lithium *improved* performance on multiple cognitive scales, suggesting that it may slow the progression of cognitive and functional deficits.<sup>17</sup>

## WHAT YOU NEED TO KNOW

# Lithium Protects the Brain

- Lithium is a mineral found in the earth's crust and in many natural bodies of water.
- Large doses of lithium have long been used to treat bipolar and other mood disorders.
- Some studies have found that bipolar patients on lithium therapy have lower rates of cognitive decline, Alzheimer's disease, and other forms of dementia than those not on lithium.
- Lithium works in a variety of ways to help the brain produce new neurons and to prevent the buildup of neurofibrillary tangles and plagues seen in the brains of Alzheimer's patients.
- Human studies demonstrate that microdoses of lithium improve cognitive performance in patients with mild cognitive impairment, and decrease cognitive decline in patients with Alzheimer's disease.

In another human study, just 300 mcg of lithium daily significantly decreased cognitive decline in Alzheimer's patients compared to a placebo.<sup>18</sup>

In a third study, the cognitive function of patients with early-stage dementia who took lithium remained more stable than in those individuals who took a placebo.19

I believe that every patient with signs and symptoms of dementia should be on microdoses of oral lithium. Further experimentation in large-scale clinical trials is still required to assess the true ability of lithium to treat or prevent dementia and cognitive decline.

### **Summary**

The mineral lithium has benefits in the brain.

It has long been used to treat mood disorders, and there is evidence that its neuroprotective properties can help prevent and slow the progression of **Alzheimer's** and other forms of **dementia**.

Studies show that lithium stimulates the growth of neurons, inhibits the development of neurofibrillary tangles seen in the brains of Alzheimer's patients, maintains and increases the length of protective **telomeres**, and much more.

Every person above the age of 60 or 65, or anyone with signs of dementia, could benefit from **microdoses of oral lithium** to promote brain health and protect cognitive function.

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

#### References

- Forlenza OV, De-Paula VJR, Diniz BSO. Neuroprotective Effects of Lithium: Implications for the Treatment of Alzheimer's Disease and Related Neurodegenerative Disorders. ACS Chemical Neuroscience. 2014;5(6):443-50.
- Nunes PV, Forlenza OV, Gattaz WF. Lithium and risk for Alzheimer's disease in elderly patients with bipolar disorder. Br J Psychiatry. 2007 Apr;190:359-60.
- Kessing LV, Forman JL, Andersen PK. Does lithium protect against dementia? Bipolar Disord. 2010 Feb;12(1):87-94.
- Kessing LV, Sondergard L, Forman JL, et al. Lithium treatment and risk of dementia. Arch Gen Psychiatry. 2008 Nov;65(11):1331-5.
- Fajardo VA, Fajardo VA, LeBlanc PJ, et al. Examining the Relationship between Trace Lithium in Drinking Water and the Rising Rates of Age-Adjusted Alzheimer's Disease Mortality in Texas. *J Alzheimers Dis.* 2018;61(1):425-34.
- Wilson EN, Do Carmo S, Welikovitch LA, et al. NP03, a Microdose Lithium Formulation, Blunts Early Amyloid Post-Plaque Neuropathology in McGill-R-Thy1-APP Alzheimer-Like Transgenic Rats. J Alzheimers Dis. 2020;73(2):723-39.
- Martinsson L, Wei Y, Xu D, et al. Long-term lithium treatment in bipolar disorder is associated with longer leukocyte telomeres. Transl Psychiatry. 2013 May 21;3:e261.
- Coutts F, Palmos AB, Duarte RRR, et al. The polygenic nature of telomere length and the anti-ageing properties of lithium. Neuropsychopharmacology. 2019 Mar;44(4):757-65.
- Quiroz JA, Machado-Vieira R, Zarate JCA, et al. Novel Insights into Lithium's Mechanism of Action: Neurotrophic and Neuroprotective Effects. Neuropsychobiology. 2010;62(1):50-60.
- Leyhe T, Eschweiler GW, Stransky E, et al. Increase of BDNF serum concentration in lithium treated patients with early Alzheimer's disease. J Alzheimers Dis. 2009;16(3):649-56.
- 11. Moore GJ, Bebchuk JM, Wilds IB, et al. Lithium-induced increase in human brain grey matter. *The Lancet*. 2000 Oct 7;356(9237):1241-2.
- 12. Chen G, Rajkowska G, Du F, et al. Enhancement of hippocampal neurogenesis by lithium. *J Neurochem.* 2000 Oct;75(4):1729-34.
- Dwivedi T, Zhang H. Lithium-induced neuroprotection is associated with epigenetic modification of specific BDNF gene promoter and altered expression of apoptotic-regulatory proteins. *Front Neurosci.* 2014 2015-January-14;8(457):457.



# Lithium's Little-Known History

Most people think of lithium as a treatment for mental illnesses. But it has a long history as a general health tonic, used to treat ailments as wide-ranging as asthma, gout, and migraines.

Lithium springs, where water contains naturally high amounts of the mineral, were popular destinations in the 19<sup>th</sup> and 20<sup>th</sup> centuries, visited by people from near and far, including famous people of the day.

Lithium was also used to fortify foods and beverages. In 1929, a soft drink inventor named Charles Leiper Grigg created a beverage called Bib-Label Lithiated Lemon-Lime Soda, now known as 7-Up. The soda contained lithium until 1950 and was originally marketed for its potential to cure hangovers and lift the mood.

Its modern use in the treatment of mental disorders began in 1948 in Australia. The U.S. Food and Drug Administration first approved its use in 1970.

- Sofola O, Kerr F, Rogers I, et al. Inhibition of GSK-3 ameliorates Abeta pathology in an adult-onset Drosophila model of Alzheimer's disease. PLoS Genet. 2010 Sep 2;6(9):e1001087.
- Takashima A. GSK-3 is essential in the pathogenesis of Alzheimer's disease. J Alzheimers Dis. 2006;9(3 Suppl):309-17.
- Sofola-Adesakin O, Castillo-Quan JI, Rallis C, et al. Lithium suppresses Abeta pathology by inhibiting translation in an adult Drosophila model of Alzheimer's disease. Front Aging Neurosci. 2014;6:190.
- Forlenza OV, Diniz BS, Radanovic M, et al. Disease-modifying properties of long-term lithium treatment for amnestic mild cognitive impairment: randomised controlled trial. *Br J Psychiatry*. 2011 May;198(5):351-6.
- Nunes MA, Viel TA, Buck HS. Microdose lithium treatment stabilized cognitive impairment in patients with Alzheimer's disease. *Curr Alzheimer Res.* 2013 Jan;10(1):104-7.
- 19. Wittenberg SM, Toxopeus KA, Schulte PFJ. [Lithium and its protective effect in Alzheimer's disease]. *Tijdschr Psychiatr.* 2017;59(9):559-63.