Science Review: Magnesium L-Threonate

Magnesium L-threonate is the magnesium salt of a naturally occurring vitamin C metabolite L-threonic acid. Magnesium, a divalent cation, is important for neuronal activity as it is a co-factor for enzymes present in the neurons or glial cells.[1,2]

Research Highlights

- ✓ Magnesium L-threonate administered at 1.5 or 2 grams daily in addition to vitamins C and D showed improvement in measures of cognitive and executive function in older adults compared to those given placebo and vitamins.[12]
- ✓ Aged animals given magnesium L-threonate showed improvement in spatial memory (memory in relation to environment) and spatial orientation; these improvements declined with discontinuation of magnesium L-threonate.[11]
- ✓ Magnesium L-threonate has been shown to upregulate expression of the NR2B subunit of the NMDA receptor in cultured hippocampal neurons.[10] This action is thought to enhance memory by increasing long-term potentiation (i.e., synaptic efficiency), which is critical for learning.[9]

Magnesium and Cognitive Health

Two observational studies found that individuals with a diet rich in magnesium have a lower risk of cognitive decline:

- 86% reduced risk in an Australian cohort of 1,400 elderly people between 60-72 years of developing mild cognitive impairment (MCI) in men (p=0.008)[3]
- 74% reduced risk in 1,081 Japanese men and women older than 60 years of developing vascular dementia and 37% reduced risk of developing all-cause-dementia[4]

Mechanism of Action

Magnesium regulates the opening of N-methyl-D-aspartate receptor (NMDAR) in the brain. This receptor plays a critical role in cognitive function and is the target of various neurological treatments.[5]

Structurally, NMDAR is made up of two glycine-binding NR1 subunits, and two of four glutamate-binding NR2 subunits: NR2A, NR2B, NR2C, and NR2D (Figure 1).

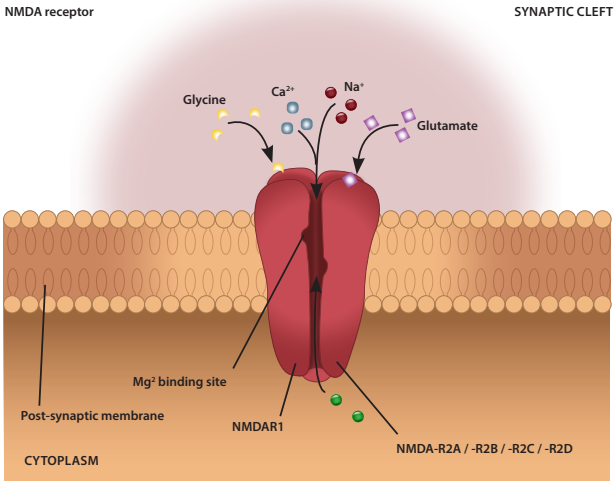

Figure 1. NMDA Receptor Structure

Long-Term Potentiation

Out of the four NR2 subunits, NR2B is of prime importance because it confers greater synaptic plasticity which helps to create and retain memories. However, the number of NR2B subunits have been shown to decrease with age in animals.[6] Overexpression of the NR2B subunit enhanced memory in transgenic rats and mice compared to wild-type littermates.[7] NR2B is also thought to influence memory formation by increasing the long-term potentiation (LTP) through the activation of calcium/calmodulin dependent protein kinase II (CaMKII) (Figure 2).[8] Long-term potentiation is long lasting increase in synaptic efficacy, which is critical for learning and memory.[9]

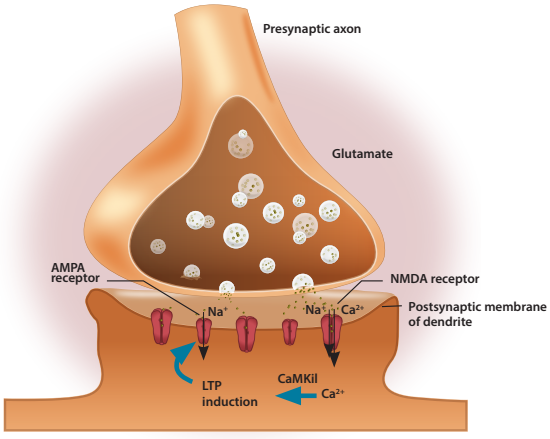

Figure 2. Long-Term Potentiation by NMDA Receptor

Magnesium L-Threonate Enhances Spatial Memory in Animals

Magnesium L-threonate upregulated the expression of NR2B subunit in cultured hippocampal neurons.[10] Compared to control, rats treated with magnesium L-threonate had:

- Increased NR2B subunit expression in the hippocampus by 60% ($p<0.001$)
- Upregulated the activation of CaMKII by 92% ($p<0.01$)
- Enhanced the magnitude of LTP by 52% in the hippocampal slices ($p<0.0001$)[11]

This increase in NR2B subunit expression and magnitude of LTP by magnesium L-threonate translates into enhanced hippocampus dependent memory. In this study, spatial working memory, memory regarding one's environment, and spatial orientation, were assessed at day 0 and day 24 by T maze. At day 0, rats in both groups made 30% fewer correct choices, but at day 24 aged rats treated with magnesium L-threonate made about 15% more correct choices than untreated rats ($p<0.05$). Interestingly, the improvement in spatial memory of aged rats declined within 12 days of stopping the treatment but improved when the treatment was reinitiated.

Magnesium L-Threonate Improves Memory in Older Adults

The effect of magnesium L-threonate on memory was studied in a randomized double-blind placebo controlled study with 50 men and women between 50-70 years of age with self-reported complaints of memory and concentration.

Subjects were treated with 1.5-2 g/day of magnesium L-threonate, along with 200 IU of vitamin D and 30 mg of vitamin C for 12 weeks. Working memory and capacity to store and process information, measured by digit span test, improved by 13.1% at week 6 compared to placebo ($p=0.023$). However, this effect on working memory approached significance at week 12, which was the end of the study ($p=0.064$).[12]

Conclusion

Preclinical studies demonstrate that magnesium L-threonate may increase synaptic plasticity through increasing the expression of one of the NMDA receptor subunits. *In vivo* and clinical study results show that magnesium L-threonate positively influences cognitive measures of memory. More clinical studies are underway to further evaluate effects of magnesium L-threonate on memory and other dimensions of cognition.

References:

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