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Human Nutrition

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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Magnesium and Brain Health

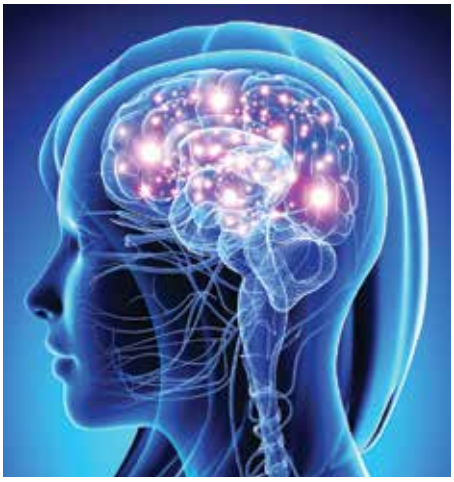
There is currently high interest in the benefits of magnesium. This should be no surprise as magnesium has a multitude of functions *(Hunt & Groff, 1990)* such as:

Cofactor for 300-600 enzymes (this number continues to grow)

- Stabilization of ATP
- Skeletal structure
- Oxidation of fatty acids
- Activation of amino acids
- Synthesis and breakdown of DNA
- Neurotransmission
- Interactions with other nutrients including potassium, pyridoxine, boron, and others

Additionally, magnesium has roles within specific body tissues and organs. One such organ is the brain. As one might expect given the roles of magnesium in energy production, it has a large role in normal brain function. Raichle has stated that in the average human adult, the brain represents only about 2% of the body weight. However, it consumes a disproportionate amount of energy that is consumed – 20 % *(Raichle, 2010)*.

Recent research on magnesium suggests that there might be additional



roles for magnesium in the brain that are not necessarily associated with energy production. In an on-line publication Adaes gives a review of the functions of magnesium in the brain *(Adaes, 2017)*. According to this review, in the brain, magnesium is a regulator of neurotransmitter signaling. It is key to the main neurotransmitters glutamate and gamma-aminobutyric acid (GABA), through modulating the activation of N-methyl-D-aspartate (NMDA) glutamate and GABA Alpha receptors. Through magnesium's regulation of the activity of calcium channels, it contributes to the maintenance of adequate calcium in brain cells. Through these roles, magnesium is important to neuronal processes. Magnesium's involvement in the mechanics of synaptic transmissions and neuronal plasticity, result in its impact on learning and memory. Increased levels of magnesium in the brain have been shown to promote multiple mechanisms of synaptic plasticity that can enhance different forms of learning and memory. Synaptic plasticity is a process that strengthens synaptic transmission. Strengthening synaptic plasticity can help delay age-related cognitive decline. It has been seen that increasing brain magnesium levels may lead to the increased and rapid production of neural stem cells. This would indicate that brain magnesium may promote neurogenesis (the generation of new neurons) in adulthood. Neurogenesis is a key process in the brain's overall adaptability, mood regulation, and cognitive flexibility. Cognitive flexibility is the mental ability to switch between thinking about two different concepts, and to think about multiple concepts simultaneously. Improved cognitive flexibility allows one to learn more quickly, solve problems more creatively, and adapt and respond to new situations more effectively. It is also helpful in enhancing the beneficial effects of exercise in the brain. Magnesium helps in the control of oxidative stress, inflammatory processes and helps maintain proper brain blood flow.

Magnesium might play other, yet-undefined, roles in brain health. In a systematic review, Veronese , et al., *(Veronese, Zurlo, & Solmi, 2016)* determined that in comparison to healthy and medical illness controls, the magnesium levels in those with Alzheimer's disease was significantly lower in cerebrospinal fluid and in hair ($p<0.05$) even though there was no difference in serum magnesium levels. In another study reported by Tzeng, et al., *(Tzeng, et al., 2018)* found that based upon the National Health Research Institute Database of Taiwan that those that had used magnesium oxide were less likely to develop dementia. They further adjusted their data to compensate for various factors including age, sex, geography and economic variation and they still found that the relationship held. Finally, Dhandapani, et al., reported that magnesium decline is likely to play a role in the pathogenesis of traumatic brain injuries *(Dhandapani, Gupta, Vivekanandhan, Sharma, & Jahapatra, 2008)*. They found that those who were parenterally administered magnesium sulfate within 12 hours of their injury had a much greater chance of a favorable outcome with no observed significant adverse effects.

From the above studies, it would appear that magnesium has multiple roles in normal brain health and function. However, magnesium must enter the brain and cross the blood brain barrier in order to support normal brain function. According to Ghabriel and Vink: "Magnesium is able to cross the blood brain barrier and is transported via the barrier with the net flux from the blood in the parenchyma. Active magnesium transport from the blood to the extracellular fluid of the brain is evidenced by its higher concentration in the cortical extracellular fluid than its concentration in the plasma-dialysate or cisternal CSF" *(Ghabriel & Vink, 2011)*. The amount of magnesium that crosses the blood brain barrier is a reflection of the amount of magnesium absorbed. To ensure that there is adequate magnesium absorbed, it stands to reason that adequate magnesium must be consumed.

Unfortunately, according to Costello et al, *(Costello, et al., 2016)* approximately 50% of the United States population consume less than the daily requirement from their diets. They further state that the 2015 Dietary Guidelines Advisory Committee characterized magnesium as a "shortfall nutrient of public health concern." This dietary inadequacy is not limited to the United States. Olza, et al., *(Olsa, et al., 2017)* reported from the ANIBES data that 72% of the Spanish population did not meet the EFSA recommended intakes of magnesium from their diets. If the diet is inadequate for magnesium content, a dietary supplement containing magnesium may be warranted to support normal brain health.

To support adequate brain health a magnesium supplement needs to be both highly bioavailable to deliver sufficient magnesium via the bloodstream. It also needs to be well tolerated. One such magnesium source is magnesium bisglycinate chelate. In a study on patients with ileal resections, Schuette, et al., as a secondary objective, found that magnesium bisglycinate was well tolerated compared to magnesium oxide *(Schuette, Lashner, & Janghorbani, 1994)*. In pregnant women consuming 300 mg daily of magnesium as a magnesium bisglycinate chelate were evaluated for leg cramping, but as a secondary objective had adverse events such as nausea and diarrhea monitored *(Supakatisant & Phupong, 2012)*. They found that there was no difference from a placebo for these events. Finally, in another study conducted by Ashmead, et al., varying dosages of magnesium bisglycinate were compared to each other and a placebo in gastric upset and fecal consistency scores *(Ashmead, et al., 2016)*. They found that at 600 mg of magnesium as a bisglycinate chelate did not differ from the placebo in regard to composite gastric upset scores and had a slight improvement in fecal scores.

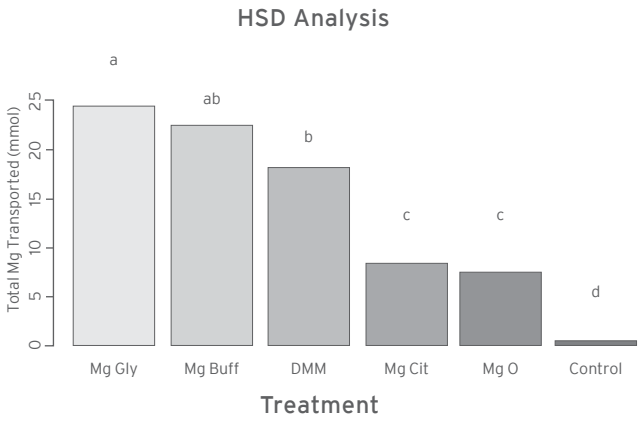
Magnesium bisglycinate chelate is highly bioavailable. There are many studies that show the bioavailability through various endpoints. A recent study by Hartle, et al., using an in vitro Caco-2 cell model was presented at the 2016 Experimental Biology Meetings. *(Hartle, Morgan, & Poulsen, 2016)* In this study, they measured absorption of various magnesium sources by

measuring the transport of magnesium across the epithelial layer while ensuring that it was not disrupted by the magnesium gradient. The results are shown in Figure 1. They concluded that magnesium bisglycinate had significantly greater absorption ($p<0.05$) and was the most bioavailable source of magnesium.

As seen in this article, magnesium bisglycinate chelate is a bioavailable source of supplementary magnesium that can help provide adequate nutrition to support the health of the brain. It is highly bioavailable with good tolerability. Albion Minerals by Balchem is the leading source of magnesium bisglycinate chelate.

Figure 1.

In-vitro absorption of various magnesium sources in Caco-2 cells. Different letters indicate statistically significant differences between treatments. Mg Gly = Mg bisglycinate, Mg Buff = Mg Bisglycinate with Mg oxide, DMM = Dimagnesium malate, Mg Cit = Mg citrate, Mg O = magnesium oxide. Data presented by Hartle, et al., at Experimental Biology, San Diego, CA, 2016



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