



Rapid recovery from major depression using magnesium treatment

George A. Eby *, Karen L. Eby

George Eby Research, 14909-C Fitzhugh Road, Austin, TX 78736, United States

Received 18 January 2006; accepted 20 January 2006

Summary Major depression is a mood disorder characterized by a sense of inadequacy, despondency, decreased activity, pessimism, anhedonia and sadness where these symptoms severely disrupt and adversely affect the person's life, sometimes to such an extent that suicide is attempted or results. Antidepressant drugs are not always effective and some have been accused of causing an increased number of suicides particularly in young people. Magnesium deficiency is well known to produce neuropathologies. Only 16% of the magnesium found in whole wheat remains in refined flour, and magnesium has been removed from most drinking water supplies, setting a stage for human magnesium deficiency. Magnesium ions regulate calcium ion flow in neuronal calcium channels, helping to regulate neuronal nitric oxide production. In magnesium deficiency, neuronal requirements for magnesium may not be met, causing neuronal damage which could manifest as depression. Magnesium treatment is hypothesized to be effective in treating major depression resulting from intraneuronal magnesium deficits. These magnesium ion neuronal deficits may be induced by stress hormones, excessive dietary calcium as well as dietary deficiencies of magnesium. Case histories are presented showing rapid recovery (less than 7 days) from major depression using 125–300 mg of magnesium (as glycinate and taurinate) with each meal and at bedtime. Magnesium was found usually effective for treatment of depression in general use. Related and accompanying mental illnesses in these case histories including traumatic brain injury, headache, suicidal ideation, anxiety, irritability, insomnia, postpartum depression, cocaine, alcohol and tobacco abuse, hypersensitivity to calcium, short-term memory loss and IQ loss were also benefited. Dietary deficiencies of magnesium, coupled with excess calcium and stress may cause many cases of other related symptoms including agitation, anxiety, irritability, confusion, asthenia, sleeplessness, headache, delirium, hallucinations and hyperexcitability, with each of these having been previously documented. The possibility that magnesium deficiency is the cause of most major depression and related mental health problems including IQ loss and addiction is enormously important to public health and is recommended for immediate further study. Fortifying refined grain and drinking water with biologically available magnesium to pre-twentieth century levels is recommended.

© 2006 Elsevier Ltd. All rights reserved.

Introduction

Major depression, one of the affective disorders, is a mood disorder characterized by a sense of inade-

quacy, despondency, decreased activity, pessimism, anhedonia and sadness where these symptoms severely disrupt and adversely affect the person's life, sometimes to such an extent that suicide is attempted or results. Irritability, insomnia, lethargy, agitation and anxiety often accompany depression. About 10% of the American

* Corresponding author. Tel./fax: +1 512 263 0805.
E-mail address: george.eby@coldcure.com (G.A. Eby).

population is affected by depression at any given moment. The World Health Organization showed that unipolar major depression was the leading cause of disability globally in 1990, and suggests that depression and heart disease will be the most common diseases on Earth by 2020 [1], with both of these diseases having strong magnesium deficiency components.

Contemporary approaches to treating unipolar major depression and manic depression (bipolar disorder) utilize a wide variety of drugs that include monoamine oxidase (MAO) inhibitors, tricyclic compounds, selective serotonin reuptake inhibitors (SSRIs), and lithium (for bipolar disorder). These drugs need several weeks to become fully functional.

Varley [2] and many others have shown concern that some antidepressant drugs promote suicide rather than prevent it, particularly in children and adolescents, wherein adverse mood-related effects, including suicide attempts is 4% in active drug versus 2% in placebo-treated patients. This wide-spread concern has resulted in "Black Box" warnings by the United States Food and Drug Administration and outright declarations of contraindications for the United Kingdom for most antidepressants. This led Varley to ask, "What options now?"

In answer to Varley's question, magnesium should again become the treatment of choice due to its: (1) wide role in brain biochemistry, (2) safety, (3) long history in treating depression and other mental health issues. Depression appears to be a magnesium deficiency disorder especially in major and suicidal depression, but not necessarily in simple "melancholy" or depression caused by other factors such as underlying disease (particularly hepatitis C), hormonal imbalance (particularly hypothyroidism and low testosterone), low cholesterol, Wilson's Disease, food allergy (particularly gluten intolerance), and adverse reaction to medications.

The benefit of magnesium to treat agitated depression was first published in 1921 by Weston [3]. Magnesium sulfate (10% elemental magnesium) was injected in doses of one to two CCs of a 25% or 50% solution resulting in nearly all of his fifty patients relaxing and sleeping from 4 to 6 h.

Magnesium is recognized in homeopathic medicine for the treatment of depression. For example, magnesium chloride (*Magnesia Muriatica*) has been used for many decades to relieve various emotional problems including anxiety, apathy, aversions, despair, depression, discontent, headaches, insecurity, irritability, over sensitiveness, restlessness, sulkiness, talkativeness and uncertainty.

Wacker and Parisi [4] reported in 1968 that magnesium deficiency could cause numerous neuromuscular symptoms including hyperexcitability, depression, behavior disturbances, tetany, headaches, generalized tonic-clonic as well as focal seizures, ataxia, vertigo, muscular weakness, tremors, irritability, and psychotic behavior, each of which were reversible by magnesium repletion.

According to Durlach and Bac [5], the mental health pattern induced through simple magnesium deficiency is always neurotic and never psychotic, for example: generalized anxiety, panic attack disorders, and depression. Other psychiatric symptoms from magnesium deficiency consisted of hyperemotionality, asthenia, headache, insomnia, dizziness, nervous fits, lipothymias (repeated fainting), and sensations of a "lump in the throat" and of "blocked breathing", all of which can be effectively treated with magnesium. Although a neurosis pattern due to magnesium deficiency is frequently observed and simply cured through oral supplementation, neuroses are preeminently conditioning factors for stress.

Cernak et al. [6] showed that chronic stress decreases both free and total plasma ionized magnesium and simultaneously increased oxidative stress in humans. These findings support the need for magnesium supplementation for people living in conditions of chronic stress. However, about 70% of United States and the West have diets containing less than the recommended 400 mg of magnesium per day and up to 20% have diets with less than one-half the recommended intake. Increased stress builds up further worsening magnesium deficiency, with health issues such as depression and cardiovascular disease resulting.

Magnesium deficiency symptoms are non-specific due to its necessity in over 325 enzymes. With most of these enzymes being brain-related, the possibility that magnesium deficiency is involved in a variety of neurosis can be safely assumed.

Opportunity arose to test the hypothesis that magnesium would be helpful in subjects with major depressive disorders. After explaining the possible risks and benefits, and obtaining informed consent, the subjects proceeded to treat their depression with magnesium.

Methods and procedures

A non-drinking, 59-year old hypomanic-depressive male, having had a long history of mild depression treatable with antidepressants, suddenly became extremely anxious, insomniac, tetanic and suicidally depressed after a year of extreme personal,

business and noise stress and poor dietary habits (fast food). He was not responsive to treatment with a number of antidepressants and lithium carbonate. After reviewing the report of Durlach concerning magnesium and depression [5], he was treated with magnesium. He was given 300 mg of magnesium, as glycinate and later as taurinate, to take orally with each meal and at bedtime.

A 23-year-old woman, who had 5 years previously suffered traumatic brain injury and lost much of her short term memory and some of her IQ, suddenly became severely depressed after experiencing long-term stress due to several stressors related to diet (fast food), work, constant noise, and especially because of very poor academic performance after having had excellent grades prior to her brain injury. Antidepressants had beneficial effects, but her concern about side effects caused her to switch to magnesium. She was given 200 mg of magnesium (as taurinate) to take with each meal and at bedtime.

A 35-year old woman, having had three children followed by severe postpartum depression (PPD) in each case, was given 200 mg of magnesium (as glycinate) to take each meal during her pregnancy to prevent PPD during her fourth pregnancy. Antidepressants had previously had some beneficial effects, but side effects were worrisome to her. Part of her decision to take magnesium was her desire to prevent preeclampsia, a known but often ignored magnesium deficiency condition [7].

A 40-year old man, irritable, anxious, extremely talkative, moderately depressed, and heavily into use of food, tobacco (smoking and chewing), alcohol and cocaine, took 125 mg of magnesium (as taurinate) with each meal and at bedtime in an effort to relieve his symptoms.

Results

The 59-year old man experienced life-saving benefit from magnesium. The first night after starting magnesium, sleep was restored essentially to normal. Within the following 4 days, depression was greatly reduced for 4–6 h after each magnesium dosage. Anxiety steadily disappeared. Tetany and headaches rapidly disappeared. On occasion, 2:00AM doses were also required to maintain a feeling of wellness. Over the following months, normalcy was maintained only by frequent magnesium ingestion. In this patient, depression always occurred 1 h after taking a 500 mg calcium (carbonate) dietary supplement, which was extinguishable within 1 h only by administration of 400 mg of magnesium. This man was extremely sensitive to cal-

cium, and elimination of all dairy and supplemental forms of calcium was mandatory for mental stability. Osteoporosis due to low calcium intake was feared, but a high magnesium and low calcium diet did not have an adverse effect on his bone density over a 5-year observation period. Normal life free of depression was difficult to maintain without frequent magnesium treatment, until Kefir, a rich source of beneficial intestinal flora and inulin (vital for magnesium absorption [8]), and indole-3-carbinol (200 mg per meal) were added to his diet. These nutrients seemed to stabilize the beneficial effect of magnesium, perhaps by improvements in intestinal absorption, digestion and immunity. After incorporation of these agents into his diet, total wellness occurred, which was easily maintained with much less magnesium.

After 1 week of magnesium treatment, the 23-year old woman became free of depression. Unexpectedly, her short term memory and IQ also returned, benefits only previously shown in rats [9] when immediately treated with magnesium after traumatic brain injury. However, her mental acuity returned nearly immediately upon magnesium treatment, even though the trauma had occurred 5 years earlier.

The 35-year old woman delivered her baby on schedule without developing any aspect of postpartum depression, preeclampsia or any other illness associated with pregnancy. The baby was healthy, full weight and quiet.

The 40-year old man found himself free of his symptoms within a week, and unexpectedly found his craving for smoking, dipping, cocaine and alcohol to disappear also. It seemed that magnesium deficiency caused his habituation. He also noted that his ravenous appetite was suppressed, and beneficial and desired weight loss ensued.

Discussion

We have shown efficacy, as have others, in treating depression and some related mental disorders with magnesium. We suggest that magnesium treatment will be found effective in future clinical trials, at least to an extent equivalent to antidepressant drugs, and perhaps more effective.

The occurrence of depression 100 years ago was rare, occurring primarily in the elderly. Only 1% of Americans born before 1905 developed depression before they were 75 years old, while 6% of Americans born in 1955 developed depression by the time they were 24 years old. [10] Previous to 1905, grains were not refined and there was adequate magnesium (over 400 mg per day) in the diet. At

that time, refining was necessary to prevent spoilage. One hundred years later, only 16% of the magnesium found in whole wheat grain remains in refined flour, [11] lowering dietary intake of magnesium in some severe cases by 250 mg per day and setting the stage for magnesium deficiency. Additionally, we often rely on diets containing too much calcium, while taking on more stressful activities.

Inadequate dietary magnesium in today's diet is clearly evident from a 4-min 16-mb video production titled, "Foods Containing 400 mg of Magnesium" located on the Internet at: <http://coldcure.com/gif/foods-containing-400mg-magnesium.wmv>. Further, some city and residential water treatment systems remove all minerals from drinking water, and bottled beverages no longer contain nearly as much minerals as they did 100 years ago. Consequently, due to widespread removal of magnesium from human food and drink, we hypothesize that most cases of major depression, including postpartum depression, may be related to magnesium deficiency.

Not only has the incidence of depression increased greatly in the last 100 years, but the age of onset has also fallen greatly. Depression was essentially unheard of in children in 1906. Today, children in the United States are taking four times the amount of psychiatric medications as children in the rest of the world combined [12], with essentially no emphasis being placed on magnesium in their food. For example, we were not able to find magnesium listed as an ingredient on any packaged food, except Planters® Peanuts, in grocery stores in the United States. Consequently, what used to be a disease risk primarily for the elderly is now common in all ages including children.

Some dietary supplements sold in the United States and the West contain magnesium, although the ligand of choice for large-scale manufacturers is "oxide" due to its compactness and ease of use in manufacturing. Unfortunately, magnesium oxide is not biologically available in the human body [13–15]. Other magnesium ligands including chloride, sulfate (Epsom Salts), citrate, lactate, malate, glycinate and taurinate produce highly biologically available magnesium complexes.

Taurine, Gamma-aminobutyric (GABA) acid and glycine are major inhibitory neurotransmitters in the central nervous system, predominantly active in the spinal cord and brain stem. Taurine and glycine also act as a modulator of excitatory amino acid transmission (glutamate) mediated by *N*-methyl-*D*-aspartate (NMDA) receptors. Shealy et al. [16] found that magnesium and taurine were deficient in nearly all depressed patients.

Magnesium glutamate and magnesium aspartate greatly worsened the 59-year old man's depression. A possible reason for this observation is that excess glutamate is more cytotoxic than cyanide to neurons in bringing into neurons toxic levels of calcium ions [17]. These magnesium compounds should be considered as neurotoxic to depressives, and perhaps all people, and should not be used during treatment of depression, anxiety or similar hyperemotional disorders. Food and drink products containing monosodium glutamate and aspartate should not be used by depressives.

This report is based on internet page <http://coldcure.com/html/dep.html> (Rapid Recovery From Depression Using Magnesium Treatment), a 135 page report that receives a quarter million accesses per year. This page is permanently archived on the WayBack machine at <http://archive.org>. Most correspondence reported that the page viewer's depression was effectively treated with high-dose magnesium. Viewers were pleased to find something natural that helped them instead of using prescription drugs. Most reported having had treatment-resistant depression, while others were simply reluctant to use psychiatric, antidepressant drugs due to their fear of side effects. While over 60,000 Internet pages were found using the search terms "major depression" and "magnesium", there were only 11 medical journal articles found with the same search terms. This suggests that the public is far more interested in magnesium for depression than is medical science.

The single largest obstacle to viewers' success in treating depression appeared to be continued, excessive intake of dietary calcium. Some viewers were found to have kidney or digestive diseases that impaired magnesium metabolism, forestalling their recovery from depression until those conditions were corrected. Apparently, the use of indole-3-carbinol to improve magnesium utilization is new.

One physician-viewer, having suffered from severe depression for two decades, reported that he had found the above web page several years earlier and totally dismissed it as being overly simplistic, recounting that "scientists are not so stupid as to have overlooked magnesium". In total desperation, he finally tried magnesium treatment and it "cured" his depression. Later, he became verbally abusive with the writer because the page made it seem too simple, and because of that, he had dismissed the idea as preposterous and continued to suffer. Irritability is a sign of modest magnesium deficiency, consequently this physician could be diagnosed as "needing more dietary magnesium". Although irritability can cause violence, no clinical

data has been published about the ability of magnesium to prevent violence, although we hypothesize that a magnesium-replete population would be less violent.

The main side effect reported from high-dose magnesium and low calcium intake as treatment for depression was diarrhea. This results mainly from the attachment of each magnesium ion to about 800 molecules of water in the intestinal tract. Any treatment to terminate diarrhea, including lowering magnesium intake, was deemed essential to promote proper absorption of nutrients. One gram of arginine with each meal helped prevent magnesium-induced diarrhea, while 3 g per meal caused severe constipation, perhaps due to the effect of excessive arginine-induced nitric oxide on nonadrenergic, noncholinergic inhibitory nerves of the colon [18]. Methods of introducing magnesium to treat depression without causing diarrhea were by injection, by rectum and topical. Of these alternatives, daily topical application to the chest and back using 25% magnesium chloride solutions as described by Shealy

[16] was preferred due to simplicity and apparent lack of side effects.

Fig. 1, by the University of California, San Diego – Department of Cognitive Science, shows magnesium ion involvement in nerve cell electrical conduction activity in a regulatory fashion for calcium ions. Magnesium ions normally block calcium ions within the *N*-methyl-*D*-aspartate (NMDA) receptor channel. When magnesium ions are missing, the channel is unblocked and calcium ions and sodium ions enter the postsynaptic neuron as potassium exits. Sapolsky [19] suggested that magnesium depletion was likely to be deleterious to neurons possibly by causing NMDA-coupled calcium channels to be biased towards opening. From our observations, Sapolsky is correct with the damage to neurons appearing to the individual as depression and related mood disorders.

Paul [20] suggested that any means of reducing pathological neuronal calcium ion flow to reduce resulting pathological nitric oxide neuronal output would have antidepressant effects. Durlach and Bac [5] reported that magnesium deficiency

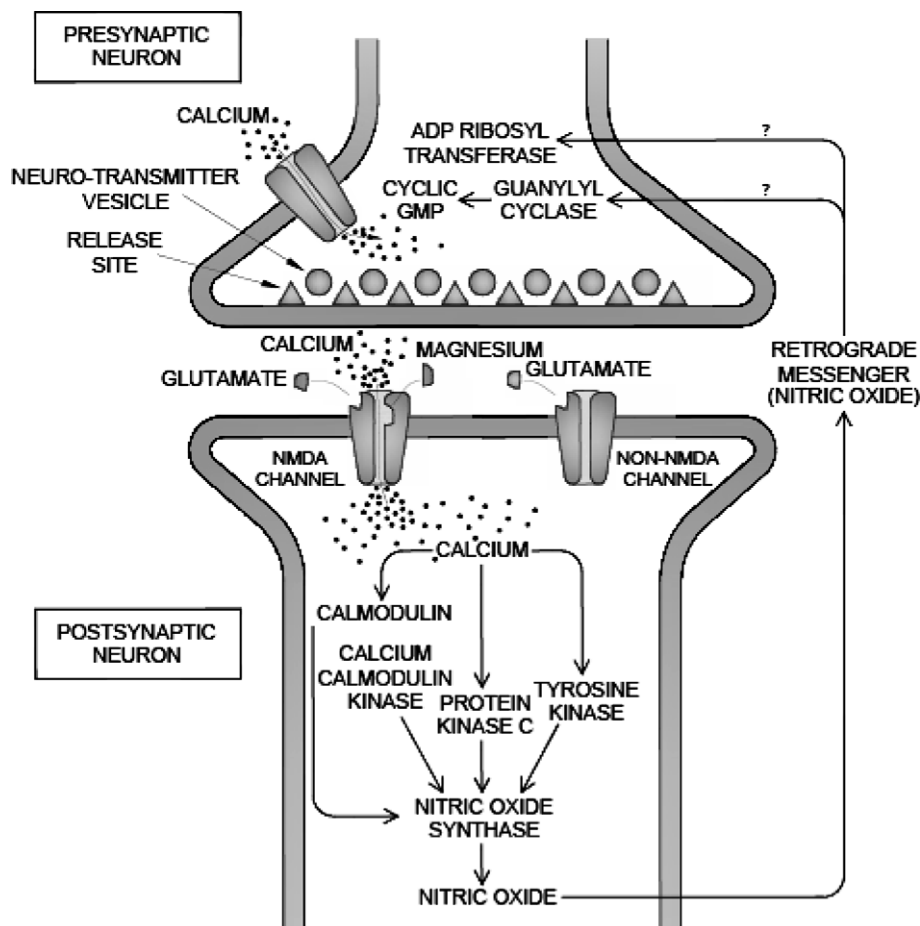


Figure 1 Magnesium has a role in regulating calcium ion flow in neurons.

increased nitric oxide production. Too much calcium ion and glutamate with insufficient magnesium ion, particularly in the hippocampus, plays a vital role in brain cell synaptic dysfunction leading to depression and other mood and behavioral disorders. These observations help explain why the 59-year old man was highly sensitive to calcium and mono-sodium-glutamate, making him nearly immediately depressed upon their consumption.

Murck [21] showed many actions of magnesium ions supporting their possible therapeutic potential in affective disorders. Examinations of the sleep-electroencephalogram (EEG) and of the endocrine system points to the involvement of the limbic–hypothalamus–pituitary–adrenocortical axis because magnesium affects all elements of this system. Magnesium has the property to suppress hippocampal kindling, to reduce the release of adrenocorticotrophic hormone (ACTH) and to affect adrenocortical sensitivity to ACTH. The role of magnesium in the central nervous system could be mediated via the *N*-methyl-*D*-aspartate-antagonistic, *g*-aminobutyric acid A-agonistic or the angiotensin II-antagonistic property of this ion. A direct impact of magnesium on the function of the transport protein p-glycoprotein at the level of the blood-brain barrier has also been demonstrated, possibly influencing the access of corticosteroids to the brain. Furthermore, magnesium dampens the calcium ion-protein kinase C related neurotransmission and stimulates the Na–K-ATPase. All these systems have been reported to be involved in the pathophysiology of depression. Singewald et al. [22] also demonstrated induced magnesium deficiency in mice to produce depression-like behavior which was beneficially influenced with antidepressants.

What remains to be explained is exactly why control of calcium ions is lost in depression, although depletion of magnesium ions certainly could cause it by impairing control of calcium ions in neuronal channels resulting in calcium ion cascades that are pathological (excitotoxic). A compelling argument for the use of calcium channel blockers, such as therapeutic doses of magnesium, is that the influx of calcium ions from the extracellular fluid to the cytosol of cells through calcium channels is important for the proper release of neurotransmitters from presynaptic neurons [23]. Interestingly, some calcium channel blocking drugs used in cardiology have been reported to increase depression and suicide risk.

Seelig and Rosanoff [24] reviewed the evidence that chronic stress depletes magnesium reservoirs,

increasing the risk of depression. Elevated cortisol in a subset of depressives is an enduring and well-replicated finding [25].

Papadopol et al. [26] in Romania compared the Intelligence Quota (IQ) of children growing up at home compared with the IQ of children growing up in a stressful orphanage. Stress from orphanage living drove down intracellular magnesium so severely that orphans lost much of their IQ (see Fig. 2). Attention, memory, psychoticism and neuroticism were also similarly, but less, affected. Magnesium deficit caused a number of neuropsychological disorders including, agitation, anxiety, depression, irritability, weakness, fatigue, confusion, asthenia, sleeplessness, headache, convulsive and nervous attacks, delirium, hallucinations and hyperexcitability [26]. Nothing could be more harmful to the minds of children than stress-induced magnesium deficiency. Yet, in search of academic excellence increasingly more stress is applied to children. Their diets are often insufficient in magnesium to protect them from stress, consequently they are treated with antidepressants and other drugs.

There are reports that there was no difference in the serum concentration of magnesium ion or calcium/magnesium ratios [27], and that magnesium was higher in serum of depressives [28], however, these observations do not represent what is

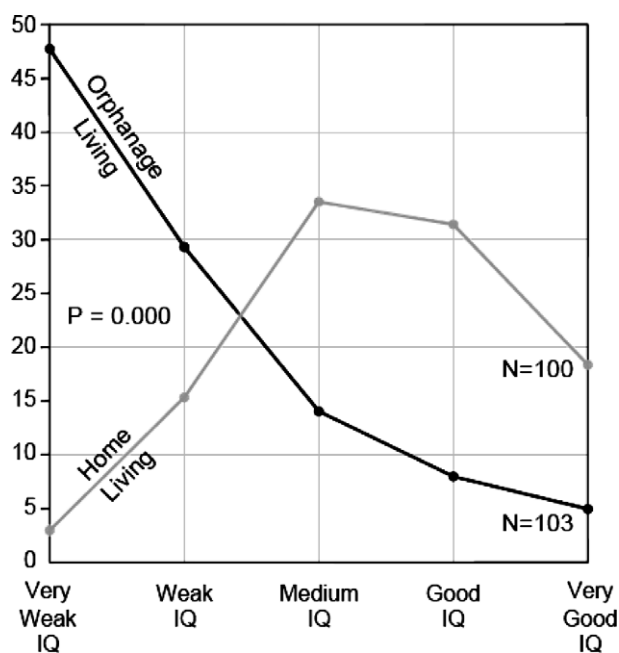


Figure 2 Distortion in children's IQ attributed to stress-induced damage to intracellular magnesium in institutionalized homes vs. home living – from Papadopol.

going on inside the central nervous system. Banki et al. [29] showed that both cerebrospinal fluid 5-hydroxyindoleacetic acid (5-HIAA) and magnesium ions are low in suicidal depressives. Levine et al. [30] showed that there were high serum and cerebrospinal fluid calcium to magnesium ratios in recently hospitalized acutely depressed patients. Kalinin et al. [31] using magnesium lactate and vitamin B-6 (required for absorption of magnesium) showed benefit in anxiety and depression treatment in patients with epilepsy. There are numerous reports showing magnesium to be extremely beneficial in treating attention deficit hyperactivity disorder (ADHD), suggesting that ADHD is a symptom of magnesium deficiency [32].

Hypothyroidism, a known cause of depression, is associated with low magnesium with circulating T4 levels being directly correlated with magnesium serum levels [33]. The depression attributable to hypothyroidism is hypothesized to be caused by resultant low magnesium, which is restored to normal only by proper treatment of hypothyroidism.

Several secondary injury factors have been identified in traumatic brain injury including oxidative stress, changes in blood flow, neurotransmitters and metal ionic changes, edema and energy failure. Of these, magnesium ion decline has been identified as playing a crucial role in the secondary injury process [34].

Postpartum depression can be much more severe than clinical depression. The fetus and placenta absorb enormous amounts of nutrients (especially magnesium) from the mother and loss of magnesium to the fetus coupled with insufficient intake of magnesium by the mother is hypothesized to be the cause of postpartum depression. Lactation is also known to deplete maternal magnesium [4]. Our observations support this otherwise unreported concept.

Consistent with our observations, elimination of cravings by magnesium for tobacco, alcohol and cocaine has been separately observed. For example, Nechifor et al. [35] found that magnesium supplements reduced the number of cigarettes smoked. Margolin et al. [36] demonstrated utility of magnesium in reducing the craving for cocaine. Murray and Berger [37] showed that magnesium was helpful in alcohol withdrawal. The Alturas [38] showed that alcohol greatly lowered serum magnesium, raising the potential for headaches, strokes and brain injury.

The process of normal aging is accompanied by changes in sleep-related endocrine activity, and in depression sleep is often highly disturbed. During aging an increase in cortisol and a decrease in renin and aldosterone concentration occur. In aged

subjects more time is spent awake and slow-wave sleep is reduced. The natural NMDA antagonist and GABA agonist, magnesium ion, plays a key role in the regulation of sleep and endocrine systems such as the HPA system and renin-angiotensin-aldosterone system. Magnesium ion partially reverses sleep EEG and nocturnal neuroendocrine changes occurring during aging [39]. The similarities of the effect of magnesium ion and lithium ion furthermore support the efficacy of magnesium ion as a mood stabilizer, and one may show that lithium ions play some of the roles normally performed by magnesium ions in the brain. Clearly, magnesium (200–400 mg) is extremely effective in promptly inducing sleep when taken at bedtime, and sleep is vital to recovery from depression.

Even national security issues may result from magnesium deficiency. Consider that Saudi Arabia, in its modernization process, removes most magnesium and other minerals, such as boron (necessary for magnesium absorption and proper brain function [40,41]), from drinking water processed by reverse osmosis. Reliance on refined grain products, rather than whole grain products, results in inadequate dietary magnesium. Inadequate magnesium intake may be the cause of the 40% depression rate among the elderly [42], and the nearly 25% depression rate in the 15–29 year old group [43], an age group that is the main source of suicidal bombers. Consider that stress depletes magnesium and increases oxidative stress in soldiers during military combat [6]. If all other factors between engaged armies are similar, surely the army having the most resistance to stress via adequate brain magnesium will prevail.

Low calcium and high magnesium (1:2 ratio) intake is vastly more beneficial to overall health, including depression, cardiovascular disease and osteoporosis than high calcium and low magnesium (2:1 ratio). The old 2:1 ratio worked well at a much earlier time when we were getting enough magnesium from food and water. Nevertheless, official governmental and highly scholarly dietary recommendations remain backward. Excessive calcium intake prevents absorption of magnesium in the intestinal tract, adversely affecting health [4,5,12,24,44].

The only “bone and joint” effect of the low calcium and high magnesium diet on the 59-year old man was complete elimination of all joint and back pain. This observation reflects terminating hyperalgesia in rats via sensitization of nociceptive pathways in the spinal cord involving NMDA and non-NMDA receptors by administration of magnesium [45], which also explains why most of Shealy’s

patients having depression with chronic pain were magnesium deficient [16].

Since magnesium has sedative properties, caution is advised when administering anesthesia and magnesium, or anesthesia to magnesium-replete patients, as less anesthesia will be required [46].

This report supports the overall hypothesis that magnesium is therapeutic for depression and related mental disorders. However, in the United States, it is effectively illegal to market nutrients to treat, cure, and prevent diseases. This disconnect between policy and reality creates artificial, insidious illnesses which are frustratingly hard to address at the policy level, as was found by Aaserud et al. [7] in 2005 in their efforts to promote magnesium for the prevention of preeclampsia, something that was first demonstrated in 1925 by Lazard [47].

It is likely that magnesium deficiency causes most major depression and related mental health illnesses, IQ loss and addictions. We suggest that magnesium deficiency as cause of these disorders is enormously important to public health and is recommended for immediate, wide-spread further study. The public should be advised to obtain more than 600 mg of dietary magnesium a day to enable them to adequately handle stress and prevent neuronal calcium ion injury. Fortifying refined grain and drinking water with biologically available magnesium is recommended.

References

- [1] World Health Organization. The World Health Report. Making a Difference. Geneva: World Health Organization; 1999.
- [2] Varley CK. Treating depression in children and adolescents : what options now?. *CNS Drugs* 2006;20:1–13.
- [3] Weston PG. Magnesium as a sedative. *Am J Psychiat* 1921;78:637–8.
- [4] Wacker WE, Parisi AF. Magnesium metabolism. *N Engl J Med* 1968;278:712–7. On Internet at <http://coldcure.com/html/magnesium-metabolism.html>.
- [5] Durlach D, Bac P. Chapter 20, Mechanisms of Action on the Nervous System in Magnesium Deficiency and Dementia. In: Yasui M, Strong MJ, Ota K, Verity MA, editors. Mineral and metal neurotoxicology. Boca Raton, New York, London, Tokyo: CRC Press; 1997. On Internet at <http://www.mgwarter.com/dur30.shtml>.
- [6] Cernak I, Savic V, Kotur J, Prokic V, Kuljic B, Grbovic D, et al. Alterations in magnesium and oxidative status during chronic emotional stress. *Magnes Res* 2000;13:29–36.
- [7] Aaserud M, Lewin S, Innvaer S, Paulsen EJ, Dahlgren AT, Trommald M, et al. Translating research into policy and practice in developing countries: a case study of magnesium sulphate for pre-eclampsia. *BMC Health Serv Res* 2005;5:68.
- [8] Coudray C, Demigne C, Rayssiguier Y. Effects of dietary fibers on magnesium absorption in animals and humans. *J Nutr* 2003;133:1–4.
- [9] Fromm L, Heath DL, Vink R, Nimmo AJ. Magnesium attenuates post-traumatic depression/anxiety following diffuse traumatic brain injury in rats. *J Am Coll Nutr* 2004;23:529S–33S.
- [10] Meyer JS, Linda F, Quenzer LF. *Psychopharmacology, Drugs the Brain and Behavior*. Sunderland, Maryland: Sinauer Associates; 2005. p. 386.
- [11] Anon.. Heart gains from whole grains. *Harvard Heart Lett*. 2002;2–4.
- [12] Dean C. *The miracle of magnesium*. New York: Ballantine Books; 2003.
- [13] Firoz M, Graber M. Bioavailability of US commercial magnesium preparations. *Magnes Res* 2001;14:257–62.
- [14] Walker AF, Marakis G, Christie Byng M. Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. *Magnes Res* 2003;16:183–91.
- [15] Lindberg JS, Zobitz MM, Poindexter JR, Pak CY. Magnesium bioavailability from magnesium citrate and magnesium oxide. *J Am Coll Nutr* 1990;9:48–55.
- [16] Shealy NC, Cady RK, Veehoff D, Houston R, Burnette M, Cox RH, et al. The neurochemistry of depression. *AJPM* 1992;2:13–6. On the Internet at <http://coldcure.com/html/shealy13.html>.
- [17] Mark LP, Prost RW, Ulmer JL, Smith MM, Daniels DL, Strottmann JM, et al. Pictorial review of glutamate excitotoxicity: fundamental concepts for neuroimaging. *Am J Neuroradiol* 2001;22:1813–24.
- [18] Tomita R, Fujisaki S, Ikeda T, Fukuzawa M. Role of nitric oxide in the colon of patients with slow-transit constipation. *Dis Colon Rectum* 2002;45:593–600.
- [19] Sapolsky RM. *Stress the aging brain and the mechanisms of neuron death*. Cambridge, MA: A Bradford Book, The MIT Press; 1992. page 192.
- [20] Paul IA. Antidepressant activity and calcium signaling cascades. *Hum Psychopharmacol* 2001;16:71–80.
- [21] Murck H. Magnesium and affective disorders. *Nutr Neurosci* 2002;5:375–89.
- [22] Singewald N, Sinner C, Hetzenauer A, Sartori SB, Murck H. Magnesium-deficient diet alters depression- and anxiety-related behavior in mice influence of desipramine and *Hypericum perforatum* extract. *Neuropharmacology* 2004;47:1189–97.
- [23] Hollister LE, Trevino ESG. Calcium channel blockers in psychiatric disorders: a review of the literature. *Can J Psychiatry* 1999;44:658–64.
- [24] Seelig MS, Rosanoff A. *The magnesium factor*. New York: Penguin Group; 2003.
- [25] Brown ES, Varghese FP, McEwen BS. Association of depression with medical illness: does cortisol play a role?. *Biol Psychiat* 2004;55:1–9.
- [26] Papadopol V, Tuchendria E, Palamara I. Magnesium and some psychological features in two groups of pupils (magnesium and psychic features). *Magnes Res* 2001;14(1/2):27–32. On the Internet at <http://coldcure.com/html/mag-iq.html>.
- [27] Young LT, Robb JC, Levitt AJ, Cooke RG, Joffe RT. Serum Mg^{2+} and Ca^{2+}/Mg^{2+} ratio in major depressive disorder. *Neuropsychobiology* 1996;34:26–8.
- [28] Imada Y, Yoshioka S, Ueda T, Katayama S, Kuno Y, Kawahara R. Relationships between serum magnesium levels and clinical background factors in patients with mood disorders. *Psychiat Clin Neurosci* 2002;56:509–14.
- [29] Banki CM, Arato M, Kilts CD. Aminergic studies and cerebrospinal fluid cations in suicide. *Ann N Y Acad Sci* 1986;487:221–30.
- [30] Levine J, Stein D, Rapoport A, Kurtzman L. High serum and cerebrospinal fluid Ca/Mg ratio in recently hospitalized

- acutely depressed patients. *Neuropsychobiology* 1999;39:63–70.
- [31] Kalinin VV, Zheleznova EV, Rogacheva TA, Sokolova LV, Polianskii DA, Zemlianaia AA, et al. [A use of Magne-B6 in the treatment of anxiety-depressive states in patients with epilepsy]. *Zh Nevrol Psikhiatr Im S S Korsakova* 2004;104:51–5.
- [32] Mousain-Bosc M, Roche M, Rapin J, Bali JP. Magnesium VitB6 intake reduces central nervous system hyperexcitability in children. *J Am Coll Nutr* 2004;23:545S–8S.
- [33] Joffe RT, Levitt AJ, Young LT. The thyroid, magnesium and calcium in major depression. *Biol Psychiat* 1996;40:428–9.
- [34] van den Heuvel C, Vink R. The role of magnesium in traumatic brain injury. *Clin Calcium* 2004;14:9–14.
- [35] Nechifor M, Chelarescu D, Mandreci I, Cartas N. Magnesium influence on nicotine pharmacodependence and smoking. *Magnes Res* 2004;17:176–81.
- [36] Margolin A, Kantak K, Copenhaver M, Avants SK. A preliminary, controlled investigation of magnesium L-aspartate hydrochloride for illicit cocaine and opiate use in methadone-maintained patients. *J Addict Dis* 2003;22:49–61.
- [37] Murray TD, Berger A. Alcohol withdrawal. *Va Med Q* 1997;124:184–7. 189.
- [38] Altura BM, Altura BT. Association of alcohol in brain injury, headaches, and stroke with brain-tissue and serum levels of ionized magnesium: a review of recent findings and mechanisms of action. *Alcohol* 1999;19:119–30.
- [39] Held K, Antonijevic IA, Kunzel H, Uhr M, Wetter TC, Golly IC, et al. Oral Mg (2+) supplementation reverses age-related neuroendocrine and sleep EEG changes in humans. *Pharmacopsychiatry* 2002;35:135–43.
- [40] Meacham SL, Taper LJ, Volpe SL. Effect of boron supplementation on blood and urinary calcium, magnesium, and phosphorus, and urinary boron in athletic and sedentary women. *Am J Clin Nutr* 1995;61:341–5.
- [41] Penland JG. Quantitative analysis of EEG effects following experimental marginal magnesium and boron deprivation. *Magnes Res* 1995;8:341–58.
- [42] Al-Shammari SA, Al-Subaie A. Prevalence and correlates of depression among Saudi elderly. *Int J Geriatr Psychiat* 1999;14:739–47.
- [43] Al-Khathami AD, Ogbeide DO. Prevalence of mental illness among Saudi adult primary-care patients in Central Saudi Arabia. *Saudi Med J* 2002;23:721–4.
- [44] Seelig MS. Magnesium deficiency in the pathogenesis of disease: early roots of cardiovascular, skeletal and renal abnormalities. 1980, Goldwater Memorial Hospital, New York University Medical Center, New York, New York. (On Internet at: <http://www.mgwater.com/Seelig/Magnesium-Deficiency-in-the-Pathogenesis-of-Disease/jacket.shtml>).
- [45] Begon S, Pickering G, Eschaliere A, Mazur A, Rayssiguier Y, Dubray C. Role of spinal NMDA receptors, protein kinase C and nitric oxide synthase in the hyperalgesia induced by magnesium deficiency in rats. *Br J Pharmacol* 2001;134:1227–36.
- [46] Dube L, Granry JC. The therapeutic use of magnesium in anesthesiology, intensive care and emergency medicine: a review. *Can J Anaesth* 2003;50:732–46.
- [47] Lazard EM. A preliminary report on the intravenous use of magnesium sulfate in puerperal eclampsia. *Am J Obst Gynec* 1925;9:178–88.

Available online at www.sciencedirect.com

