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The Soy Connection

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HEALTH AND NUTRITION NEWS ABOUT SOY

Research Updates

Soy and Mineral Bioavailability

By Mark Messina, Ph.D.

Mineral bioavailability is a consideration regarding the impact of soyfoods on overall nutrition. This issue is particularly germane when soyfoods are substituted for animal products since red meat is an excellent source of iron and zinc, and dairy products are an excellent source of calcium. Mineral bioavailability is not generally an issue for those who use dairy milk as a source of calcium and consume modest amounts of red meat, since it takes little meat to meet iron and zinc needs.

In general, iron bioavailability from plants is quite poor, generally less than five percent, which is why the iron needs of vegetarians are thought to be as much as 80 percent higher than non-vegetarians.¹ Soybeans are quite high in iron but due to the inhibitory effects of phytate, which is present in soybeans in high amounts, and to a lesser extent soy protein, soybeans are not considered a good source of iron. However, new research suggests this conclusion may not be justified.

Murray-Kolb and colleagues in the department of nutrition at Pennsylvania

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New Studies: Soy Appears To Benefit Cognitive Function

By Sandra E. File, Ph.D.
King's College London

A QUICK TASTE

Animal studies and three short-term human trials have found that soyfoods and isoflavones exert beneficial effects on several aspects of cognition and memory. Although a single epidemiologic study published three years ago found tofu consumption to be associated with age-related cognitive impairment among Japanese men in Hawaii, the majority of preliminary data look encouraging and certainly justify conducting longer term studies into the potential cognitive benefits of soyfoods stemming from the estrogen-like effects of soy isoflavones.

There has been considerable interest in the possible beneficial cognitive effects of estrogen supplements, particularly, but not exclusively, in postmenopausal women. Thus, it is not surprising that there is interest in the effects of soyfoods on cognitive function. This is because soy isoflavones bind to estrogen receptors and, following dietary administration, enter the brain in sufficient concentrations to activate estrogen β receptors. Estrogen receptor beta is the newly discovered estrogen receptor and recent data indicate isoflavones have a greater binding affinity to this receptor than the classic estrogen receptor, estrogen receptor alpha.

The first evidence that dietary soy might improve cognitive function came from a study in which ovariectomized female rats were fed a diet high in soy isoflavones for 10 months.¹ A second study confirmed a positive effect of a life-long high soy diet in female rats,

but found that the same diet impaired performance in male rats.² An uncontrolled epidemiological study also provided some indication that a life-long dietary intake of soy might impair cognitive function in men.

White et al³ tested elderly Japanese-American men in a cognitive abilities screening test for dementia. No measures were taken of their diet at the time of cognitive testing, but they had been asked about their dietary intake of tofu on two previous occasions, 25 and 20 years prior to cognitive testing. There was a low correlation (0.29) between their reports on the two occasions, but there was an increased incidence of mild cognitive impairment with increasing frequency of reported tofu intake 25 years earlier.

The group with the higher tofu intake was older, had a lower level of education, less complex occupations, and had spent longer in Japan as children. These factors were all independently associated with cognitive impairment, but did not totally account for the association with reported tofu intake. It was assumed that the tofu intake of the wives was similar to that of their husbands, but in the women the presumed higher tofu intake was not significantly associated with cognitive impairment.

While the actual level of intake of soy isoflavones is unknown, the duration of this diet is likely to have been for several decades. The uncontrolled nature of this study and the many confounding factors make it hard to be confident about the conclusions. Nonetheless, it raises the important possibility

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New Studies: Soy Appears To Benefit Cognition *(Continued from Page 1)*

that the cognitive effects of a soy diet may depend on the levels of soy isoflavones, the duration and timing of the diet and, perhaps, gender.

However, the results of a more recent prospective study indicate that men can show cognitive benefits from a high soy diet⁴. In a double-blind, placebo-controlled study, both male and female young (25.5 y) men and women were randomly allocated to 10 weeks of supervised diets that had high (100 mg/day total isoflavones) or low (0.5 mg/day) soy content. The groups did not differ in age, IQ, education, anxiety or depression. Both the men and women allocated to the high soy diet showed significantly greater improvements in episodic memory (immediate recall of a story, short-term recognition of patterns, delayed picture recall) and in a task measuring frontal lobe function (rule shifting and reversal).

The results of two recent studies provide evidence that it may also be possible to obtain cognitive benefits from supplements containing soy-extracted isoflavones. Both of these studies examined the effects in post-menopausal women. In a double-blind placebo controlled trial,^{5,6} 33 women (50-65 y) were randomly allocated to placebo or soy (60 mg total isoflavone equivalents) for 3 months. Those receiving the soy supplement showed significantly greater improvements in episodic memory (immediate recall of a story, delayed recall of pictures) and in tasks measuring frontal lobe function (rule reversal and ability to plan). The groups were closely matched in age, IQ and education. There were no effects of soy on anxiety, depression, menopausal symptoms or sleepiness and therefore the improved cognition was not secondary to other effects of soy.

Kritz-Silverstein et al⁷ studied a group of 56 women (55-74 y) who were randomly allocated to placebo or soy (110 mg isoflavones/day) for 6 months. Those receiving the soy showed significantly greater improvement in category fluency. They also showed greater improvements in story recall and in a planning task, but these just missed significance. It

is possible that the lower level of significance in this study is due to a greater diversity in the group, compared with that in the File et al study.^{5,6} Indeed, an age-stratified analysis showed that there was greater cognitive benefit of soy in the sub-group of older women.

Thus, in three prospective studies in which volunteers were randomly allocated to treatments and in which the groups were well matched, there were cognitive benefits from soy supplementation of between 60 and 110 mg/day total isoflavones for a period of 3-6 months. It would be of great importance to study the effects of soy supplements in older men and to determine whether the benefits would remain with longer periods of treatment. It would also be important to determine whether lower levels of soy supplementation would be of benefit, since results from animal studies on one of the possible underlying mechanisms (brain derived neurotrophic factor) indicate that soy may have bidirectional effects that depend on the soy concentration and duration of the diet.^{8,9}

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Dementia History, Type, Causes Explained

By Ronni Chernoff, Ph.D., R.D., F.A.D.A.

As the population ages, the prevalence of cognitive impairment, known as dementia, will become an increasing burden on the health care system. While it may seem that the incidence of dementia is increasing, the reality is that older adults now have an extended life expectancy. The likelihood becomes greater that elderly individuals will demonstrate loss of cognitive ability the longer they survive.

One of the challenges that many health professionals encounter is distinguishing among depression, delirium and dementia. Depression is more common among older adults than most health professionals are aware. It can be treated but it first must be diagnosed. Depressed individuals often experience memory impairment but demonstrate intact cognitive function and appropriate language skills for their age. Delirium is frequently a rapid onset condition of short duration associated with some disorientation and variable recall of events. Dementia tends to be progressive, with disorientation, aphasia, and memory loss.

Before an individual is diagnosed with dementia, there is a condition known as mild cognitive impairment (MCI)¹ that may be apparent. Individuals with MCI may complain about memory problems, but they generally score well on diagnostic tests such as evaluation of activities of daily living (the ability to care for self) and the mini-mental state examination, a standardized test of cognition.² Patients who demonstrate symptoms of MCI have a higher risk for developing Alzheimer's disease (AD). Early diagnosis will contribute to early intervention which may be helpful for individuals who have reversible forms of dementia.

There are many etiologies for dementia but most contribute to the loss of intellectual function, memory impairment, loss of judgment, and personality changes. Dementia tends to be progressive and often irreversible. However, there are dementias that can be resolved with

treatment of the underlying disease process. Reversible causes of dementia include central nervous system infection, brain trauma or tumors, multi-infarct dementia which is related to chronic cerebrovascular disease, normal pressure hydrocephalus, Wernicke-Korsakoff syndrome, vitamin deficiency diseases, and neurological disorders such as multiple sclerosis, Parkinson's disease and others.³

Diagnosing dementia as early in its development as possible allows for aggressive intervention that may slow the progression of disease.⁴ The two most common and irreversible causes of dementia are vascular disease and Alzheimer's disease. Vascular dementia has been described as the second most common type of dementia in older adults.⁵ Because the two leading causes of morbidity and mortality are related to vascular disease, stroke and ischemic heart disease, it is possible that vascular disease is also a factor in other dementias as well. Large vessel disease in the brain is associated with multi-infarct dementia where there is a progressive loss of tissue. Small vessel disease usually leads to lacunar strokes.⁵ Cardiovascular diseases, particularly coronary artery bypass grafts (CABG) associated with the use of cardiopulmonary bypass machines, and congestive heart failure are also associated with progressive dementia. CABG patients may develop dementia from emboli associated with their surgery; emboli may occur because of bubbles from nitrous oxide or anesthetic gases, thrombi from the vessels in the heart, or fat or inorganic emboli. It seems that there may be more vascular disease related dementia than is currently being diagnosed.⁵

The most common form of dementia is Alzheimer's disease. The progression of AD dementia is variable and symptoms may develop at different rates among individuals.⁶ Dr. Alois Alzheimer first described the syndrome in 1903 but it was not seen often, probably because life expectancy was much

shorter a century ago. When it became more prevalent as people lived longer, a variety of etiologies were postulated, including the use of aluminum cookware and foil. This theory has been discarded when, under strong scientific investigation, a relationship between the neurofibrillary plaques characteristically seen in patients who had AD were noted on autopsies of Down's syndrome patients. Exploration of the physiologic etiology and processes of AD is active and continues to identify characteristics, such as the presence of Lewy bodies⁷ (characteristic eosinophilic structures in neuron cytoplasm) that may offer more information that will result in prevention or treatment of this terrible disease. Acetyl cholinesterase inhibitors, non-steroidal anti-inflammatory drugs, hormones, vitamins and herbal remedies have all been tried to inhibit the progression of disease. Although some of these remedies hold promise, carefully controlled, conclusive clinical trials have not yet been reported.

Recently, a newer syndrome, called mixed dementia (MD) has been identified. It seems to have pathologies and manifestation of both vascular dementia and AD.⁸ Virtually all of the current literature strongly recommend that additional research is essential to determine the etiology of dementia, its diagnosis, and treatment modalities that slow or stop progression of disease, or at the very least, permit a greater quality of life for those who devel-

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Focus On Aluminum

Questions & Answers

Q. What is aluminum?

A. Alumina (aluminum oxide) is one of the most abundant natural resources in the earth's crust. It is the third most common element after oxygen and silicon. It is frequently found in cans, foil, and cookware. It is widespread in food and water supplies because of its presence in soil, water, and air.

Q. How much aluminum does one consume?

A. According to the Food and Drug Administration's Total Diet Study, 6-11 month old infants intake an estimated 0.7 mg of aluminum per day, considerably below the Provisional Tolerable Weekly intake of a maximum of 7 mg aluminum/kg of body weight per week established by a FAO/WHO Joint Expert Committee. Average intake for 14-16 year old males was estimated to be 11.5 mg/day, and for adult men and women, 8-9 and 7mg/day, respectively.¹

Q. What are the major food contributors of aluminum in the diet?

A. Foods with aluminum-containing food additives, e.g. grain products and processed cheese. Foods with naturally occurring alumina include legumes or vegetables grown in aluminum-containing soil.

Q. Is aluminum important for bodily functions?

A. There is no known biological function for aluminum but the adverse health effects of aluminum have received attention in two areas related to soy intake – one is **infant health** and the

other is **Alzheimer's disease (AD)**.

INFANT HEALTH

Q. What impact does soy formula have on infant health?

A. Soy infant formulas are known to contain high levels of aluminum.² This is due to the plant itself – plants tend to accumulate aluminum since it is present in the soil and they lack an excretory mechanism for this element – and due to incidental aluminum (use of aluminum salts) from other ingredients used in the making of soy formula. Aluminum from infant formula is not of a concern for individuals with normal kidney function, since the human body absorbs very little aluminum, and that which is absorbed is excreted by the kidney and eliminated via the urine. However, infants with impaired renal function may have a high concentration of aluminum in the brain. A 1985 study published in the journal *Lancet*, attributed the very high concentration of aluminum in the brain of two infants with congenital kidney disease to the consumption of soy formula.³ However, five years later, these authors acknowledged that unrecognizable sources of aluminum, such as intravenous fluids, may have contributed to the excessive brain aluminum concentrations.⁴ No other case reports have found problems with aluminum in soy formula and soy formula has been used safely by millions of infants over the course of the last several decades.

Q. How do the aluminum levels in soy formula compare with cow's milk formulas?

A. Studies indicate the aluminum content of soy formula may be 10 times higher than cow's milk formula, and that the content of cow's milk formula is about 5 times higher than human milk.² However, despite the higher aluminum concentration, serum aluminum levels in breast fed infants do not differ significantly from levels in infants fed soy formula.⁵ And in neither case, do they come close to the serum aluminum levels known to be associated with toxicity in *adults*.⁶ These findings strongly suggest, but do not prove, that aluminum exposure from the use of soy formula is unlikely to be problematic. Tissue concentrations of aluminum would likely provide more insight than serum levels. Interestingly, one study did find significantly elevated serum levels in infants fed a casein-hydrolyzed formula.⁷

Q. Do soy based formulas present an aluminum toxicity risk?

A. The aluminum intake of infants using soy formula is only about 25 percent that of the upper tolerable level established by the Food and Agriculture Organization.⁸ And according to the American Academy of Pediatrics, term infants with normal renal function do not seem to be at substantial risk for aluminum toxicity from soy protein-based formulas. Thus, the aluminum content of soy formula is not viewed as a contraindication to its use.⁹

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Questions & Answers *(Continued from Page 4)*

ALZHEIMER'S DISEASE

Q. What affect does soy and its association with aluminum have on Alzheimer's disease?

A. The etiology of AD is unknown, but some data suggest that elevated aluminum intake may increase risk of this disease.¹⁰ However, this hypothesis is still very speculative.

Q. What studies have been conducted on this topic?

A. In 2000, a prospective epidemiologic study conducted in Hawaii found that Japanese men who consumed tofu 2-4 times per week were more likely to

develop impaired cognitive function than men who did not consume tofu.¹¹ Of course, epidemiologic studies can not be used to establish cause and effect relationships. These studies only identify associations.

Given the possible connection between aluminum intake and AD, and the reported association between tofu intake and impaired cognitive function, speculation has arisen that the high aluminum content of soybeans might have been responsible for the reported relationship. One study did find that the aluminum concentration of soymilk was higher than cow's milk but it was only about twice as high.⁸ Thus, the aluminum naturally

found in the soybean does not appear to be remarkable.

More importantly, a recent 10-week clinical trial found that young men and women who consumed a high soy diet experienced improvement in several measures of cognitive function in comparison to subjects who consumed a diet devoid of soy.¹² Also, two other unpublished but presented studies lasting in duration from 12 weeks to 6 months have found that soy isoflavone supplements lead to improvements in cognitive function in postmenopausal women. Thus, although the available evidence is far too limited to draw conclusions, the data are suggestive of soy having a beneficial, not a harmful, effect on cognitive function. ☺

Research Updates *(Continued from Page 1)*

State University examined iron absorption from soybeans.² Eighteen women with marginal iron deficiency (low iron stores without anemia) were fed soup containing 46g of intrinsically labeled soybeans or muffins containing 23g of intrinsically labeled soybeans in the flour. Women were fed a breakfast containing soy and then a regular lunch and dinner that did not include soyfoods. The radioactivity in red blood cells was measured 14 and 28 days following the consumption of the meals. Mean iron absorption was 27 percent, quite high compared to other plant foods and to most previous studies of the absorption of iron from soy. The authors of this study speculated that iron bioavailability from soy is so high because much of the iron is in the form of ferritin. Ferritin is a large protein that reversibly concentrates iron as a solid mineral. In this particular study, approximately half of the iron was stored as ferritin and half as phytate.

Soybean varieties differ markedly in their ferritin con-

centration which suggests iron bioavailability from different soybean varieties differs.

Murray-Kolb et al recommended that more research aimed at identifying factors that are responsible for the amount of ferritin in different soybean varieties be conducted.

In addition to phytate, soybeans are also high in oxalate, another component that inhibits calcium absorption. The high oxalate content of spinach is why this vegetable, although high in calcium, is not considered a good source of this mineral.³ Surprisingly however, although phytate does affect calcium absorption, calcium absorption from soybeans is still quite good. More than ten years ago Heaney and colleagues showed that the absorption of calcium from soybean varieties that were naturally high and low in phytate was 31.0 percent and 41.4 percent, respectively.⁴ The difference between the two varieties was statistically significant. However, even the lower value is still quite high, just a bit lower than the 37.7 percent

found for dairy milk in this study and much higher than for other legumes.⁵

Some concern was raised three years ago when the absorption of calcium from calcium fortified soymilk was found to be about 25 percent lower than dairy milk.⁶ Although the absorption from fortified soymilk was good, the authors of this study noted that soymilk would need to be fortified with 500 mg of calcium/cup to provide the same amount of absorbable calcium as provided by one cup of dairy milk. However, Heaney and colleagues also concluded that the lower absorption was due to the specific type of calcium salt used to fortify the soymilk. In this case, it was tricalcium phosphate.

More recently, Weaver and colleagues from Purdue University examined calcium absorption from calcium fortified tofu.⁷ In one experiment, premenopausal Caucasian women were fed tofu that was made by coagulating the

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soymilk with calcium chloride, and in a second experiment, premenopausal Asian women were fed tofu made by coagulating the soymilk with calcium sulfate. The researchers found there was essentially no difference between calcium absorption from either tofu and

calcium absorption from dairy milk. Thus, the absorption of calcium from soymilk fortified with calcium salts other than tricalcium phosphate might be similar to calcium absorption from dairy milk, although this conclusion needs to be established experimentally.

Also, neither tofu made without the use of a calcium salt nor unfortified soymilk are high calcium.

In summary, although soyfoods have been commonly regarded as poor sources of bioavailable iron, newer data suggests that this may not be the case. ☺

Dementia History, Type, Causes Explained *(Continued from Page 3)*

op dementia in later life.

No nutritional etiologies for dementia have been definitively identified other than B vitamin deficiencies (notably vitamin B6 and vitamin B12) although the roles of vitamins C and E are under investigation. However, there are a number of nutritional challenges. There have been theories about dementia patients becoming hypermetabolic, however, reports in the literature indicate no consistency among dementia patients. Some patients become hyperactive while others become sedentary and lethargic.

Nutritional problems are most likely associated with a decrease in consumption or, in some cases, consumption of non-food items such as paper, flowers, plant soil, and other brightly colored or

attractive items. Dementia patients have short or sporadic attention spans and may be easily distracted. Successful meal experiences occur more often in settings where there are few distractions, it is quiet and the lighting is good. Advanced dementia patients may need to be fed; when possible, meal time should be designed to meet each patient's eating skills, favorite foods, and nutritional needs. Regardless of the etiology of dementia, nutrition and food are quality of life issues that demand and deserve attention from health professionals.

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