Soy and Brain Damage

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By John D. MacArthur

"Tofu Shrinks Brain!" Not a science fiction scenario, this sobering soybean revelation is for real. But how did the "poster bean" of the '90s go wrong? Apparently, in many ways -- none of which bode well for the brain.

In a major ongoing study involving 3,734 elderly Japanese-American men, those who ate the most tofu during midlife had up to 2.4 times the risk of later developing Alzheimer's disease. As part of the three-decade long Honolulu-Asia Aging Study, 27 foods and drinks were correlated with participants' health. Men who consumed tofu at least twice weekly had more cognitive impairment, compared with those who rarely or never ate the soybean curd. [1,2]

"The test results were about equivalent to what they would have been if they were five years older," said lead researcher Dr. Lon R. White from the Hawaii Center for Health Research. For the guys who ate no tofu, however, they tested as though they were five years younger.

What's more, higher midlife tofu consumption was also associated with low brain weight. Brain atrophy was assessed in 574 men using MRI results and in 290 men using autopsy information. Shrinkage occurs naturally with age, but for the men who had consumed more tofu, White said "their brains seemed to be showing an exaggeration of the usual patterns we see in aging."

Phytoestrogens -- Soy Self Defense

Tofu and other soybean foods contain isoflavones, three-ringed molecules bearing a structural resemblance to mammalian steroidal hormones. White and his fellow researchers speculate that soy's estrogen-like compounds (phytoestrogens) might compete with the body's natural estrogens for estrogen receptors in brain cells.

Plants have evolved many different strategies to protect themselves from predators. Some have thorns or spines, while others smell bad, taste bad, or poison animals that eat them. Some plants took a different route, using birth control as a way to counter the critters who were wont to munch.

Plants such as soy are making oral contraceptives to defend themselves, says Claude Hughes, Ph.D., a neuroendocrinologist at Cedars-Sinai Medical Center. They evolved compounds that mimic natural estrogen. These phytoestrogens can interfere with the mammalian hormones involved in reproduction and growth -- a strategy to reduce the number and size of predators.

Toxicologists Concerned About Soy's Health Risks

The soy industry says that White's study only shows an association between tofu consumption and brain aging, but does not prove cause and effect. On the other hand, soy experts at the National Center for Toxicological Research, Daniel Sheehan, Ph.D., and Daniel Doerge, Ph.D., consider this tofu study very important. "It is one of the more robust, well-designed prospective epidemiological studies generally available. . . We rarely have such power in human studies, as well as a potential mechanism."

In a 1999 letter to the FDA (and on the ABC News program 20/20), the two toxicologists expressed their opposition to the agency's health claims for soy, saying the Honolulu study "provides evidence that soy (tofu) phytoestrogens cause vascular dementia. Given that estrogens are important for maintenance of brain function in women; that the male brain contains aromatase, the enzyme that converts testosterone to estradiol; and that isoflavones inhibit this enzymatic activity, there is a mechanistic basis for the human findings." [3]

Although estrogen's role in the central nervous system is not well understood, White notes that "a growing body of information suggests that estrogens may be needed for optimal repair and replacement of neural structures eroded with aging."

One link to the puzzle may involve calcium-binding proteins, which are associated with protection against neurodegenerative diseases. In recent animal studies at Brigham Young University's Neuroscience Center, researchers found that consumption of phytoestrogens via a soy diet for a relatively short interval can significantly elevate phytoestrogens levels in the brain and decrease brain calcium-binding proteins. [4]

Concerns About Giving Soy to Infants

The most serious problem with soy may be its use in infant formulas. "The amount of phytoestrogens that are in a day's worth of soy infant formula equals 5 birth control pills," says Mary G. Enig, Ph.D., president of the Maryland Nutritionists Association. She and other nutrition experts believe that infant exposure to high amounts of phytoestrogens is associated with early puberty in girls and retarded physical maturation in boys. [5]

A study reported in the British medical journal Lancet found that the "daily exposure of infants to isoflavones in soy infant-formulas is 6-11 fold higher on a bodyweight basis than the dose that has hormonal effects in adults consuming soy foods." (A dose, equivalent to two glasses of soy milk per day, that was enough to change menstrual patterns in women. [6]) In the blood of infants tested, concentrations of isoflavones were 13000-22000 times higher than natural estrogen concentrations in early life. [7]

Soy Interferes with Enzymes

While soybeans are relatively high in protein compared to other legumes, Enig says they are a poor source of protein because other proteins found in soybeans act as potent enzyme inhibitors. These "anti-nutrients" block the action of trypsin and other enzymes needed for protein digestion. Trypsin

inhibitors are large, tightly folded proteins that are not completely deactivated during ordinary cooking and can reduce protein digestion. Therefore, soy consumption may lead to chronic deficiencies in amino acid uptake. [8]

Soy's ability to interfere with enzymes and amino acids may have direct consequence for the brain. As White and his colleagues suggest, "isoflavones in tofu and other soyfoods might exert their influence through interference with tyrosine kinase-dependent mechanisms required for optimal hippocampal function, structure and plasticity." [2]

High amounts of protein tyrosine kinases are found in the hippocampus, a brain region involved with learning and memory. One of soy's primary isoflavones, genistein, has been shown to inhibit tyrosine kinase in the hippocampus, where it blocked "long-term potentiation," a mechanism of memory formation. [9]

Tyrosine, Dopamine, and Parkinson's Disease

The brain uses the amino acids tyrosine or phenylalanine to synthesize the key neurotransmitters dopamine and norepinephrine, brain chemicals that promote alertness and activity. Dopamine is crucial to fine muscle coordination. People whose hands tremble from Parkinson's disease have a diminished ability to synthesize dopamine. An increased incidence of depression and other mood disorders are associated with low levels of dopamine and norepinephrine. Also, the current scientific consensus on attention-deficit disorder points to a dopamine imbalance.

Soy has been shown to affect tyrosine hydroxylase activity in animals, causing the utilization rate of dopamine to be "profoundly disturbed." When soy lecithin supplements were given throughout perinatal development, they reduced activity in the cerebral cortex and "altered synaptic characteristics in a manner consistent with disturbances in neural function." [10]

Researchers at Sweden's Karolinska Institute at the National Institutes of Health and are finding a connection between tyrosine hydroxylase activity, thyroid hormone receptors, and depleted dopamine levels in the brain -- particularly in the substantia nigra, a region associated with the movement difficulties characteristic of Parkinson's disease. [11-13]

Soy Affects the Brain via the Thyroid Gland

Tyrosine is crucial to the brain in another way. It's needed for the body to make active thyroid hormones, which are a major physiological regulator of mammalian brain development. By affecting the rate of cell differentiation and gene expression, thyroid hormones regulate the growth and migration of neurons, including synaptic development and myelin formation in specific brain regions. Low blood levels of tyrosine are associated with an underactive thyroid gland.

Scientists have known for years that isoflavones in soy products can depress thyroid function, causing goiter (enlarged thyroid gland) and autoimmune thyroid disease. In the early 1960s, goiter and hypothyroidism were reported in infants fed soybean diets. [14] Scientists at the National Center for Toxicological Research showed that the soy isoflavones genistein and daidzein "inhibit thyroid peroxidase-catalyzed reactions essential to thyroid hormone synthesis." [15]

Japanese researchers studied effects on the thyroid from soybeans administered to healthy subjects. They reported that consumption of as little as 30 grams (two tablespoons) of soybeans per day for only one month resulted in a significant increase in thyroid stimulating hormone (TSH), which is produced by the brain's pituitary gland when thyroid hormones are too low. Their findings suggested that "excessive soybean ingestion for a certain duration might suppress thyroid function and cause goiters in healthy people, especially elderly subjects." [16]

Thyroid Hormones and Fetal Brain Development

Thyroid alterations are among the most frequently encountered autoimmune conditions in children. Researchers at Cornell University Medical College showed that the "frequency of feedings with soy-based milk formulas in early life was significantly higher in children with autoimmune thyroid disease." [17] In a previous study, they found that twice as many diabetic children had received soy formula in infancy as compared to non-diabetic children. [18]

Recognizing the risk, Swiss health authorities recommend "very restrictive use" of soy for babies. In England and Australia, public health agencies tell parents to first seek advice from a doctor before giving their infants soy formula. The New Zealand Ministry of Health recommends that "Soy formula should only be used under the direction of a health professional for specific medical indications. . . Clinicians who are treating children with a soy-based infant formula for medical conditions should be aware of the potential interaction between soy infant formula and thyroid function." [19]

Thyroid hormones exert their influence during discrete windows of time. Inappropriate hormone levels can have a devastating effect on the developing human brain, especially during the first 12 weeks of pregnancy when the fetus depends on the mother's thyroid hormones for brain development. After that, both maternal and fetal thyroid hormone levels affect the central nervous system.

A 1999 study published in the New England Journal of Medicine showed that pregnant women with underactive thyroids were four times more likely to have children with low IQs if the disorder is left untreated. The study found that 19% of the children born to mothers with thyroid deficiency had IQ scores of 85 or lower, compared with only 5% of those born to mothers without such problems. [20]

Thyroid, Brain, and Environmental Toxins

Children exposed prenatally and during infancy to common environmental toxins like dioxin and polychlorinated biphenyls (PCBs) can suffer behavioral, learning, and memory problems because these chemicals may be disrupting the normal action of thyroid hormone. [21]

Combinations of insecticides, weed killers, and artificial fertilizers -- even at low levels -- have measurable detrimental effects on thyroid and other hormones as well as on the brain. [24] EPA scientists now want to upgrade the commonly used herbicide, atrazine, to a "likely carcinogen." In animal tests, atrazine attaches to sites on the hypothalamus, a crucial brain region involved with regulating levels of stress and sex hormones. [25]

Individuals newly diagnosed with Parkinson's disease were more than twice as likely to have been exposed to insecticides in their home, compared to those without the disease. [26]

Soy formulas for infants can contain other neurotoxins: aluminum, cadmium, and fluoride. Studies found that aluminum concentrations in soy-based formulas were a 100-fold greater compared to human breast milk, while cadmium content was 8-15 times higher than in milk-based formulas. In an Australian study, the fluoride content of soy-based formulas ranged from 1.08 to 2.86 parts per million. The authors concluded that "prolonged consumption (beyond 12 months of age) of infant formula reconstituted with optimally-fluoridated water could result in excessive amounts of fluoride being ingested." A study of Connecticut children revealed that mild-to-moderate fluorosis was strongly associated with soy-based infant formula use. [27-30]

In May 2000, Boston Physicians for Social Responsibility released their report, "The Toxic Threats to Child Development." In the section on neurotoxins, they concluded: "Studies in animals and human populations suggest that fluoride exposure, at levels that are experienced by a significant proportion of the population whose drinking water is fluoridated, may have adverse impacts on the developing brain." [31]

Iodine vs. Fluorine

The thyroid gland uses tyrosine and the natural element iodine to make thyroxine (T4), a thyroid hormone containing four iodine atoms. The other, much more biologically active thyroid hormone is tri-iodothyronine (T3), which has three iodine atoms. Lack of dietary iodine has long been identified as the problem in diminished thyroid hormone synthesis.

According to the International Council for the Control of Iodine Deficiency Disorders: "Iodine deficiency has been called the world's major cause of preventable mental retardation. Its severity can vary from mild intellectual blunting to frank cretinism, a condition that includes gross mental retardation, deaf mutism, short stature, and various other defects. . . The damage to the developing brain results in individuals poorly equipped to fight disease, learn, work effectively, or reproduce satisfactorily."

This crucial role of iodine is another reason why the thyroid gland is especially vulnerable today. Canadian researcher Andreas Schuld has documented more than 100 studies during the last 70 years that demonstrate adverse effects of fluoride on the thyroid gland. [32] Schuld says, "Fluorine, being the strongest in the group of halogens, will seriously interfere with iodine and iodine synthesis, forcing more urinary elimination of ingested iodine as fluoride ingestion or absorption increases."

Fluorides were actually used in the past, specifically to reduce thyroid function. In the 1930s through to the 1960s fluorides at 0.9mg to 4.5mg/day were given as effective anti-thyroid medication to hyperthyroid patients." [33] Russian researchers in the 1980s concluded that prolonged consumption of drinking water with a raised fluorine content was a risk factor of more rapid development of thyroid pathology. [34]

A major source of fluoride exposure in the United States is fluoridated drinking water -- including foods and drinks manufactured and processed with this treated water. (Only about 5% of the world's

population is fluoridated, and more than half live in North America. 99% of western continental Europe has rejected, banned, or stopped the addition of fluoride compounds to their drinking water. [35]) Also, approximately 45 million pounds of hydrogen fluoride are released from U.S. coal-fired plants every year into the environment.

Soy Phytates Inhibit Zinc Absorption

Another way that soybeans may affect brain function is because of their phytic acid content. Phytic acid is an organic acid present in the outer portion of all seeds. Also known as phytates, they block the uptake of essential minerals in the intestinal tract: calcium, magnesium, iron, and especially zinc. According to research cited by the Weston A. Price Foundation, soybeans have very high levels of a form of phytic acid that is particularly difficult to neutralize -- and which interferes with zinc absorption more completely than with other minerals.

The soy industry acknowledges the problem, noting that "one-half cup of cooked soybeans contains one mg of zinc. However, zinc is poorly absorbed from soyfoods." As for iron, "both phytate and soy protein reduce iron absorption so that the iron in soyfoods is generally poorly absorbed." [36]

Nutritionist Sally Fallon, author of Nourishing Traditions: The Cookbook that Challenges Politically Correct Nutrition and the Diet Dictocrats, says that as early as 1967, researchers testing soy formula found that it caused negative zinc balance in every infant to whom it was given. Even when the diets were additionally supplemented with zinc, there was a strong correlation between phytate content in formula and poor growth. She warns that "a reduced rate of growth is especially serious in the infant as it causes a delay in the accumulation of lipids in the myelin, and hence jeopardizes the development of the brain and nervous system."

Zinc and the Brain

Relatively high levels of zinc are found in the brain, especially the hippocampus. Zinc plays an important role in the transmission of the nerve impulse between brain cells. Deficiency of zinc during pregnancy and lactation has been shown to be related to many congenital abnormalities of the nervous system in offspring. In children, "insufficient levels of zinc have been associated with lowered learning ability, apathy, lethargy, and mental retardation." [37]

The USDA references a study of 372 Chinese school children with very low levels of zinc in their bodies. The children who received zinc supplements had the most improved performance -- especially in perception, memory, reasoning, and psychomotor skills such as eye-hand coordination. Three earlier studies with adults also showed that changes in zinc intake affected cognitive function. [38]

New research has identified a specific contingent of neurons, called "zinc-containing" neurons, which are found almost exclusively in the forebrain, where in mammals they have evolved into a "complex and elaborate associational network that interconnects most of the cerebral cortices and limbic structures." This suggests the importance of zinc in the normal and pathological processes of the cerebral cortex. [39] Furthermore, age-related tissue zinc deficiency may contribute to brain cell death in Alzheimer's dementia. [40]

Safe Soy

To produce soy milk, the beans are first soaked in an alkaline solution, then heated to about 115 degrees C in order to remove as much of the trypsin inhibitors as possible. Fallon says this method destroys most, but not all of the anti-nutrients, however it has the "unhappy side effect of so denaturing the proteins that they become very difficult to digest and much reduced in effectiveness." Furthermore, phytates remain in soy milk to block the uptake of essential minerals.

Only a long period of fermentation will significantly reduce the phytate content of soybeans, as well as the trypsin inhibitors that interfere with enzymes and amino acids. Therefore, fermented soy products such as tempeh and miso (not tofu) provide nourishment that is easily assimilated.

Links to Further Information:

Soy Online Service (http://www.soyonlineservice.co.nz/)
Weston A. Price Foundation (http://www.westonaprice.org/)

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