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Antioxidant-Rich Diet Plus Mental Activity Work Together to Keep Minds Sharp

Psychologists and biologists have long argued whether biology – in this case diet – or mental stimulation plays the bigger role in mental development. Now, a study with “man’s best friend” has confirmed that both do: specifically, the combination of an antioxidant-rich diet and a stimulating environment can help keep the bodies and minds of older dogs relatively young.

The study, led by N. William Milgram, PhD, a psychology professor at the University of Toronto, tracked the progress of 48 older beagles and 17 younger ones over two years. The older dogs were divided into four groups: the first group received a diet fortified with antioxidants and “mitochondrial” nutrients, and the second group was fed standard chow but was exposed to a stimulating environment. A third group received both the fortified diet and enhanced environment, and the fourth received no special diet or activity.

Dogs were used in the experiment because they have a brain structure similar to that of people. They also have a digestive tract somewhat like that of people, and they suffer from age-related memory and learning problems.

The dietary supplements added to the food included vitamins E and C, alpha-lipoic acid, carnitine, and small amounts of antioxidant-rich foods, including spinach, tomato and grape pomace, carrots, and citrus pulp. The environmental enhancements consisted of regular exercise and various training activities.

After two years, the differences between the four groups of older dogs were striking. The inactive dogs fed standard chow showed an expected age-related decline in learning, remembering, and other cognitive functions. Meanwhile, the antioxidant-fed and environmentally enhanced dogs fared much better.

But the sharpest dogs were those that had both an antioxidant-rich diet and a stimulating environment. They did the best at finding treats and in

distinguishing between black and white objects.

“Possibly the most important outcome of this study was the demonstration that the behavioral enrichment and the antioxidant supplementation condition combined were more effective than either alone,” wrote Milgram.

According to Milgram, the younger dogs did not benefit substantially from the antioxidant-fortified diet or enhanced learning experiences.

Reference: Milgram NW, Head E, Zicker SC, et al. Learning ability in aged beagle dogs is preserved by behavioral enrichment and dietary fortification: a two-year longitudinal study. *Neurobiology of Aging*, 2005;26:77-90. □

Perspectives...

Vioxx versus Natural Alternatives

Late last year, the Cox-2 inhibitor drug Vioxx was withdrawn from the market when researchers reported that it increased the chances of having a heart attack. Then questions were raised about Celebrex, the drug’s main competitor. And within weeks, naproxen and over-the-counter analgesics came under suspicion as well.

The truth is that serious side effects with Cox-2 inhibitors were apparent five years ago when these drugs hit the market. But the problems were smothered with extensive advertising and deceiving medical reports. In at least one case, in a *JAMA* article, all of the article’s researchers were either employees or paid consultants to the drug company that made Vioxx. In the January 24, 2005, issue of *JAMA*, researchers estimated that the drug caused 140,000 cases of serious heart disease.

The theory behind Cox-2 inhibitors was originally praised, but also seriously flawed. The idea was to reduce activity of the Cox-2 enzyme, which is involved in the body’s production of pro- and anti-inflammatory substances. But as I wrote two years ago in *The Inflammation Syndrome*, Cox-2 also plays

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key roles in brain activity, memory, ovulation, and pregnancy – and now, apparently in heart function. It wasn't smart to manipulate Cox-2.

Chronic inflammation is usually the result of an injury combined with nutritional deficiencies. It would have been far more sensible to increase the body's levels of some of the substances that Cox-2 acts on, such as the omega-3 fish oils. For example, fish oils boost the body's production of prostaglandin E1, which suppresses the far more inflammatory prostaglandin E3.

Similarly, glucosamine and chondroitin provide some of the natural building blocks of joint cartilage, and more than 40 studies have shown that they reduce osteoarthritic pain and can help regenerate new cartilage.

But neither fish oils nor glucosamine and chondroitin are proprietary, and they cannot easily be patented. Economically, that discourages any single company from exclusively marketing these nutritional products. For this reason, the drug companies are not interested in promoting nutrients.

Fish oils, glucosamine, and chondroitin help offset the dietary imbalances that prime many people for sustained inflammatory reactions. They are safe, they work, and you don't need a prescription for them. —JC

Supplements of Folic Acid May Reduce Risk of High Blood Pressure

Hypertension affects an estimated 65 million Americans, many of whom take medications to lower their blood pressure. But a new study suggests that supplemental folic acid, a B vitamin, may help prevent high blood pressure.

John P. Forman, MD, of the Harvard Medical School, and his colleagues tracked the health of two groups of women nurses for eight years. One group included 93,803 women, ages 27 to 44 years old, and the other included 62,260 nurses, ages 43 to 70 years old. None of the women had a history of high blood pressure when the study began.

Forman found that younger women who consumed the most folic acid – at least 1,000 mcg daily – were 46 percent less likely to develop high blood pressure. The benefit was less pronounced among the older women, who had only an 18 percent lower risk of hypertension if they took folic acid. Only the large amounts of folic acid in supplements, not foods, were related to a lower risk of hypertension.

Women who consumed less than 200 mcg of folic acid daily were those most likely to develop high blood pressure. The findings accounted for intake of other nutrients, weight, physical activity,

and family history of hypertension.

According to Forman, two small clinical trials found that folic acid and a combination of folic acid and vitamin B6 led to reductions in blood pressure.

Folic acid reduces levels of homocysteine, which can damage blood vessel walls and thereby contribute to hypertension.

Reference: Forman JP, Rimm EB, Stampfer MJ, et al. Folate intake and the risk of incident hypertension among US women. *JAMA*, 2005;292(3):320-329. □

Baked and Broiled Fish Lower Risk of Ischemic Stroke – Fried Does Not

Regularly eating baked or broiled fish can significantly reduce the risk of ischemic stroke, the most common type. In contrast, eating fried fish, fish sandwiches, or fish burgers increases the risk of all types of stroke.

Dariusz Mazaffarian, MD, of the Harvard School of Public Health, and colleagues studied the eating habits of 4,775 men and women 65 years of age or older, then tracked their risk of stroke for 12 years.

The more baked or broiled fish the people ate, the lower their risk of ischemic stroke. Those who ate fish five or more times weekly were 30 percent less likely to suffer a stroke, and those who ate fish one to four times a week were 27 percent less likely to have a stroke.

But those who regularly ate fried fish had a sharply increased risk of stroke. Eating fried fish one a week increased the risk of ischemic stroke by 44 percent and 37 percent for all types of strokes.

Mazaffarian wrote that baked and broiled fish are generally species rich in omega-3 oils, which are known to reduce the risk of heart disease. Fish used for deep frying use white fish than contain few of these oils. Furthermore, fried fish is high in trans fats and oxidized omega-6 fats, which may increase the risk of heart disease and stroke.

Reference: Mazaffarian D, Longstreth WT, Lemaitre RN, et al. Fish consumption and stroke risk in elderly individuals. *Archives of Internal Medicine*, 2005;165:200-206. □

The Herb Butterbur Found Helpful in Reducing Migraine Headaches

An herb known as butterbur can significantly reduce the frequency of migraine headaches.

Richard B. Lipton, MD, of the Albert Einstein College of Medicine, the Bronx (New York City), and his colleagues treated 245 patients with one of three protocols: 75 mg of butterbur (*Petasites hybridus*) root, 50 mg of butterbur root, or placebos twice daily for four months. All of the subjects had experienced two to six migraine headaches monthly during the three

months before the study began.

Overall, the higher dose of butterbur reduced the frequency of migraine headaches by half. Sixty-eight percent of the patients taking 75 mg of butterbur twice daily had more than a 50 percent reduction in migraine frequency. Only about one-fourth of those taking placebos improved.

Lipton wrote that “this levels of treatment effect is broadly comparable with results obtained with prescription preventive medications.”

The butterbur product used in the study is a standardized extract made from the herb’s root. It has been sold as Petadolex in Germany since 1988.

Reference: Lipton RB, Gobel H, Einhaupl KM, et al. *Petasites hybridus* root (butterbur) is an effective preventive treatment for migraine. *Neurology*, 2004;63:2240-2244. □

Low-Dose Vitamin D Supplements May Be Helpful in Treating Vaginal Atrophy

Postmenopausal women often experience vaginal atrophy and dryness. But vitamin D, which is actually a hormone, may reverse these problems.

Basak Yildirim, MD, and colleagues in Denizli, Turkey, treated 30 postmenopausal women with a small daily dose of vitamin D – 20 IU – for four months. None of the women were taking hormone-replacement therapy or drugs for osteoporosis, which might have thrown off the results.

By the end of the study, women taking vitamin D had improvements in vaginal tissue, leading Yildirim to write that the treatment of vaginal atrophy might be a new use for vitamin D.

The Reference Daily Intake for vitamin D is 200 IU, although some researchers have recommended amounts in the range of 2,000 to 10,000 IU daily.

Reference: Yildirim B, Kaleli B, Duzcan E, et al. The effects of postmenopausal Vitamin D treatment on vaginal atrophy. *Maturitas*, 2004;49:334-337. □

Nutrient Diversity of Avocados May Protect Against Prostate Cancer

Eating avocados may reduce the risk of prostate cancer, according to a recent cell study.

David Heber, MD, of the University of California, Los Angeles, and his colleagues conducted experiments on two types of prostate cells: LNCaP, which are hormone dependent, and PC-3, which are not hormone dependent. (Hormone-dependent prostate cancer cells are stimulated by testosterone.) Both types of cells were grown with an extract of the whole edible portion of avocados.

Avocados are rich in many nutrients known to have anti-cancer properties, including mono-unsaturated fats, lutein, alpha-carotene, beta-carotene,

vitamins E and C, and B vitamins. Because avocados are high in lutein, some LNCaP and PC-3 cells were treated with lutein alone.

The avocado extract inhibited the growth of both types of prostate cancer cells, with higher concentrations of the extract having the greatest effect. By itself, lutein had only a slight effect on the PC-3 cells and no effect on the LNCaP cells.

Reference: Lu QY, Arteaga JR, Zhang Q, et al. Inhibition of prostate cancer cell growth by an avocado extract: role of lipid-soluble bioactive substances. *Journal of Nutritional Biochemistry*, 2005;16:23-30. □

Acetyl-L-Carnitine Helps Diabetic Patients with Nerve Pain

Acetyl-L-carnitine, a form of carnitine, can reduce pain and help normalize nerve function in people with diabetic neuropathy.

Anders A.F. Sima, MD, PhD, of the Wayne State University School of Medicine, Detroit, and his colleagues tracked the health of 1,257 diabetic patients who were enrolled in two related clinical trials. The patients were asked to take 500 mg of acetyl-L-carnitine (ALCAR) three times daily, 1,000 mg of ALCAR three times daily, or placebos for one year.

Patients taking the higher dose of ALCAR – a total of 3,000 mg daily – had more than a 50 percent decrease in neuropathic pain when followed up after six months and a year. Further tests found that they were able to grow new nerve fibers and developed better feeling in their fingers and toes.

Patients taking the lower dose of ALCAR did not appear to benefit. In addition, patients with type 1 diabetes did not improve as much as those with type 2 diabetes.

Other clinical trials have found that alpha-lipoic acid (600 mg daily) is also helpful in treating diabetic neuropathy, and animal studies have found that a combination of alpha-lipoic acid and ALCAR have an age-reversing effect.

Reference: Sima AAF, Calvani M, Mihra M, et al. Acetyl-L-carnitine improves pain, nerve regeneration, and vibratory perception in patients with chronic diabetic neuropathy. *Diabetes Care*, 2005;28:96-101. □

Omega-3 Fish Oils Enhance Brain Cell Activities in Bipolar Disorder

Omega-3 fish oils alter the “membrane fluidity” of brain cells and may be helpful in treating bipolar (manic-depressive) disorder.

Perry F. Renshaw, MD, PhD, of McLean Hospital, Belmont, Mass., and his colleagues studied 21 women diagnosed with bipolar disorder and 12

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Quick Reviews of Recent Research

• Carotenoids may protect against colon cancer

Researchers analyzed dietary intake of antioxidant carotenoids and other nutrients in 402 men and women with colon cancer, comparing them to 688 people without cancer. Among people who never smoked, high intake of beta-carotene was associated with a 56 percent lower risk of developing colon cancer. For current and former smokers, high lycopene intake was associated with a 37 percent lower risk of colon cancer.

Nkondjock A, et al. *International Journal of Cancer*, 2004;110:110-116.

• Smoking tobacco lowers vitamins E and C levels

Ten smokers and 10 nonsmokers received 150 IU of vitamin E for six consecutive evenings. Blood levels of vitamin E decreased more quickly among

Omega-3 Fish Oils, Bipolar Disorder...

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women without the disorder. Some of the women were asked to take high doses of omega-3 fats (5 to 5.2 grams of EPA and 3 to 3.4 grams of DHA) daily for four weeks. Other women were asked to take low doses of omega-3 fats (1.3 grams of EPA and 0.7 grams of DHA).

Using magnetic resonance imaging (MRI), Renshaw and his colleagues measured T2 values in the women's brains. T2 refers to a technique used to measure membrane fluidity, which modulates how cells communicate with each other.

The T2 activity decreased significantly among the women with bipolar disorder who took the omega-3 fish oil supplements, indicating an increase in brain cell membrane fluidity. The effect was more pronounced in women taking the higher dose of omega-3 fish oils.

Renshaw reported that women who experienced the greatest change in T2 activity had a modest improvement in a clinical test used to measure depression.

The findings supported earlier reports that omega-3 fish oils are helpful in bipolar disorder. "Although the biological effects of omega-3 fatty acids were detectable within four weeks of treatment, the effects on mood state may require a longer time interval," wrote Renshaw and his colleagues.

T2 measures the movement of protons from water in brain cells.

Reference: Hirashima F, Parow AM, Stoll AL, et al. Omega-3 fatty acid treatment and T2 whole brain relaxation times in bipolar disorder. *American Journal of Psychiatry*, 2004;161:1922-1924. □

the smokers. In addition, lower levels of vitamin E were associated with low levels of vitamin C. In addition, smokers had higher blood markers of free radicals compared with nonsmokers.

Bruno RS, et al. *American Journal of Clinical Nutrition*, 2005;81:95-103.

• Chamomile tea found to be biologically active

Chamomile is a traditional herbal remedy for upset stomach and anxiety. Researchers analyzed urine samples from subjects before and after they consumed chamomile tea. After drinking the tea, the subjects' urine contained high levels of hippurate, which forms during the breakdown of antioxidant polyphenolic compounds. In addition, the urine contained high levels of glycine, an amino acid known to function as a nerve relaxant. These findings support the traditional use of chamomile.

Wang Y, et al. *Journal of Agricultural and Food Chemistry*, 2005;53:191-196.

• Vitamin B12 deficiency common among seniors

Researchers noted that the prevalence of vitamin B12 deficiency may be as high as 43 percent among senior citizens. The most common cause of this type of deficiency is atrophic gastritis, related to an age-related decrease in digestive enzymes. Low vitamin B12 may affect cognitive function.

Wolters M, et al. *Preventive Medicine*, 2004; 39: 1256-1266.

• High maternal vitamin C levels protect infant

Infants have a relatively low risk of developing allergies if their mother's breast milk contains high levels of vitamin C. Researchers analyzed levels of the vitamin in breast milk from 65 women, while also assessing the prevalence of atopic dermatitis in one-month-old infants. The highest levels of vitamin C in breast milk were associated with a 30 percent lower risk of allergies in their infants.

Hoppu U, et al. *European Journal of Clinical Nutrition*, 2005;59:123-128.

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