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Children's Brains, Behavior Sensitive to Omega-3 Levels – Supplements Help

Three new studies underscore the importance of omega-3 fats – eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) – in the developing brains of children.

Paul Montgomery, PhD, of the University of Oxford, United Kingdom, and his colleagues tracked 493 school children ages seven to nine years, all of whom had been selected for the study because of their below average reading skills.

After analyzing the children's blood levels of omega-3s, Montgomery found that lower levels of DHA were associated with poorer reading ability and working memory—that is, with more difficulty managing information for a relatively short periods of time. "Lower DHA was also associated with higher levels of parent-rated oppositional behavior and emotional lability," he wrote.

Meanwhile, Bita Moghaddam, PhD, of the University of Pittsburgh, and her colleagues investigated the effects of multigenerational deficiencies of omega-3s on the cognitive function and behavior of adolescents. Because such a study would be difficult to conduct in several generations of people, she used multiple generations of laboratory rats, but focused specifically on the behavior of adolescent animals.

Multiple generations of "deficient animals would best mimic the current state of human adolescent omega 3...deficiency, given that dietary trends toward consumption of omega-3 deficient fats began in the 1960s and 1970s when most parents of current adolescents were born," wrote Moghaddam and her colleagues.

She reported that deficiencies of omega-3s interfered with cognitive function and reduced motivation in ways different from in adult animals. Moghaddam suggested that omega-3 deficiencies may disrupt normal dopamine activity in the brain.

Finally, John Columbo, PhD, of the University of Kansas, Lawrence, and his colleagues studied 81

children who, as infants, were fed formulas containing omega-3s or formulas without these nutrients. Both types of formulas were provided to parents in double-blind fashion so they didn't know which their child was consuming.

Starting at age 18 months, the children were tested every six months using age-appropriate standardized cognitive tests.

The omega-3s did not influence test performance at 18 months, but positive effects were seen at ages three to five years. Children who had consumed omega-3s as infants scored better on rule-learning, inhibition tasks, vocabulary and preschool intelligence.

Colombo wrote that the effects of omega-3s "may not always be evident on standardized developmental tasks at 18 months...[but] significant effects may emerge later on more specific or fine-grained tasks."

References: Montgomery P, Burton JR, Sewell RP, et al. Low blood long chain omega-3 fatty acids in UK children are associated with poor cognitive performance and behavior: a cross-sectional analysis from the DOLAB study. *PLoS One*, 2013;8:e66697. Bondi CO, Taha AY, Tock JL, et al. Adolescent behavior and dopamine availability are uniquely sensitive to dietary omega-3 fatty acid deficiency. *Biological Psychiatry*, 2013: epub ahead of print. Colombo J, Carlson SE, Cheatham CL, et al. Long-term effects of LCPUFA supplementation on childhood cognitive outcomes. *American Journal of Clinical Nutrition*, 2013;98:403-412.

Perspectives Prostate Cancer: Fishy Research

With so many PhD researchers and way too many public relations folks churning out news releases, I'm not surprised at the huge number of low-quality studies getting undeserved attention. One of the latest, published in the *Journal of the National Cancer Institute*, claimed to link fish oil supplements with a greater risk of aggressive prostate cancer.



The study was simply bad science. And that's putting it politely.

First, other research strongly suggests that fish oils protect against prostate cancer. (See the next story.)

Second, the *JNCI* study was based on data extracted from a larger study on vitamin E and selenium and prostate cancer risk. Because fish oils were not the primary focus, the findings are inherently weak statistically.

Third, the study's conclusions were based on a single blood test, and not a very good one at that. The researchers measured omega-3 levels in blood plasma, the watery portion of blood, which can reflect significant day-to-day variations. They would have done much better if they had measured red blood cell levels of omega-3s (Thanks to my editorial colleague Robert Rountree, MD for pointing this out.)

Fourth, almost three-fourths of the men who went on the develop prostate cancer had a PSA level of 2 or higher when the study began. Among the men who remained cancer free, only about one-fourth had PSA levels that high.

Fifth, 30 percent of the cancer patients had a close relative with prostate cancer, which would increase their risk. In addition, 80 percent of the cancer patients were overweight or obese, which would also increase their risk.

Sixth, the researchers had no idea whether the men were eating fish, what type of fish, or were taking fish oil supplements.

As the lead researcher, Anthony D'Amico, PhD, admitted in a radio interview, "The scientific strength of it [the study] is weak, at best."

So why did this study get so much attention? -JC

Fish Oil Supplements Reduce The Risk of Prostate Cancer

A carefully conducted study of fish and fish oil consumption in Iceland has found that eating salted or smoked fish increased the risk of prostate cancer, whereas taking fish oil supplements reduced the risk of the disease.

Johanna E. Torfadottir, PhD, of the University of Iceland, Reykjavik, and her colleagues studied 2,268 men, ages 67-96 years, of whom 410 had been diagnosed with prostate cancer. The researchers asked the subjects to complete a food-frequency questionnaire to assess their eating habits in early life, midlife, and later years.

The most common types of fish consumed were cod and haddock, which are low in the omega-3s.

However, many of the men also consumed fish oils, particularly cod liver oil, with a recommended daily intake of 400 mg.

Men who consumed fish oils (liquids or capsules) in later life had a 57 percent lower risk of advanced prostate cancer.

Torfadottir and her colleagues added: "High intake of salted or smoked fish was associated with a twofold increased risk of advanced prostate cancer both in early life and in later life."

You can download a free copy of the study at http://www.ncbi.nlm.nih.gov/pmc/articles/ PMC3629172/pdf/pone.0059799.pdf

Reference: Torfadottir JE, Valdimarsdottir UA, Mucci LA, et al. Consumption of fish products across the lifespan and prostate cancer risk. *PLoS One*, 2013;8:e59799.

High Intake of Omega-3 Fish Oils Lowers the Risk of Breast Cancer

An analysis of 21 studies, which included more than 1.2 million participants, has found that the consumption of omega-3 fish oils reduces a woman's risk of developing breast cancer.

Duo Li, PhD, of Zheijiang University, China, and his colleagues analyzed data from the studies and determined that diets high in fish oils were associated with a 14 percent lower risk of breast cancer. When they looked at studies that measured blood levels of omega-3s, they found virtually the same reduction in disease risk.

The researchers calculated that each 100 mg of dietary omega-3s was related to a 5 percent reduction in the risk of breast cancer.

Li and his colleagues also examined the relationship between plant sources of alpha-linolenic acid – the "parent" molecule of omega-3s – but they found no significant reduction in breast cancer risk.

Reference: Zheng JS, Hu XJ, Zhao YM, et al. Intake of fish and marine n-3 polyunsaturated fatty acids and risk of breast cancer: meta-analysis of data from 21 independent prospective cohort studies. *BMJ*, 2013;346: doi 10.1136/bmj.f3706.

New Antioxidant Combination Helps Reduce Low Back Pain

Neuropathic, or nerve, pain contributes to low back pain, a condition that affects millions of people. In a new study, Italian researchers combined alphalipoic acid with superoxide dismutase to successfully treat patients with low back pain.

Both substances function as important cellular antioxidants, and alpha-lipoic acid is also used in the treatment of diabetic nerve pain.

Emilio Battisti, MD, of the University of Siena,

and his colleagues treated 98 patients with chronic low back pain, giving them 600 mg of alpha-lipoic acid and 140 IU of superoxide dismutase daily for 60 days. The study was open and nonrandomized, meaning there was no placebo group.

By the end of the study, only 8 percent of the patients were still using analgesic drugs, compared with 73.5 percent when the study began. The patients had significant improvements in perceived pain and functional disabilities. Battisti wrote that "pain ameliorated after 40 days of therapy and the improvement was significant both statistically and clinically."

Only four patients dropped out of the study because of severe pain unrelated to the treatment.

Reference: Battisti E, Albanese A, Guerra L, et al. Alpha lipoic acid and superoxide dismutase in the treatment of chronic low back pain. *European Journal of Physical and Rehabilitation Medicine*, 2013;49:1-6.

Some People with Celiac Disease Have Greater Risk of Lymphoma

People with celiac disease whose intestines do not fully heal have a much higher risk of developing lymphoma, an immune system cancer, compared with other celiac patients and the general population.

Celiac disease is characterized by an abnormal immune reaction to gluten, a family of proteins found in wheat, barley, and rye. Biopsies of celiac patients show a flattening of intestinal villi, fingerlike extensions from the gut wall that normally absorb nutrients and fluids. When most celiac patients adopt a gluten-free diet, the villi return to normal.

Benjamin Lebwhohl, MD, of Columbia University Medical Center, New York City and collaborators at the Karolinka Institute, Sweden, studied 7,625 patients with celiac disease, of whom 3,308 had persistent villous atrophy – that is, continued flattening of intestinal villi. People with this problem often have difficulty eating a gluten-free diet.

Over an average of nine years of follow up, celiac patients were almost three times more likely to develop lymphoma compared with people who did not have celiac disease. Those with persistent villous atrophy had a four-time greater risk of developing lymphoma compared with nonceliac patients. They were also three times more likely to develop lymphoma compared with celiac patients whose intestines had healed.

Reference: Lebwohl B, Granath F, Ekbom A, et al. Mucosal healing and risk for lymphoproliferature malignancy in celiac disease. A population-based cohort study. *Annals of Internal Medicine*, 2013;159:169-175.

Supplements Help Women Suffering from Dry Eye

Several studies have found that people with dry eye, technically known as keratoconjunctivitis sicca, have low levels of omega-3 fats. In a new study, researchers at the Eastern Virginia Medical School, Norfolk, found that a combination of omega-3s with gamma-linolenic acid (GLA), a plant oil, led to significant improvement in dry eye.

John D. Sheppard, Jr., MD, and his colleagues treated 38 post-menopausal women who had dry eye. Some of the women received supplements while others took placebos daily for six months. The supplements included 126 mg of eicosapentaenoic acid (EPA), 99 mg of docosahexaenoic acid (DHA), and 240 mg of GLA, along with modest amounts of several other vitamins and minerals.

By the end of the study, women taking the supplements had significant improvements in eye irritation symptoms, better corneal smoothness, and lower levels of blood markers of inflammation.

The omega-3s and GLA suppress proinflammatory compounds, such as prostaglandin E2.

Reference: Sheppard JD Jr, Singh R, McClellan AJ, et al. Long-term supplementation with n-6 and n-3 PUFAs improves moderate to severe keratoconjunctivitis sicca. *Cornea*, 2013: epub ahead of print.

Vitamin D Levels May Affect Success of In Vitro Fertilization

A woman's vitamin D levels may influence her ability to conceive after in vitro fertilization (IVF), according to a Canadian study.

Kimberley Garbedian, MD, and her colleagues studied 173 women undergoing IVF at Mount Sinai Hospital in Toronto. The women had their vitamin D levels measured. About 45 percent had normal levels – above 30 ng/ml (75 (nmol/L) – and 55 percent had low levels.

Women with normal levels of vitamin D were far more likely to become pregnant after IVF - 52.5percent versus only 34.7 percent of women with low levels. In addition, egg implantation rates were higher among women with higher vitamin D levels.

"Infertility affects 15 percent of couples in North America," the researchers wrote. "Recent studies support the role of vitamin D in human reproduction and suggest that vitamin D levels predict reproductive success following IVF."

Reference: Garbedian K, Boggild M, Moody J, et al. Effect of vitamin D status on clinical pregnancy rates following in vitro fertilization. *Canadian Medical Association Journal*, 2013: doi 10.9778/cmajo.20120032.



Quick Reviews of Recent Research

• Indian gooseberry improve blood vessels

Supplements of Indian gooseberry extract (*Phullanthus emblica*) can improve blood vessel tone in people with type 2 diabetes. Researchers from India asked 80 subjects to take either 250 or 500 mg of the extract or placebos twice daily for 12 weeks. Poor blood vessel tone, which can contribute to hypertension and coronary artery disease, is influenced by the endothelium, a thin layer of cells that line the inside wall of blood vessels. Levels of nitric oxide, the principal regulator of endothelial function, increased while a marker of free radical stress decreased.

Usharani P. Diabetes, Metabolic Syndrome and Obesity, 2013;6:275-284.

• Green tea may reduce blood sugar

Drinking green tea or taking green tea extract supplements can lead to a slight decrease in blood sugar and insulin levels. Chinese researchers analyzed data from 17 studies in which people either drank green tea or took green tea supplements. People consuming green tea had a modest decrease in HbA1c and a significant decrease in fasting insulin levels.

Liu K. American Journal of Clinical Nutrition, 2013: doi 10.3945/ajcn.112.052746.

Eat fruits and vegetables to live longer

Researchers at the Karolinska Institute in Sweden analyzed fruit and vegetable consumption by 71,706 men and women whose average age was 45 to 83 years. During 13 years of follow up, 11,439 of the subjects died. People who never consumed fruits and vegetables lived three years shorter and had a 53 percent higher mortality rate, compared with those who ate five servings daily.

Bellavia A. American Journal of Clinical Nutrition, 2013; 98:454-459.

Higher glucose levels boost dementia risk

Having higher blood sugar levels – even without diabetes – increases the risk of developing dementia. Researchers from the University of Washington, Seattle, and other institutions analyzed blood sugar levels from 2,067 people whose average age was 76 years. After almost seven years of follow up, 524 of the subjects developed dementia (of which Alzheimer's is one type). People with a blood sugar level of 115 mg/dl, compared with those whose blood sugar was 100 mg/dl, were 18 percent more likely to develop dementia. People whose blood sugar level was less than 100 mg/dl had a lower risk of dementia.

Crane PK. New England Journal of Medicine, 2013;369:540-548.

• Antibiotics damage normal cells

Antibiotics have saved millions of lives, but a new study suggests it's best to use them only when absolutely necessary. Researchers at Boston University tested the effects of antibiotics on mice and human cells. The antibiotics increased levels and free radicals and damaged mitochondria, the energy centers of cells. However, N-acetylcysteine, an overthe-counter antioxidant, protected the mice and cells from damage.

Kalghatgi S. Science Translational Medicine, 2013;5:192ra85.

• Drinking water boosts reaction times

Researchers from the Universities of East London and Westminster noted anecdotal evidence suggesting that water consumption might enhance cognitive performance. In a study of 34 people, drinking about three cups of water before a battery of tests led to faster reaction times, compared with when the subjects did not drink water.

Edmonds CJ. Frontiers in Human Neuroscience, 2013: doi 10.3389/fnhum.2013/00363.

• Chemical combination increases cancer risk

Thousands of industrial chemicals are considered safe in small amounts, but doubts have long been raised about the risks when these chemicals interact. A recent study suggests that those risks may be very real. Researchers at Texas Tech University, Lubbock, started with the knowledge that both arsenic (found in many groundwater supplies) and estrogen can cause cancer, but each are believed to be harmless in tiny amounts. So the researchers exposed prostate cells to a combination of small and apparently safe amounts of arsenic and estrogen. Together, the chemicals nearly doubled the risk of cancer cells developing, in part by inhibiting a gene that would otherwise help abnormal cells self-destruct. Treas J. *The Prostate*, 2013: doi: 10.1002/pros.22701

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Post Office Box 30246 • Tucson AZ 85751-0246 USA Editor and Publisher: Jack Challem Copy Editor: Mary E. Larsen

Medical and Scientific Advisors

Ronald E. Hunninghake, MD Wichita, Kansas• Ralph K. Campbell, MD Polson, Montana Peter Langsjoen, MD Tyler, Texas • Marcus Laux, ND San Francisco, Calif. James A. Duke, PhD Fulton, Maryland • Andrew W. Saul, PhD Rochester, New York