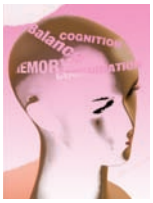

SECOND IN A SERIES
NUTRITION AND BRAIN FUNCTION

Metals Essential to the Brain's Hardwiring

The standard element for moving telecommunications signals across phone wires is copper. Key bioactive enzymes and proteins in the brain also depend on copper to function. At least one copper-dependent enzyme supports the formation of neurotransmitters that allow brain cells to "talk" to one another.

Associations between copper deficiency and impaired brain function were noted nearly 75 years ago. The owner of a sheep station in Australia found that his lambs had become uncoordinated to the point of falling. Eventually, it was found that the lambs—all of which died—were born from mothers that had been pastured during pregnancy on forage with extremely low copper content.

ARS chemist W. Thomas Johnson recently authored "Copper and Brain Function," a review chapter in the book *Nutritional Neuroscience.* Johnson is a lead scientist at the ARS Grand Forks Human Nutrition Research Center (GFHNRC) in North Dakota. He heads projects on dietary copper requirements for health. In the book, Johnson described current research into the biochemical mechanisms underlying impaired brain development and function that have been associated with copper deficiency.

Dietary Copper Traffic

Many proteins and enzymes depend on copper for their catalytic activity. Some contain copper, and some are affected by the presence or absence of sufficient copper. Some proteins act as escorts that deliver copper to copper-containing enzymes in the brain. These enzymes will not function properly with insufficient copper.

In exploring abnormal brain development and function, ARS researchers have been looking at changes in two copper-dependent enzymes in particular: cytochrome c oxidase (CCO) and dopamine-B-monooxygenase (DBM). These enzymes function within the brain's billions of nerve cells, or neurons.

GFHNRC studies have found that the activity of various copper-containing enzymes is lower in rats subjected to copper deficiency during either pre- or postnatal brain development—with varying outcomes.

CCO, for example, contains about 20 percent of the rat brain's total copper content. It is involved in what's called the "electron transport chain"—a critical aerobic pathway producing energy in the body.

"The electron transport chain is involved in mitochondrial energy production," says Johnson. Impaired CCO activity—associated with copper deficiency—can damage rat brain mitochondria and their critical metabolic pathways.

An early GFHNRC animal study led by biologist Curtiss Hunt showed that even moderate copper deprivation in pregnant rats led to underdevelopment of memory-control areas of their pups' developing brains. The study rats were fed low-copper diets during gestation, lactation, or both. Their pups—when compared to pups born to mothers fed copper-sufficient diets—exhibited slowed development of the dentate gyrus and hippocampal areas of their brains. These areas are important for higher brain functions, such as learning.

More recently, now-retired GFHNRC psychologist James Penland participated in an animal study with lead author and copper expert Joseph R. Prohaska at the University of Minnesota-Duluth. Their tests showed that rat pups from mothers made copper-deficient during pregnancy never achieved their full motor function.

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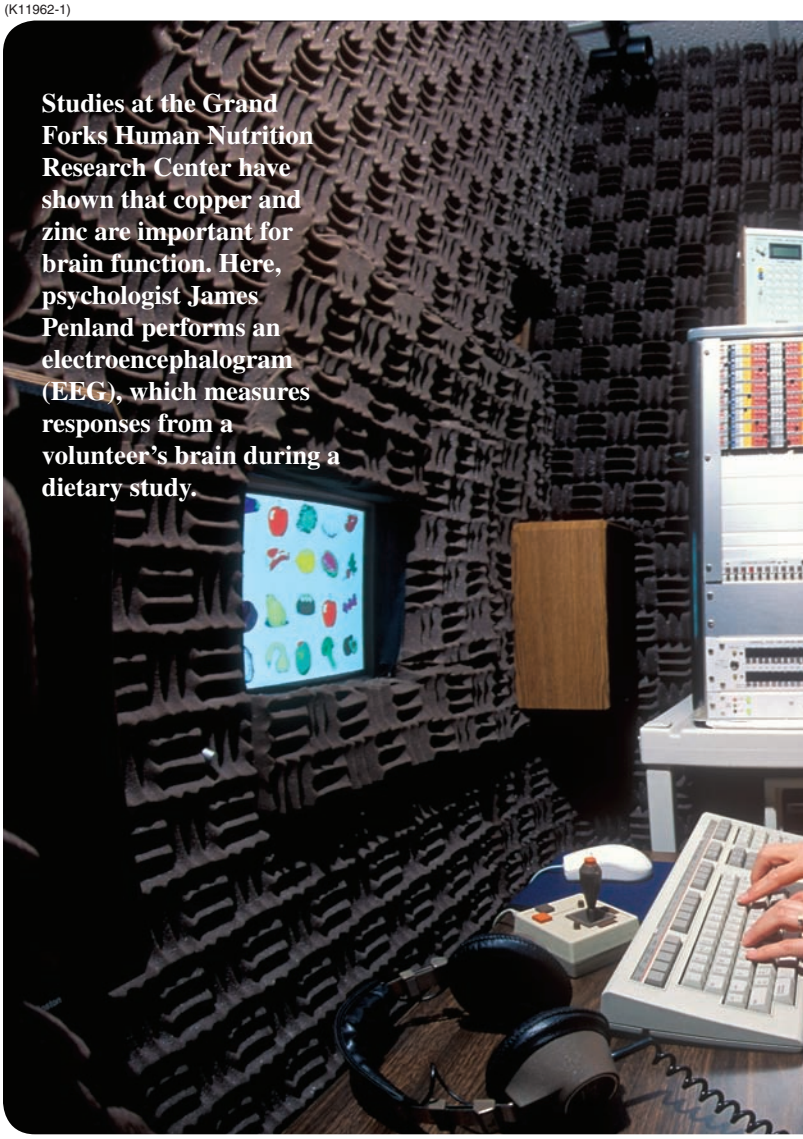

Studies at the Grand Forks Human Nutrition Research Center have shown that copper and zinc are important for brain function. Here, psychologist James Penland performs an electroencephalogram (EEG), which measures responses from a volunteer's brain during a dietary study.

Penland was also interested in the effects of diminished DBM activity. DBM contains just a fraction of 1 percent of the brain's copper content, but it catalyzes an important reaction: formation of the neurotransmitter norepinephrine from dopamine. "A deficiency of norepinephrine during critical brain development

might decrease synaptic connections and, thus, the maturing process of brain cells," says Penland. "That could affect behavioral and motor responses."

Two major factors have been found to lead to impaired motor and brain function due to copper deficiency in laboratory animals: the timing and the degree of the deficiency. For example, during gestation, neonatal genes are turned on or off in response to various factors, such as maternal diet and nutrition. This

"nutritional programming" can affect susceptibility to health risks later in life.

Research on nutritional programming is part of Life Stage Nutrition and Metabolism, one of four new research components within the ARS Human Nutrition national program, according to Molly Kretsch, the program's leader.

"Our animal model studies suggest that levels of copper intake are critical during pregnancy," says Johnson. "The effects of low copper intake are very subtle and might not be seen until offspring are in their adult years."

The Zinc-Think Connection

During the last several decades, scientists have also demonstrated the effects of zinc deficiency on brain function and mental performance.

Penland conducted a study at GFHNRC that examined the effects of restricted zinc intakes on the neuropsychological functions of 11 men. For the study, neither the researchers nor the volunteers knew which participants received specific quantities of dietary zinc. The volunteers' diets were closely controlled to limit confounding of test variables.

In random order, the men were fed one of four relatively low amounts of zinc daily for 35 days: either 1, 2, 3, or 4 milligrams (mg). Then they were given adequate zinc (10 mg) for 35 days. Before-and-after cognitive and psychomotor task tests showed that the men's performance—while on *any* of the four low-zinc diets—deteriorated in 9 out of 15 tasks.

The study was described in "Zinc Nutriture as Related to Brain," a chapter Penland coauthored for the book *Trace Elements in Man and Animals 10.*

Penland also conducted a study of the effects of zinc nutrition in adolescents. He found that seventh graders given 20 mg of zinc 5 days a week for 10 to 12 weeks responded more quickly and accurately and had more sustained attention than classmates who received no additional zinc.

"The beneficial effects were seen regardless of the youngsters' previous zinc status," says Penland.

Adequate amounts of copper and zinc are clearly important to overall health and brain function. But the idea that "a little is good, so a lot must be better" does not apply. The human body regulates copper so that it does not accumulate to unsafe levels. But zinc competes with copper for absorption sites in the intestine, and too much zinc can affect copper levels.

Even though copper deficiency is not generally a public health concern in the United States, 8 to 16 percent of childbearing-age women had inadequate copper intake, according to ARS national food-intake survey data from 2001 and 2002.

"A balanced diet containing a variety of nutritious foods is always the best approach," says Johnson.—By **Rosalie Marion Bliss,** ARS.

This research is part of Human Nutrition, an ARS national program (#107) described on the World Wide Web at www.nps.ars.usda.gov.

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