

Looking for answers on how to keep older brains healthy

addes as Alzheimer's, Parkinson's or Huntington's disease. "We have extremely well-trained physicians who are seeing patients all the time and are bringing data back to scientists," said Andrew Dillin, PhD, assistant professor at the Salk Molecular and Cell Biology Laboratory, in LaJolla, Calif. Since the cause of these diseases is unknown, "we really have to throw everything at it," he said. "It's a huge field with a lot of different approaches coming out of it."

Dr. Dillin, working with researchers at Scripps Research Institute in LaJolla, unveiled new findings in the Aug. 10 *Science Express*, the online version of *Science*, that could lead to the development of drugs to prevent build-up of harmful beta-amyloid.

1 in 10 people older than 65 and nearly half of those 85 and older are affected by Alzheimer's disease.

Their research also found that the aging process impedes two molecular clean-up crews from getting rid of the toxic aggregates of this protein fragment. Although beta-amyloid production occurs in all brains, healthy cells clear away excess amounts. The brains of people with Alzheimer's can't control this build-up, and scientists have struggled for years to find out why.

To determine whether aging or simply time's passage was the culprit, Dr. Dillin, working with Scripps chemistry professor Jeffrey Kelly, PhD, experimented with roundworms that were engineered to age at different rates. Roundworms can produce human beta-amyloids in their body wall muscles. The scientists then postulated: If it just takes time to accumulate the harmful protein fragments, then the round-

Ridding the brain of harmful beta-amyloid plaques is a common target for new therapies.

SUSAN J. LANDERS
ANNEX STAFF

Washington Researchers are pursuing numerous leads in their quest for the secrets of a healthy, aging brain.

One recent study focuses on the genes that allow us to reach age 90 with robust mental faculties. Another opens the door to new drug treatments that sweep out toxic bits of protein that build up in the brains of people with Alzheimer's disease. A third homes in on the dangers posed by high-fat, copper-rich diets.

The role of exercise and the wear and tear of stress on the brain also are being explored, and Swedish researchers even have assembled a risk predictor for dementia that weighs low education, advanced age, hypertension, cholesterol levels and obesity.

If any of these promising projects reach fruition, the yield in terms of public health benefits would be enormous as thousands of baby boomers approach the age at which diseases such as Alzheimer's take an increasing toll. Advanced age is the greatest risk factor for this illness, with one in 10 people older than 65 and nearly half of those 85 and older affected, according to the Alzheimer's Assn.

Research in the healthy aging field has exploded as attempts are made to uncover the cause of such puzzling mal-

DEMENTIA RISK

Swedish researchers examined data on 1,409 people who were examined in middle and again 20 years later to gather a set of predictors for the development of dementia. The findings might be important for assessing factors and could help identify people who might benefit from intensive lifestyle changes and pharmaceutical treatments.

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The quest to keep older brains healthy

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worms designed to live for 25 days and those that live for 50 days should evidence the onset of disease at the same time. But that didn't happen. "The roundworms treated to live longer managed to do so successfully, while those who lived a normal 25 days exhibited an incapacitating build up of beta-amyloid aggregates."

"Our study revealed that the age onset of these diseases is not simply a matter of time but that the aging process plays an active role in controlling the onset of toxicity," Dr. Dillin said. The researchers also found that cells use an unexpected two-pronged strategy to rid themselves of harmful aggregates, thus opening the way to new drug targets.

Meanwhile, Martha Clare Morris, ScD, associate

professor of medicine at Rush University Medical Center in Chicago, zeroed in on diet to determine why there is an increased rate of cognitive decline among older people.

She found that people who consume high amounts of food with saturated and trans fats and have a higher intake of copper may show a decline in thinking, learning and memory abilities — signs of Alzheimer's. Her findings were published in the August *Archives of Neurology*.

Plus, it seemed to take both the high fats and the copper to produce the result. "In people who did not have a high-fat diet, there was no association of the copper cognitive decline," she said.

While copper is an essential nutrient, fats are not, she said. "This is another reason that a diet high in

ABSTRACTS ARCHIVES JOURNALS

ARCHIVES OF NEUROLOGY Dietary Copper and High Saturated and Trans Fat Intakes Associated With Cognitive Decline

Background: Evidence from prospective epidemiologic studies and animal models suggests that intakes of dietary fats and copper may be associated with neurodegenerative diseases.

Objective: To examine whether high dietary copper intake is associated with increased cognitive decline among persons who also consume a diet high in saturated and trans fats.

Design: Community-based prospective study.
Setting: Chicago, Ill.

Patients: Chicago residents 65 years and older.

Main Outcome Measures: Cognitive function was assessed using 4 cognitive tests administered during in-home interviews at 3-year intervals for 6 years. Dietary assessment was performed with a food frequency questionnaire. Dietary intakes of copper and fats were related to change in global cognitive score (the mean of the 4 tests) among 3718 participants.

Results: Among persons whose diets were high in saturated and trans fats, higher copper intake was associated with a faster rate of cognitive decline. In multiple-adjusted mixed models, the difference in rates for persons in the highest (median, 2.75 mg/d) vs lowest (median, 0.88 mg/d) quintiles of total copper intake was -6.14 standardized units per year ($P < .001$) or the equivalent of 19 more years of age. There was also a marginally statistically significant association ($P = .07$) with the highest quintile of food intake of copper (median, 1.51 mg/d) and a strong dose-response association with higher copper dose in vitamin supplements. Copper intake was not associated with cognitive change among persons whose diets were not high in these fats.

Conclusion: These data suggest that high dietary intake of copper in conjunction with a diet high in saturated and trans fats may be associated with accelerated cognitive decline.

Morris MC, Evans DA, Tangney CC, et al. 2006;63:1055-1088.

saturated and trans fat tends to cause problems." Previous studies also have shown that copper can cause the harmful amyloid plaques to form. Based on this research, a focus in Alzheimer's research has been to find medications that can mimic the action of the healthy brain and clear out these dangerous plaques, said Sam Gandy, MD, PhD, chair of the Alzheimer's Assn.'s medical and scientific advisory council. "That's the most popular hypothesis of how Alzheimer's begins."

In July, the 10th International Conference on Alzheimer's Disease and Related Disorders was held in Madrid and attended by 5,000 researchers and clinicians. A similar meeting in 1988 attracted 500 attendees.

But the sad part is that funding is being cut, Dr. Gandy said. "Just as we are bringing medicine into the clinic, we are being knee-capped by losing the support we need to keep it going." ♦