

# Report Highlights Gaps in Alzheimer's Research

BY JEFF EVANS

FROM A NATIONAL INSTITUTES OF HEALTH STATE-OF-THE-SCIENCE CONFERENCE

BETHESDA, MD. — Current knowledge about the epidemiology of Alzheimer's disease and cognitive decline has not provided enough evidence to recommend specific, preventive interventions, according to a draft "state-of-the-science" report issued by a panel of experts assembled by the National Institutes of Health.

The 15-member panel found that there is not enough evidence to support the use of pharmaceutical agents or dietary supplements to prevent cognitive decline or Alzheimer's disease, but ongoing additional studies of antihypertensive medications, omega-3 fatty acids, physical activity, and cognitive engagement "may provide new insight into the prevention of delay of cognitive decline or Alzheimer's disease."

"We're hoping that our report is going to supply physicians with accurate information that they can give to their patients" to clarify what interventions may be worth continuing or pursuing and



**The report aims 'to clarify what interventions may be worth continuing ... and which should be discontinued.'**

DR. BELL

which should be discontinued, said panelist Dr. Carl C. Bell, director of public and community psychiatry at the University of Illinois at Chicago, said at a press telebriefing.

A wide range of modifiable factors has been reported to be associated with risk for Alzheimer's disease, such as diabetes

diet, medication, or lifestyle, but the overall quality of evidence from these studies is low, the panel said.

Panel member Arnold L. Potosky, Ph.D., of Georgetown University in Washington said that it is important for physicians to discuss participation in clinical studies with their patients.

The panel recommended that further research should include:

- ▶ The development and use of rigorous, consensus-based diagnostic criteria for Alzheimer's disease and mild cognitive impairment.

- ▶ The development and use of a standardized, well-validated, and culturally sensitive battery of outcome measures across research studies.

- ▶ The collection of data from caregivers of people with mild cognitive impairment or early Alzheimer's disease in a systematic manner in observational studies and randomized, controlled trials.

- ▶ The conduct of large-scale, long-term

population-based studies with well-validated exposure and outcome measures in people followed from middle to old age.

- ▶ The leveraging of alternative research resources and platforms that facilitate long-term longitudinal assessments, such as a multicenter Alzheimer's disease registry or observational studies within large health care delivery systems with defined populations and well-developed electronic health records.

- ▶ The creation of a simple, inexpensive, quantitative instrument that can be administered by a trained nonexpert to assess change in cognitive status over time.

The panel based its draft statement on an evidence report from the Evidence-Based Practice Center at Duke University's Clinical Research Institute, which was commissioned by the Agency for Healthcare Research and Quality. ■

## Healthy Lifestyle Linked To Lower Mortality Risk For Stroke Patients

BY AMY ROTHMAN SCHONFELD

FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF NEUROLOGY

TORONTO — Even after having a stroke, people who maintain a healthy lifestyle can reduce the risk of death, and the more healthy lifestyle practices they follow, the greater the benefit, according to data from 388 stroke survivors.

Those who did not smoke and exercised regularly were less likely to die, and those who ate fruits and vegetables routinely were less likely to die from cardiovascular causes, Dr. Amytis Towfighi said at the annual meeting of the American Academy of Neurology. "The benefits of five simple healthy lifestyle factors had been shown in the general population, but had not been shown before for the stroke survivor population," said Dr. Towfighi, of the University of Southern California, Los Angeles.

Dr. Towfighi analyzed data from the National Health and Nutrition Examination Survey (NHANES). From an initial sample of more than 33,000, 649 subjects were identified who had a prevalent stroke during

1988-1994 and were followed through 2000.

In the final analysis, 388 stroke survivors met all criteria, including information on such covariates as age, sex, race, and prior myocardial infarction. The sample was 80% white and 53% female, with a mean age of 67 years. Of the 388 stroke patients, 206 died by 2000, with 126 deaths attributed to cardiovascular causes. Of the stroke survivors, 75% said they did not smoke, and 23% used alcohol moderately (although most did not drink).

Of the five healthy lifestyle factors, abstaining from smoking (hazard ratio, 0.57; confidence interval, 0.34-0.98) and regular exercise (HR, 0.66; CI, 0.44-0.99) were associated with a lower all-cause mortality. Eating at least five servings of fruits and vegetables was associated with lower risk of cardiovascular death (HR, 0.30; CI, 0.09-1.04).

Compared with those who did not report any of the healthy practices, the HR for all cause-mortality was 0.07 (CI 0.01-0.51) for five practices, 0.04 (CI 0.01-0.19) for four practices, and 0.13 (CI 0.03-0.55) for three practices.

Dr. Towfighi said she had no relevant conflicts. ■

## Brain Exercises Fail To Improve Memory, Cognitive Function

BY LEANNE SULLIVAN

"Brain training" does not improve general cognitive function, according to a 6-week trial of more than 11,000 participants.

The study results "provide no evidence for any generalized improvements in cognitive function following brain training in a large sample of healthy adults," Adrian M. Owen and his colleagues reported.

The participants were divided into three groups: the experimental group 1 (4,678 subjects), which did six tasks emphasizing reasoning, planning, and problem solving; experimental group 2 (4,014 subjects), which practiced six tasks

focusing on short-term memory, attention, visuospatial processing, and mathematics; and a control group (2,738 subjects), which answered various research questions using the Internet, said Mr. Owen of the Medical Research Council Cognition and Brain Sciences Unit, Cambridge, England, and his colleagues.

The participants were assessed before and after the intervention using benchmarking tests that measuring reasoning, verbal short-term memory, spatial working memory, and paired-associates learning.

All three groups improved on the tasks they had been assigned to during the trial, but postinter-

vention improvements were much smaller (effect sizes: 0.01-0.22 for all groups).

No relationship was seen between number of training sessions performed or age of participants and postintervention benchmarking test scores. The scores on two tests reflected small gender differences.

Although participants improved at their assigned tasks, "training-related improvements may not even generalize to other tasks that use similar cognitive functions," the researchers said (Nature 2010 Apr. 20 [doi: 10.1038/nature09042]).

The authors reported no financial conflicts of interest. ■

### Credible Study on Complex Question

MY TAKE

The notion of exercising the mind to reduce its deterioration is popular in the world of Alzheimer's disease.

Do more crossword puzzles and you will slow the progression of dementia. But is it true? Epidemiological studies have shown mixed results, possibly reflecting presymptomatic-stage disease, confounding medical issues, and medications influencing outcomes. Functional brain imaging studies show activation of prefrontal



cortices during the early attentional practice stage that diminishes and ultimately vanishes as any skill becomes automatic (Proc. Natl. Acad. Sci. USA 1998;95:853-60).

Cognitive tasks, in contrast to sensorimotor tasks, rely on the integration of multiple brain regions that are geographically distant and serve different functions. Because a related, nonidentical task might use this network, it is conceivable that related tasks may be performed with greater

facility and dexterity.

Given the effort required to achieve even a "simple" practice effect, studies such as that of Adrian M. Owen and his colleagues that fail to show any major translational skill differences after a mere 6 weeks of "brain exercises" that sound far less grueling than the practice of professional musicians and athletes are certainly credible.

RICHARD J. CASELLI, M.D., is a professor of neurology at the Mayo Clinic Arizona, Scottsdale. He has no financial conflicts of interest related to this subject.