NIH Points to Gaps in Alzheimer's Research

BY JEFF EVANS

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 clinical 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 which should be discontinued, panelist Dr. Carl C. Bell, director of the Institute for Juvenile Research in the department of 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, elevated blood cholesterol in midlife, and depression, but also relatively benign changes in diet, medication, or lifestyle.

The report should clarify what interventions may be worth continuing and which should be discontinued.

DR. BELL

However, the overall quality of evidence from these studies is low, the panel said, and they did not find enough evidence to draw firm conclusions about the association of modifiable risk factors with cognitive decline or Alzheimer's disease.

In light of the fact that there are no proven interventions that prevent cognitive decline or Alzheimer's disease, 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. Existing cohorts from ongoing studies of this type also could be explored for timely, cost-effective identification of individuals at high risk of cognitive decline or Alzheimer's disease.

► 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 scope of the statement was restricted to studies of people aged 50 years or older that were conducted in developed countries. The minimum sample size in these studied was at least 50 patients in randomized, controlled trials and at least 300 patients in observational studies.

The duration between exposure to a preventive intervention and study outcomes had to be at least 1 year for studies of mild cognitive impairment and at least 2 years for studies of Alzheimer's disease.

The panel based their 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. ■

The evidence report is available at www.ahrq.gov/clinic/tp/alzcogtp.htm. The finalized statement is available at consensus.nih.gov.

Brain Training Exercises Fail to Boost 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: 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 math; and a control group (2,738 subjects), which answered various questions using the Internet. The groups were matched in size initially, but more of the control group members dropped out before the final assessment. Participants were recruited from viewers of a British science TV show.

The tasks given to group 2 were considered to be most like those of commercially available "brain training" programs, 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 measured reasoning, verbal short-term memory, spatial working memory, and paired-associates learning. These validated cognitive assessment tools (available at www.cambridgebrainsciences.com) were chosen for their proven sensitivity to small cognitive changes because of disease or neuropharmacologic therapy.

Participants completed an average of 24 training sessions over the 6-week period (range, 1-188). The tasks were performed for a minimum of 10 minutes a day, three times a week.

All three groups improved on the tasks they had been assigned to practice (effect sizes: group 1, 0.73-1.63; group 2, 0.72-0.97; controls, 0.33). However, postintervention improvements on the benchmarking tests were much smaller (effect sizes: 0.01-0.22 for all groups).

The control group improved slightly more than the experimental groups on two measures.

The groups were similar in age (average, 39-40 years) and gender (each group had 4-5 times as many female participants). 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 April 20 [doi:10.1038/nature09042]).

"Six weeks of regular computerized brain training confers no greater benefit than simply answering general knowledge questions using the Internet," the study authors concluded. ■

Disclosures: *The authors reported having no conflicts.*

MY TAKE

A Credible Study on a Complex Question

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.

Most people "exercise" their brain during their daily activities whether they conceptualize it in this way or not. The term "brain training" implies some kind of special activity that the term "practice" lacks, but acquiring any new skill requires enhanced attention, and with increasing task familiarity comes greater automaticity and increasing dexterity.

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.

The background of the question is complex, but 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.

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