

Nonpharma Intervention Cuts Dementia Risk by a Third

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Healthy, well-functioning seniors who undertake a type of computerized cognitive training that targets processing speed have a 29% reduced risk for dementia after 10 years, with those completing the most training sessions having the greatest benefit, new results suggest.

Cognitive training that focused on memory or reasoning did not significantly reduce the risk for dementia.



Dr Jerri Edwards

"This study is the only randomized clinical trial to ever show that any kind of intervention — pharmaceutical or nonpharmacological — can reduce the risk of dementia," Jerri Edwards, PhD, professor, College of Medicine, Department of Psychiatry and Behavioral Neurosciences, University of South Florida, Tampa, said at a press conference.

The study results, first presented at the 2016 Alzheimer's Association International Conference (AAIC) in Toronto and [reported by Medscape Medical News](#) at that time, [were published in *Alzheimer's & Dementia: Translational Research & Clinical Interventions*](#).

"Mental Quickness"

The new results differ somewhat from those presented at the AAIC because the researchers narrowed the definition of dementia, which affected the number of dementia cases and hazard ratios (HRs).

The multisite Advanced Training in Vital Elderly (ACTIVE) study included 2785 community-dwelling seniors (mean age, 73.6 years) who were initially cognitively intact, with a mean Mini-Mental State Examination [MMSE] score of 27.3. The study group was predominantly white (73.3%) and female (76.2%).

Participants were randomly assigned to one of three types of cognitive training — memory, reasoning, or speed of processing — or to a control group that received no cognitive training.

Each training arm consisted of ten 60- to 75-minute sessions over 5 to 6 weeks. The memory and reasoning training took place in a classroom format with pencil-and-paper types of exercises.

"The memory training taught people strategies they can use to better remember lists of information, and the reasoning training taught strategies to recognize patterns to be able to better solve problems," said Dr Edwards.

The speed of processing training was the only computerized intervention. This training targets "mental quickness," which, said Dr Edwards, declines with age.

"Mental quickness starts to decline as early as 25 years of age and is a hallmark of aging, if you will. I think that speed of processing training is particularly important because it's targeting the very basic ability that can affect all aspects of your life."

During the computerized intervention, users are asked to identify visual targets, for example, cars or trucks, that are briefly flashed on the screen. The task can be made more difficult by adding more stimuli, having targets appear for a briefer period of time, and/or adding distractors.

A subset of participants who completed at least 80% of the training sessions were randomly selected to receive booster training, which consisted of four 75-minute sessions, at 11 and 35 months after the initial training.

For the memory composite outcome, researchers used the Hopkins Verbal Learning Test, Rey Auditory-Verbal Learning Test, and Rivermead Behavioral Memory Test. For the reasoning composite, they used the Letter Series, Letter Sets, and Word Series. And for the speed composite outcome, they used the four subtests of the Useful Field of View, reverse-scaled so that higher scores indicated better performance.

Researchers also considered participants' vocabulary scores.

Test scores were normalized to the control group to form Z-scores. The average of the component Z-scores formed four domain-specific cognitive composites.

Assessments were completed immediately after training and at 1, 2, 3, 5, and 10 years.

Dementia Criteria

For this latest analysis, dementia was defined as any of these three criteria:

- Cognitive and functional impairment (memory, reasoning, or speed composite score, or vocabulary score, at or below – 1.5 standard deviations of the baseline mean, and Minimum Data Set Instrumental Activities of Daily Living [MDS-IADL] total score at or below the 10th percentile of the baseline);
- A score of less than 22 on the MMSE, with all scores on subsequent MMSE assessments at less than 22 or missing; or
- A diagnosis of dementia or Alzheimer's disease during follow-up.

In the earlier analysis, the dementia definition included two additional criteria. These included institutionalization and deactivation from the study due to family refusal. The three criteria used in the study "are more widely accepted," said Dr Edwards.

Of the 2785 original participants, 1220 completed the 10-year follow-up. The rate of nonparticipation due to death, withdrawal, and loss to follow-up did not differ by training arm.

During the decade-long follow-up, 260 study participants developed dementia according to the updated criteria.

Compared with the control group, the risk for dementia was 29% lower in the speed training group (HR, 0.71; 95% confidence interval [CI], 0.50 - 0.998; $P = .049$).

The risk for dementia was not significantly different compared with the control group for the memory training group ($P = .177$) or for the reasoning training group ($P = .163$).

Each additional speed training session was associated with a 10% lower hazard for dementia (HR, 0.90; 95% CI, 0.85 - 0.95; $P < .001$). This was the case even after adjustment for age, sex, race, depressive symptoms, diabetes, and congestive heart failure.

The authors acknowledged that the association between the number of training sessions and the risk for dementia could be due to reverse causality.

It's not clear what the "right dose" or scheduling of speed training sessions should be for the lowest dementia risk, said Dr Edwards.

Researchers carried out several sensitivity analyses. In one, they compared results using different combinations of dementia criteria and found that the hazard of dementia was consistently lower for participants in the speed training arm compared with controls.

Underlying Mechanism Unclear

An analysis examining effects of early dropout (before 5 years), late dropout (after 5 years), and completers consistently indicated a similar magnitude of speed training effects on dementia risk reduction.

Another analysis showed that the relation of increased training exposure to lower risk for dementia was detected to the same degree in the groups who were and were not randomly assigned to booster training, two relatively homogenous groups.

The authors concluded from this that differential participant characteristics linked to booster assignment is "likely not responsible for our pattern of findings."

The authors noted that the attrition rate in the study, at 5.5% per year over the 10 years, falls within the typical range for studies of older adults with a long-term follow-up.

The relationship between speed training and dementia risk was not detected at 5-year follow-up. However, Dr Edwards noted the earlier analysis looked at all three training arms together and had "a statistical power issue."

In that 5-year analysis, there were only 189 dementia cases compared with 260 cases at 10 years. The increased number of outcomes improved the power to detect a relationship, said Dr Edwards.

The underlying mechanism by which speed training reduces dementia risk is not clear but may be related to changes in brain reserve.

Speed training may increase brain reserve capacity through compensatory changes in function. For example, enhanced capacity or efficiency of the brain, or via direct effects promoting viability of healthy tissue or decreasing the amount or effect of pathologic proteins and processes, the authors note.

Results of previous research using electrodes to measure brain activity before and after speed training sessions suggest that this intervention "improves allocation of attention," said Dr Edwards. "So it improves your ability to pay attention to everything around you."

The authors acknowledged that there are limitations to the dementia criteria used in the study. For example, MDS-IADL function was self-reported and therefore biased, and low MMSE score is not a sensitive dementia marker.

This new study adds to the growing literature on cognitive training. To date, some 17 randomized controlled trials looking at the effects of speed training have been published, said Dr Edwards.

Six of these studies showed positive effects on everyday function, meaning participants had a better chance of remaining independent and in their own home. Other studies showed that such interventions improve health-related quality of life, gait and balance, and increase the sense of control over one's life, she said.

Cautiously Encouraging

Commenting on the findings for *Medscape Medical News*, David Knopman, MD, professor of neurology at the Mayo Clinic, Rochester, Minnesota, whose research interests include late-life cognitive disorders, described the findings as "cautiously encouraging."

However, he noted several "caveats" or limitations.

Among these, said Dr Knopman, is that the analysis showing that speed training lowered dementia risk was post hoc; the primary designated outcome was at 5 years, not 10 years.

Also, the effect — a 29% reduction in dementia risk — was relatively small and was confounded by attrition as only 44% of the original cohort was included in the analysis, said Dr. Knopman.

The results were also potentially subject to bias as the researchers "cherry picked" the speed training outcome.

"The authors had three possible arms in which to find one with a positive outcome. They didn't specify ahead of time which one they expected to work. If you toss a coin three times, you are more likely to get 'heads' at least once compared to tossing the coin only once."

The sort of cognitive training used in the study represents "far too low a dose of cognitively stimulating activity to be useful," Dr Knopman maintained.

"For people to obtain a benefit from cognitive stimulation, they need such activity in their lives every day. An hour a few times a week on a computer in the context of little other cognitive or social stimulation is doomed to show the smallest of benefits."

However, Dr Knopman said computer-delivered cognitively stimulating activities are "better than nothing."

The speed training program used in the ACTIVE study is available as an exercise called Double Decision. It is one of the exercises in BrainHQ, an online cognitive training program from Posit Science. The study was supported by grants from the National Institute of Nursing Research and the National Institute on Aging. Dr Edwards has had relationships with Posit Science and Visual Awareness Inc and serves on the data safety and monitoring board for National Institutes of Health grants awarded to employees of Posit Science. Dr Knopman has disclosed no relevant financial relationships.

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