Cognitive Training and Dementia: Media FAQ
The ACTIVE Study 20-Year Dementia Medicare Results

Summary

Q: What are the new scientific results?
A: Researchers have evaluated data from a 20-year study of cognitive training and shown that a relatively modest amount of one specific type of cognitive training can significantly reduce the risk of developing of dementia (including Alzheimer's disease and related dementias) over a 20-year period as evaluated with Medicare data.

Q: Why are these results newsworthy?
A: According to the Alzheimer's Association, more than 7 million Americans are living with Alzheimer's dementia, a figure expected to nearly double to almost 14 million by 2060, with a new person developing Alzheimer's every 65 seconds. Alzheimer's disease accounts for approximately 70% of the cases of dementia, and in 2025, the costs of Alzheimer's are estimated at over $384 billion. This is the first result from a large randomized controlled trial to show that any intervention—cognitive training, brain game, physical exercise, diet/nutrition, or drug—can cut the incidence of dementia. Also, 80% of the general public is reported to have a fear of developing dementia at some point in their lives, and dementia is the most feared disease of people as they age. According to the Pew Research Center most consumers of news are older, with 62% of Americans aged 65+ saying they follow the news "all or most of the time," compared to just 15% of adults under 30, and with median ages for network news ranging from 55 to 58**.**

Design of the ACTIVE Study

Q: How was the ACTIVE Study conducted?
A: These new results come from the ongoing Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study, a large multi-site randomized controlled trial organized and funded by the National Institutes of Health. The ACTIVE Study commenced participant enrollment in March 1998 and completed enrollment in October 1999. ACTIVE enrolled 2,832 community-dwelling and generally healthy participants aged 65 and older, with an average age of almost 74, at six research sites across the United States. Participants were randomly assigned to one of three cognitive training groups (referred to in the study as "speed," "memory," or "reasoning" training), or to a control group. Participants engaged in a comprehensive set of cognitive assessments before training, immediately after training, and 1, 2, 3, 5, and 10 years after training. For this 20-year follow-up, researchers accessed participants' medical records through Medicare to determine which participants were diagnosed over the 20-year follow-up period with dementia. At the time of the 20-year follow-up an average surviving participant would have been almost 94.

Q: What cognitive training programs were used in ACTIVE?
A: ACTIVE evaluated three different cognitive training programs:

- In *speed training,* participants performed computerized training that was designed to improve the speed and accuracy of visual information processing, while expanding the visual area over which a person could pay attention and make rapid decisions. The training was adaptive and personalized, starting each participant at a task difficulty appropriate for their abilities, and getting more challenging as a participant succeeded at the task, and getting easier when a participant struggled with the task.
- In *memory training*, participants were taught mnemonic strategies for remembering word lists and sequences of items, text material, and main ideas and details of stories. For example, participants were instructed how to organize word lists into meaningful categories and to form visual images and mental associations to recall words and texts.
- In *reasoning training,* participants focused on the ability to solve problems that follow a serial pattern, like identifying the pattern in a letter or number series or understanding the pattern in an everyday activity such as prescription drug dosing or travel schedules.

Q: How much training did people in the ACTIVE study do?
A: Everyone assigned to a cognitive training program group was asked to do 10 sessions of training at first. People trained twice per week for 60-75 minutes per session, over the course of five weeks. They also met together to talk about how this training might be relevant to their everyday lives. To examine whether subsequent training at a later time was beneficial, about half of the people in each cognitive training group, who completed at least 8 of the initial 10 sessions, were randomly assigned to do “booster” training, where they did an additional 4 sessions of their assigned training at the end of the first year (in the 11th month), and another 4 hours of training at the end of the third year (in the 35th month). This means that people did up to 22.5 hours in total of training for those in the booster subgroups.

Q: What kinds of people enrolled in ACTIVE? How many? What was the procedure?
A: Study participants were a volunteer sample, living independently in their communities – in 6 geographical areas – Detroit, Baltimore, Birmingham, Indianapolis, Boston, and central PA. To be enrolled in the study, participants had to be 65 or older, and not have dementia, functional limitations, or terminal illnesses. Approximately 25% were African Americans; 75% were women. The average age at the beginning of the study was 74 years (range 65 – 94).

Q: Who were the scientists who organized the ongoing ACTIVE study?
A: ACTIVE was organized and funded by the National Institutes of Health (specifically, The National Institute on Aging and the National Institute for Nursing Research). Six principal investigators originally designed, executed, and analyzed the study:

- Dr. Karlene Ball (University of Alabama, Birmingham), Professor and Director of the UAB Edward R. Roybal Center for Research on Applied Gerontology
- Dr. George Rebok (Johns Hopkins University), Professor and Core Faculty, Center on Aging and Health

- Dr. Sherry Willis (Pennsylvania State University, University of Washington), Research Professor
- Dr. Michael Marsiske (Wayne State University, University of Florida), Professor of Clinical & Health Psychology and Program Director for Graduate Education
- Dr. Fred Unverzagt (Indiana University School of Medicine), Professor of Clinical Psychology in Clinical Psychiatry
- Dr. John Morris (Hebrew SeniorLife), Senior Scientist and Alfred A. and Gilda Slifka Chair in Social Gerontological Research

The current analyses of the ACTIVE study and Medicare dementia data and the preparation of the manuscript were led by Dr. Marilyn Albert (Johns Hopkins University), Professor of Neurology and Director of Cognitive Neuroscience and Director of the Johns Hopkins Alzheimer's Disease Research Center; School of Medicine, and Dr. Norma Coe (University of Pennsylvania), Professor of Medical Ethics & Health Policy, Perelman School of Medicine.

Scores of other investigators have made significant contributions over time to the ACTIVE Study, including Dr. Alden Gross (Johns Hopkins University), Professor, Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health, Dr. Jerri Edwards (University of Alabama, Birmingham), Professor, Heersink Endowed Chair in Mental Health Research, and Dr. Rich Jones, (Brown University), Professor of Psychiatry and Director of Quantitative Science Program.

New Results from the ACTIVE Study

Q: What did the ACTIVE Study 20-Year dementia results show?
A: The participants who were randomly assigned to the speed training group and then randomly assigned to the booster sub-group showed a statistically significant 25% reduction in the risk of diagnosis with dementia in Medicare records over the course of the 20-year follow-up period compared to participants in the control group. Participants randomly assigned to the speed group but not to the booster group and participants in the other two cognitive training programs showed no significant benefit. As further confirmation that the booster training was important, the participants who were randomly assigned to the speed booster group showed a significant 19% risk reduction when compared to participants who were eligible for booster training but were randomly assigned to the non-booster group.

Q: How did researchers diagnose and analyze Alzheimer's disease?
A: The researchers were provided with access to Medicare records for participants in the ACTIVE study. When a person who has Medicare is diagnosed with Alzheimer's disease or a related dementia by their doctor, these data are recorded in their medical records. This record-keeping system has already been demonstrated to be highly accurate, with an 85-90% agreement with a full dementia workup by a neurologist. The researchers had to apply for special permission to access this data and follow careful security processes to ensure that while analyzing the data the privacy of the study participants was protected.

Q: How do the researchers know that the results aren't just due to chance?
A: The ACTIVE Study was a randomized clinical trial, which means that participants were randomly assigned to each group and every effort was made to statistically adjust for variables that might differ among the groups The research team has already shown that the groups randomly assigned to each of the three cognitive training programs and the control group were statistically equivalent at the start of the study. Furthermore, the groups who were eligible for and were randomly assigned to do the booster training were statistically equivalent to the groups who were eligible for but not randomly assigned to do the booster training. This means that all groups had equivalent risks for going on to develop dementia, and the primary difference in the group with reduced dementia risk was that they had done the speed training program with booster sessions.

Q: Are there specific effects on different types of dementia and related conditions, like Alzheimer's, vascular dementia, or fronto-temporal dementia?
A: In the Medicare data that were analyzed by the investigators, Alzheimer's, vascular dementia, and fronto-temporal dementia are all grouped into a single category, referred to as "Alzheimer's disease and related dementias" (ADRD), so the researchers were not able to investigate specific effects on specific dementia types.

Previous Scientific Results from ACTIVE

Q: What other results has the ACTIVE study shown?
A: Previous results from the ACTIVE study have been published in scores of peer-reviewed, academic journals including the *Journal of the American Medical Association* and the *Journal of the American Geriatrics Society* (among many others). Results have shown that all three types of cognitive training can improve their target cognitive functions (speed, memory, and reasoning) and all three reduce the risk of declines in instrumental activities of daily living—the skills required for a person to live independently in their own home.

In other analyses of ACTIVE study data, speed training has been shown to improve everyday speed (activities like looking up a phone number, or reading a medication label), protect against declines in health-related quality of life and depressive symptoms, reduce predicted medical expenditures, improve locus of control, lessen fall risk, and reduce the incidence of at-fault car crashes.

Q: How do these results confirm, extend or differ from the 10-year ACTIVE Study Dementia Results?
A: In 2017, the ACTIVE team published an analysis of dementia risk over a 10-year follow up period. The researchers defined dementia using cognitive and functional performance scores and showed that that speed training caused a 29% reduction in dementia across all speed training participants and a higher 48% reduction in those who had the most booster training (with no significant benefits seen in the other types of cognitive training).

The new study extends these results in two significant ways: (1) the new study followed participants for a follow-up period of 20 years (instead of 10 years), and (2) the new study assessed dementia with gold-standard Medicare records (instead of study-specific cognitive and functional tests).

Both analyses agree that speed training with additional booster sessions uniquely reduces the risk of dementia.

The Science of Speed Training

Q: How can this unique type of cognitive training reduce the incidence of dementia?
A: Researchers are investigating this important question. It's likely that a combination of mechanisms explains the results. First, neuroscientists now recognize that the brain is "plastic"—or capable of change—at any age, adaptively rewiring itself in response to experience, learning, and training. Speed training may be uniquely effective at driving physical brain change because it employs brief, strong stimuli that activate large neuronal populations across brain networks in synchrony – perfect for engaging Hebb's law ("neurons that fire together, wire together"). As these neurons wire together – strengthening existing synapses, physically forming new synapses, thickening myelination – there are changes in connections between brain networks which may help to build "brain reserve" – the ability of the brain to resist the effects of developing dementia. Numerous studies have shown that speed training improves structural, functional, and chemical measures of brain health, including a recent study (INHANCE) showing that speed training improved the health of the brain's acetylcholine system (involved in attention, learning, and memory). Preserving its health may confer resistance to the onset of Alzheimer's disease. Second, it's been shown in numerous studies (including ACTIVE and others) that speed training causes improvements in driving safety, depressive symptoms, health-related quality of life, locus of control, and the ability to perform everyday activities associated with independent living. These functional benefits themselves may cause a resistance to the onset of dementia, because engagement with such everyday activities is associated with dementia resistance. It is likely that both "bottom-up" brain plasticity/brain health and "top-down" real-world engagement mechanisms work synergistically to reduce the risk of the onset of dementia as seen in the ACTIVE study. Further studies should investigate these (and other) possibilities.

Q: Does this result mean that speed training affects amyloid plaques or tau tangles, the pathological hallmarks of Alzheimer's disease?
A: Researchers do not know the answer to this question yet. One possibility is that speed training reduces the risk of the onset of Alzheimer's disease by directly affecting the amyloid plaques and tau tangles. Another possibility is that speed training builds what scientists call "brain reserve" – the ability of a healthy brain to resist the effects of amyloid and tau and continue functionally well even as biomarkers of Alzheimer's disease grow. Further studies should investigate these (and other) possibilities.

Q: What changes in the brain as a result of plasticity-based brain training?
A: Thousands of scientific papers in the field of brain plasticity document physical, functional, and chemical brain changes in animal models as a result of training. Researchers have specifically studied an animal model of speed training and have shown that training drives brain plasticity-based changes at the molecular, cellular, and systems level of the brain. At the molecular level, brain training has been shown to improve markers of neuromodulatory chemical synthesis and neural wiring integrity. At the cellular level, speed training has been shown to revivify the number of interneurons that coordinate coherent global brain activity. And at the systems level, this type of training improves the speed and accuracy of neural information processing.

Q: How can just 10 to 22½ hours of cognitive training show such significant effects that last such a long time?
A: Speed training is a task that involves what is often called “implicit learning” (also called perceptual learning, or non-declarative learning). This kind of learning is like learning to ride a bicycle—the individual is not memorizing facts but rather is practicing procedures. A child can learn to ride a bike in about 10 hours—a learning activity that requires a tremendous amount of brain rewiring across the visual, motor, and balance systems. And once the child has learned how to ride a bike, they will retain that brain-based skill for decades – even with no additional practice. Speed training appears to work in the same way, driving a long-lasting, important brain change in the course of 10 to 22½ hours of learning.

Q: Why did speed training (with boosters) show a benefit on the development of dementia while memory and reasoning training did not?
A: Scientists are very interested in this question. One possibility is the program speed training was *adaptive* – it adapted its level of challenge for each participant’s individual performance level on each day. People who were faster at the start moved to even faster challenges quickly, and people who were slower at the start began at a slower level appropriate for their brains. The memory and reasoning programs were not adaptive – everyone in the group learned the same strategies Additionally, speed training drives *implicit* learning (as discussed in the previous question, more like an unconscious habit or a skill), while memory training and reasoning training drive *explicit* learning (more like learning facts and strategies). Scientists already know that implicit learning works very differently in the brain than explicit learning, and this may contribute to the results on the development of dementia seen in the current analysis.

The Speed Training Program

Q: Who invented speed training?
A: The “speed training” used in the ACTIVE Study was originally developed by Dr. Karlene Ball and Dr. Daniel Roenker. In their original studies of the basic science of visual attention, they developed a computerized assessment tool to measure the “Useful Field of View”—the visual

area over which information can be extracted at a brief glance without eye or head movements. In initial studies, they showed that this assessment was highly predictive of auto crashes in older adults. They also showed that the fundamental skill could be trained with an adaptive computerized program they called "speed training." Through a number of NIH-funded studies, Drs. Ball and Roenker and their colleagues showed that speed training generalized to improvements in a variety of real-world measures, including on-road driving safety and timed instrumental activities of daily living. These results led to the inclusion of speed training in the ACTIVE study.

Q: Where is speed training now?
A: The inventors of speed training, Dr. Karlene Ball and Dr. Daniel Roenker, initially made the program available with the help of NIH small business innovation research (SBIR) grants through Visual Awareness Inc. In 2007, as Posit Science began to build visual speed training exercises to complement its existing auditory speed training exercises, researchers from Posit Science met with Drs. Ball and Roenker to discuss collaborative opportunities. Those discussions led to the acquisition of the speed training program by Posit Science. Developers at Posit Science then worked closely with Drs. Ball and Roenker to port speed training from the original MS-DOS platform to modern computing platforms including the web and mobile devices as part of the BrainHQ app. The exercise is patented and is not available on any other website or program.

Q: Is this speed training available to the public?
A: Yes. The speed training exercise used in the ACTIVE study has been updated and is now available as an exercise called Double Decision, one of the exercises in the BrainHQ brain training app from Posit Science. To access Double Decision, people can go to BrainHQ at www.BrainHQ.com or download the BrainHQ from the Apple (iOS) or Google Play (Android) app stores. People who want to match the training regimen used in the ACTIVE study can select the ACTIVE study focus, which will configure BrainHQ to provide only the Double Decision (speed training) exercise, and configure their weekly goal to 2 hours of training per week.

Other Approaches for Dementia Prevention

Q: How do these results compare to the benefits of physical exercise, the Mediterranean or MIND diets, or other healthy living habits?
A: Many *observational studies* have associated various healthy living habits, including physical exercises, good sleep, or a healthy diet with lower risk of dementia. However, in these observational studies, researchers cannot distinguish cause and effect – does physical exercise prevent dementia, or does not having dementia allow people to exercise more. Similarly, researchers can't be sure of the true cause of the benefit - it's not possible to tell if a healthy diet is the specific cause of lower dementia risk, or if people who eat a healthy diet also have other healthy habits or differences that lower their risk of dementia. To determine if a specific intervention actually causes a lower dementia risk, researchers must do a *randomized control trial* - randomly assigning people to either engage in the intervention or not engage in the

intervention, and then, evaluating the differences between the groups over time. At this time, while there have been randomized controlled trials of physical exercise and dietary intervention that have shown benefits to cognitive function, there have been no trials that have evaluated the effects on dementia risk. The ACTIVE study is the first randomized controlled trial to show a benefit of any intervention – cognitive activity, physical activity, or diet/nutrition – on the risk of developing dementia.

Q: What about other cognitively stimulating activities, like crossword puzzles?
A: Crossword puzzles (and sudoku, and the like) are a great way to spend an afternoon. But no randomized controlled trials have ever shown that doing crossword puzzles improves cognitive function, and no study has ever shown that doing crossword puzzles reduces the risk of dementia. In fact, crossword puzzles have been used as the control group in certain randomized controlled trials of cognitive training. While observational studies (see above) have shown a correlation between doing cognitively stimulating activities (like crossword puzzles) and reduced risk of dementia, those studies have not been able to untangle cause and effect—perhaps people who aren't experiencing the earliest subtle signs of dementia are more likely to engage in crossword puzzles and other mentally stimulating activities.

Q: What about other brain games? Do these results show that all brain games can reduce the risk of dementia?
A: There are hundreds and perhaps thousands of brain games now available. In 2016, the FTC began enforcing existing consumer protection laws to stop brain game companies from making false advertisements and claims of efficacy without the science to support those claims. The current results show that different cognitive training programs are different – only speed training with booster sessions showed a significant benefit, while other types of cognitive training did not.

Q: What about medications, like cholinesterase inhibitors or anti-amyloid antibodies?
A: Cholinesterase inhibitors (like Aricept, Reminyl, or Exelon) have been shown to slow the rate of decline of people who already have Alzheimer's disease. However, in several large- scale randomized controlled trials, they have failed to protect people with early memory loss from going on to develop Alzheimer's disease. Anti-amyloid antibody treatments (like Leqembi /lecanemab and Kisunla/donanemab)) have similarly been shown to slow the rate of decline of people who already have the disease – but no studies have yet been done to evaluate if these drugs can prevent the development of the disease in otherwise healthy people.