Lifestyle Intervention Slows Cognitive Decline in Randomized Trial

Sue Hughes

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Targeting multiple lifestyle factors, including physical activity, diet, vascular risk factors, and brain training, slowed cognitive decline among older healthy individuals in the first randomized, controlled trial of its kind.

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study, <u>published online</u> in *The Lancet* on March 12, was led by Professor Miia Kivipelto, Karolinska Institute, Stockholm, Sweden.

"This is the first time that it has been shown in a longitudinal study that it is possible to reduce the risk of cognitive decline with lifestyle changes," Professor Kivipelto told *Medscape Medical News*.

"We have seen epidemiological studies suggesting associations between various risk factors and cognitive impairment or dementia but now we actually have a randomized study showing that lifestyle interventions can reduce the risk. That is a real breakthrough and feels very exciting.

"It has been very difficult to prove anything works for reducing dementia or cognitive impairment in a randomized trial. Now we have done it. Our results suggest prevention is key. We can do things before memory problems develop to lower the risk," she added. "And our interventions are not difficult to do—they are very simple and pragmatic."

"Major Implications" for Clinical Practice

Commenting on the study for *Medscape Medical News*, Joe Verghese, MBBS, MS, chief of cognitive and motor aging, Albert Einstein College of Medicine, New York, said, "The result of the FINGER study is exciting and has major implications for clinical practice."

Dr Verghese pointed out that the study design does not shed light on which of the multiple interventions is the most beneficial. "For instance, the intervention group was seen at a much greater frequency than the control group, and increasing social interactions might have cognitive protective effects."

Maria Carrillo, PhD, chief science officer for the Alzheimer's Association, said, "The FINGER study is the first large-scale, long-term randomized controlled trial of a lifestyle intervention and the first to demonstrate that multiple changes in lifestyle can improve memory and thinking in older adults who are at risk for cognitive decline. The Alzheimer's Association is pleased to have provided some of the funding for this study."

Dr Carrillo added that the study design was robust and the findings significant, but more research is needed to confirm the outcomes in larger, more diverse groups over similar, long periods of time.

For the study, 1260 people from across Finland, aged 60 to 77 years, were randomly assigned to the multidomain intervention group or control group, who received regular health advice only.

The participants had not yet developed substantial memory problems but were thought to be at risk for cognitive impairment on the basis of a dementia risk score of 6 or more (on a scale of 0 to 15) that

considered age, sex, education, blood pressure, cholesterol, body mass index, and physical activity. They also underwent cognitive testing; individuals with cognitive performance at the mean level or slightly lower than expected for age according to Finnish population norms were selected.

Professor Kivipelto noted: "The population we included was still quite healthy at the starting point and quite representative of the general population in their 60s and 70s."

The intervention group underwent a program concentrated on four major areas:

- Physical exercise based on international guidelines guided by physiotherapists at the gym and consisting of individually tailored programs for progressive muscle strength training (one to three times per week) and aerobic exercise (two to five times per week).
- Nutritional advice based on the Finnish Nutrition Recommendations delivered by study nutritionists (three individual sessions and seven to nine group sessions)
- Cognitive training (10 group sessions with a trained psychologist and individual sessions consisting of computer-based training) conducted in two periods of 6 months each, with each period including 72 training sessions (three times per week, 10 to 15 minutes per session).
- Management of metabolic and vascular risk factors based on national guidelines. This included
 regular measurements of blood pressure, weight, body mass index, hip and waist circumference,
 physical examinations, and recommendations for lifestyle management. Study physicians did not
 prescribe medication but strongly recommended participants to contact their own physician or
 clinic if needed.

Cognitive tests were repeated at the end of the 2-year study period. The intervention group had a 25% improvement in the overall cognitive score compared with the control group.

The primary outcome — mean change in cognition as measured through the comprehensive neuropsychological test battery Z score at 2 years — was 0.20 in the intervention group and 0.16 in the control group. Between-group difference in the change of neuropsychological test battery total score per year was 0.022 (P = .030).

Professor Kivipelto pointed out that the benefit was particularly noticeable in the domains of processing ability and executive function. Processing ability (the speed at which a individual can conduct different tasks using both the brain and motor function together) improved by 150% (P = .029), while executive function (the ability to organize thoughts) improved by 83% (P = .039) vs control.

Overall memory scores were not improved in the active group, but there was a benefit on complex memory tasks, she added.

The researchers report that the interventions were feasible and safe; dropout rates were low (12%) and adherence to interventions was high.

Adverse events occurred in 46 (7%) participants in the intervention group compared with 6 (1%) participants in the control group; the most common adverse event was musculoskeletal pain (5% for intervention vs 0% for control).

Professor Kivipelto believes these findings should be put into practice immediately.

"While it is only one study and there is obviously much more to do, I think we can start to give advice based on our results. I think it would be unethical not to," she said. "This trial puts dementia in the same place as coronary heart disease or diabetes. It is a chronic condition that is partly preventable. Our interventions are simple and pragmatic that we can all start following today to lower our risk of future cognitive problems."

She pointed out that the physical activity, diet, and vascular risk factor interventions are already recommended for the prevention of heart disease and diabetes, and now there is the added benefit that these interventions also have a positive effect on cognitive decline. "This is a win-win situation."

"And we can also now advise people to keep their brain active. We used a specific brain training computer-based program because it is standardized and validated as necessary for research purposes. But I would say do anything that challenges your brain: memory games, puzzles, problem-solving, time tests, learning a new skill.

"When you are a bit older it is easy to get stuck in the same routine," she added. "But we should be challenging our brain to learn new things all the time."

Long Period of Intervention

Professor Kivipelto believes the key factors in the success of this study were the multi-interventional approach and the relatively long intervention period.

"We know that multifactorial issues increase the risk of dementia so it makes sense that addressing multiple factors will reduce that risk. You can't just focus on one risk factor. Our study involved multiple interventions — we can't tell exactly which ones were more beneficial than others. We believe they all make a contribution, so we would recommend trying to do them all to some extent. But we all have different risk factors so we should each try and do what is best for ourselves — start with addressing the risk factor that is the biggest problem for you."

In addition, she points out that previous studies have looked at interventions only for relatively short durations: a few weeks or months. "We thought there would be a greater chance of showing an effect if we continued for a longer period."

The researchers are also continuing to follow the study participants to see whether further benefits are seen over time. During the next phase, the intensity of the intervention in the active group will lessen; the participants will not receive the same personal guidance but will be sent supportive messages. "We are hoping that they will carry the good practices that they have learned forwards," Professor Kivipelto said.

She noted that the current paper documents the results in a scientific way, but she and her team are planning to produce a practical model of how people can put these results into practice.

"Part of the benefit may have come from social interaction. Some of the interventions involved group physical activity or cooking sessions learning healthy new recipes. This is a double benefit in that the individual gains from the activity itself but also gains from the social interaction. It is impossible separate these two things."

She suggests that activities combining social, cognitive, and physical factors are the ideal. "Go to a group to learn a new language; join a dance class, a walking group or a book group."

In the *Lancet* paper, the researchers report that about a third of cases of Alzheimer's disease worldwide could be attributable to low education, physical inactivity, obesity, hypertension, diabetes, smoking, and depression.

"The worldwide prevalence of Alzheimer's disease could be reduced by 8.3% by 2050 with relative reductions of 10% per decade in the prevalence of each of these factors. Such small changes imply large effects, and if the beneficial effects on cognition observed in FINGER will lead to even a modest delay in onset of dementia and Alzheimer's disease, it would have a huge effect on both individual and societal levels," they conclude.

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