Higher levels of cognitive activity in childhood, middle age, and old age were associated with slower rate of cognitive decline, after controlling for disease pathology on brain autopsy, a new study has shown.

Lead author Robert S. Wilson, PhD, Rush University Medical Center, Chicago, Illinois, told Medscape Medical News that it has been fairly well established that reduced cognitive activity is associated with an increased rate of cognitive decline, but what has not been known is which comes first.

“This basic association has been out there for several years, but it has been suggested that the reduced cognitive activity could be just a sign of disease pathology. So if you're developing Alzheimer's, you will be less likely to engage in cognitive activities. But in our study, we have actually controlled for disease pathology, and we still see a strong association, so that blows that theory out of the water,” he said.

“We have proved for the first time that increased cognitive activity has an association with reduced cognitive decline independent of cognitive-related pathology. I think it is likely to be causal, but as this is an observational study, we can't make that leap definitely. But as it is virtually impossible to conduct a prospective, randomized clinical trial of a lifestyle factor such as cognitive activity, we have to look at observational studies for this information,” Dr. Wilson added.

“Our results suggest that it is a good idea to start doing some sort of cognitive activity every day if you're not already doing it.”

The study was published online July 3 in Neurology.

Important at All Stages of Life

Part of the larger Rush Memory and Aging Project, the current analysis included 294 older persons with an average age of 80 years at baseline.

On enrollment, participants rated late-life (ie, current) and early-life participation in cognitively stimulating activities such as reading, writing, visiting museums, playing challenging card games such as bridge, doing puzzles, and the like. They also took part in annual cognitive function testing until they died (mean of 5.8 years of follow-up), after which brain autopsies were performed.

After adjustment for plaques, tangles, infarcts, and Lewy bodies — pathologies signifying cognitive disease processes — as well as age at death, sex, and education, higher levels of cognitive activity in both early and later life were associated with a slower rate of cognitive decline in old age.

Table. Rate of Cognitive Decline vs Average in Highest and Lowest Percentiles of Cognitive Activity in Later and Earlier Life

<table>
<thead>
<tr>
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<th>Lowest 10% Cognitive Activity</th>
<th>Highest 10% Cognitive Activity</th>
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<tbody>
<tr>
<td>Older life</td>
<td>+48.4%</td>
<td>-32.3%</td>
</tr>
<tr>
<td>Younger life</td>
<td>+41.5%</td>
<td>-31.9%</td>
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When early- and late-life activity were modeled together, late-life cognitive activity was related to level of cognitive function, but early-life cognitive activity was not. However, both activity measures were related to change in cognition, accounting for 14% of variability in cognitive decline, after brain pathology had been accounted for.

When looking at 3 individual times in earlier life, the results showed a significant association between cognitive activities in childhood (age 6-12 years) and at age 40 years and cognitive decline in old age, but the results showed no effect for cognitive activity at young adulthood (age 18 years). However, Dr. Wilson said that he would not read too much into these differences.
"I would say that engaging in cognitive activities is important at all stages of life."

**Supports Cognitive Reserve Hypothesis**

The researchers note that these results show that more frequent cognitive activity can counterbalance the cognitive loss associated with neuropathologic conditions.

"This finding supports the cognitive reserve hypothesis and suggests that the association of cognitive activity with loss of cognition is not the result of reverse causality," they write.

"It might be that the buildup of pathology may be unstoppable — a fact of life — but it also might be possible to make people more resilient to it. It appears that life experience has some impact on an individual's vulnerability to these diseases," said Dr. Wilson.

He added that they are now trying to figure out how this is happening.

"We have been doing neuroimaging in this study, too, looking for changes in the brain that might explain our results. That will be the subject of another paper. If we can understand the neurobiology, we may be able to intervene further."

Dr. Wilson admits that the study does have limitations, for example, the fact that they relied on individuals' self reporting of activities participated in decades previously.

"Yes, this is a source of bias, but we can't really start this sort of study in childhood and follow until death. That would be completely impractical," he said.

**Keeping Dementia at Bay**

In an accompanying editorial, Prashanthi Vemuri, PhD, and Elizabeth C. Mormino, PhD, from the Mayo Clinic, Rochester, Minnesota, note that the these new findings "potentially address a question that all of us ask from time to time — can we do anything to slow down late-life cognitive decline? The results suggest yes — read more books, write more, and do activities that keep your brain busy irrespective of your age."

They note that ongoing research in the field will soon be able to educate neurologists on the cognitive outcomes that can be expected in a patient with high cognitive reserve vs low cognitive reserve and the steps that may alter the course of disease. Until then, they say the best advice is simple: "a busy mind to keep dementia at bay."

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