

Cognitive Decline in Women Starts Midlife

Pauline Anderson | January 27, 2017

For women, mental sharpness, particularly processing speed, begins to decline as early as age 50, a large, longitudinal study shows.

Unlike previous research, the new study controlled for menopausal symptoms and "practice effects," which can occur with repeat testing of the same individuals using the same tests.

The findings suggest that cognitive problems experienced by middle-aged women are a normal part of the aging process, said lead author Arun S. Karlamangla, MD, professor of medicine, Division of Geriatrics, David Geffen School of Medicine, University of California, Los Angeles.

"Don't be surprised when your 50-year-old female patients come in saying that they're forgetting where they left their keys," said Dr Karlamangla.

"This is cognitive aging, and it's very common, very usual, and it's just like aging of other organ systems. It's not a harbinger for dementia later on."

The study was [published online](#) January 3 in *PLOS ONE*.

Longitudinal Data

Most previous studies of cognitive decline have been conducted in older individuals or have used cross-sectional comparisons that are typically not very reliable, said Dr Karlamangla. "Very few studies have looked at cognitive functioning in midlife that have been longitudinal."

The new longitudinal study included 2124 women from the Study of Women's Health Across the Nation (SWAN), a community-based analysis of midlife women at seven US sites. At entry, SWAN participants were aged 42 to 52 years, had an intact uterus, at least one ovary, did not use estrogen, and had had at least one menstrual period in the previous 3 months.

After baseline visits in 1996/97, participants were followed annually. Visits included cognitive testing. Results of the third cognitive test were used as the baseline for the current analysis.

Almost half of the study sample were white, and about a quarter had a postgraduate education. The median age of participants was 54 years, and half were 2 or more years beyond the final menstrual period (FMP).

Starting the analysis a few years after menopause helped control for symptoms related to menopause, including depression, anxiety, and vasomotor and sleep disturbances, said Dr Karlamangla.

"We wanted to isolate actual aging-related declines after getting rid of these symptoms of menopausal transition," he said.

The researchers created a subsample of 1224 women for whom the date of the FMP was known. This sample was very similar to the main study group. At baseline, half of these women were at least 2 years past the FMP.

In both samples, the mean number of cognitive tests for which results were available for analysis was 3.4.



By using the third cognitive testing visit as baseline, the researchers were able to minimize the impact of practice effects, which may mask cognitive decline during the menopause transition.

"Practice effects are largest from the first testing to the second, smaller from second testing to the third testing, and minimal from then on," said Dr Karlamangla.

Age-Related Changes

The median length of follow-up was 6.5 years for both study samples. During this time, 7185 cognitive assessments were conducted.

The researchers assessed four cognitive domains, including cognitive processing speed, verbal episodic memory, and working memory.

They employed two adjusted models – an ovarian aging model that quantifies the change in cognitive test performance in relation to time from FMP, and a chronologic aging model that quantifies the change in cognitive test performance in relation to the time elapsed since the third cognitive testing (baseline).

In each model, the investigators assessed between-women and within-women longitudinal differences in cognitive domains.

In the main group, for whom the exact date of menopause was unknown, after controlling for practice effects, menopause transition, and symptoms associated with the menopause transition, women showed longitudinal declines in some cognitive performance.

The mean decline in scores reflecting cognitive speed was 0.28 points per year (95% confidence interval [95% CI], 0.20 - 0.36), or 4.9% in 10 years. The mean decline in scores for delayed verbal episodic memory was 0.02 points per year (95% CI, 0.00 - 0.03), or 2% in 10 years.

As women age, they experience cognitive decline and other changes, such as slower gait speed, reduced muscle mass, and loss of reflexes.

"We think this is essentially just age-related changes," said Dr Karlamanga. "As time passes, there is some degeneration. It's not something people need to be shocked or worried about."

Consistent with previous work, the researchers did not find longitudinal decline in immediate recall or working memory. However, "more sensitive measures of episodic and working memory might indeed show declines in midlife," they write.

Use It or Lose It

In the ovarian aging model, in which the FMP was known, the within-woman rate of decline (longitudinal aging effect) in processing speed (0.28 points per year) was essentially identical to the average between-women difference by age at time of FMP (0.31 points per year).

"This is really suggesting that it has nothing to do with the menopausal transition but simply the passing of time," said Dr Karlamangla. "It's saying that we had done a good job of removing all possible confounders."

However, in the chronologic aging model, the cross-sectional differences by chronologic age at time of testing were substantially greater than the longitudinal aging effects (0.54 points per year vs. 0.25 points per year).

"This means that something is happening, that there is some confounding in the cross-sectional comparison that we haven't controlled for," said Dr Karlamangla.

He noted that the only difference between the chronologic model and the ovarian model was that in the latter, the researchers knew the date of the FMP. This, he said, suggests that the decline in estrogen may be a missing factor that contributes to cognitive decline.

One possible way to slow cognitive decline is to keep the brain active – the "use it or lose it" approach, said Dr Karlamangla.

"Lots of studies have shown that the more cognitively active you are, the less decline you have in the domains in which you're active. So if you do a lot of crossword puzzles, you'll continue to be able to do them well, but that doesn't mean it translates to other domains."

Physical activity and controlling cardiovascular risk factors — blood pressure, blood glucose level, and cholesterol level – are other important brain savers.

A limitation of the study was that it did not include men. However, Dr Karlamangla pointed to a previous study (Whitehall II) that also looked at cognitive decline longitudinally and found that certain cognitive domains declined among both male and female middle-aged civil servants.

Terrific Study

Reached for a comment, Pauline Maki, PhD, professor of psychiatry and psychology, University of Illinois, Chicago, called the study "terrific."

"It kind of tells us what portion of our cognitive decline as we age is not due to the fact that we transition through menopause and have these symptoms."

To estimate the effect of chronologic aging independently of ovarian aging "is really important," and the authors' approach to doing that "was really key," said Dr Maki.

The study also shed light on what normal cognitive decline looks like in middle-aged women.

"We finally have this estimate – of 5% in 10 years – and that's good, because it tells us what normal is and it gives us a benchmark to understanding what we can expect."

But as with all research, the findings should be replicated, said Dr Maki. "We need to be very cautious and make sure we are using the most sensitive tests that we can."

SWAN is supported by grants from the National Institutes of Health (NIH), the National Institute on Aging, the National Institute of Nursing Research, and the NIH Office of Research on Women's Health. The authors have disclosed no relevant financial relationships.

PLoS One. Published online January 3, 2017. [Full text](#)

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Cite this article: Cognitive Decline in Women Starts Midlife. *Medscape*. Jan 27, 2017.

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