

Higher dementia risk in women with prolonged fertility

17 September 2020, by Margareta G. Kubista



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Women with a longer reproductive period had an elevated risk for dementia in old age, compared with those who were fertile for a shorter period, a population-based study from the University of Gothenburg shows.

"Our results may explain why women have a higher risk of developing dementia and Alzheimer's disease than men after age 85, and provide further support for the hypothesis that estrogen affect the risk of dementia among women," says Jenna the form of Najar, a medical doctor and doctoral student at Sahlgrenska Academy who also works at AgeCap, the Center for Aging and Health at the University of Gothenburg.

The study, now published in the journal Alzheimer's & Dementia, covers 1,364 women who were followed between 1968 and 2012 in the population studies collectively known as the "Prospective Population-based Study of Women in Gothenburg" (PPSW) and the "Gothenburg H70 Birth Cohort Studies in Sweden" (the H70 studies). The "reproduction period" spans the years between menarche (onset of menstruation) and menopause, when menstruation ceases.

Of the women studied with a shorter reproductive period (32.6 years or less), 16 percent (53 of 333 individuals) developed dementia. In the group of women who were fertile a longer period (38 years or more), 24 percent (88 of 364) developed dementia. The difference was thus 8 percentage points.

The study shows that risk for dementia and Alzheimer's disease increases successively for every additional year that the woman remains fertile. The association was strongest for those with dementia onset after age 85, and the effect was most strongly associated with age at menopause.

Endogenous estrogen over time

These results persisted after adjustment for other factors with an influence, such as educational attainment, physical activity, BMI, smoking, and cardiovascular disease. On the other hand, no association was found between dementia risk and age at menarche, number of pregnancies, duration of breastfeeding, or exogenous estrogen taken in the form of hormonal replacement therapy (HRT) or oral contraceptives.

Several studies have investigated how estrogen in the form of HRT affects dementia risk. Some studies show that dementia risk falls and others that it rises, especially in women who take estrogen late in life.

In the current study Jenna Najar has, instead, investigated the long-term association between factors related to endogenous estrogen and dementia.

"What's novel about this study, too, is that we've had access to information about several events in a woman's life that can affect her estrogen levels. Examples are pregnancies, births, and breastfeeding. Being pregnant boosts estrogen levels tremendously; then they decline once the



baby is born, and if women breastfeed the levels fall to extremely low levels. The more indicators we capture, the more reliable our results are," Najar says.

Many factors involved

Ingmar Skoog, professor of psychiatry at Sahlgrenska Academy, University of Gothenburg and head of AgeCap, led the study.

"The varying results for <u>estrogen</u> may be due to it having a protective effect early in life but being potentially harmful once the disease has begun."

At the same time, Skoog points out that the duration of women's fertile periods is one risk factor for dementia among many.

Most women whose menopause is delayed do not develop dementia because of this factor alone. However, the study may provide a clue as to why women are at higher risk than men for dementia after age 85, the most common age of onset. Alzheimer's disease, on the other hand, starts developing some 20 years before symptoms of the disorder become apparent.

"Most people affected are over 80 and female," Najar says.

"As a result of global aging, the number of people affected by dementia will increase. To be able to implement preventive strategies, we need to identify people with an elevated risk of dementia."

More information: Jenna Najar et al. Reproductive period and dementia: A 44?year longitudinal population study of Swedish women, *Alzheimer's & Dementia* (2020). <u>DOI:</u> 10.1002/alz.12118

Provided by University of Gothenburg

APA citation: Higher dementia risk in women with prolonged fertility (2020, September 17) retrieved 27 August 2022 from

https://medicalxpress.com/news/2020-09-higher-dementia-women-prolonged-fertility.html



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