'Stressors' in middle age linked to cognitive decline in older women

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A new analysis of data on more than 900 Baltimore adults by Johns Hopkins Medicine researchers has linked stressful life experiences among middle-aged women—but not men—to greater memory decline

in later life.

The researchers say their findings add to evidence that stress hormones play an uneven gender role in brain health, and align with well-documented higher rates of Alzheimer's disease in women than men.

Although the researchers caution their study was designed to show associations among phenomena, and not determine cause and effect, they say that if future studies demonstrate that stress response does factor into the cause of dementia, then strategies designed to combat or moderate the body's chemical reactions to stress may prevent or delay onset of cognitive decline.

The findings are published in the July issue of the *International Journal of Geriatric Psychiatry*.

According to the Alzheimer's Association, 1 in 6 women over age 60 will get Alzheimer's disease, compared with 1 in 11 men. There currently are no proven treatments that prevent or halt progression of the disease.

"We can't get rid of stressors, but we might adjust the way we respond to stress, and have a real effect on brain function as we age," says Cynthia Munro, Ph.D., associate professor of psychiatry and behavioral sciences at the Johns Hopkins University School of Medicine. "And although our study did not show the same association for men, it sheds further light on the effects of stress response on the brain with potential application to both men and women," she adds.

Munro says prior research by other investigators shows that the effect of age on the stress response is three times greater in women than in men. Separately, other research has shown that stressful life experiences can result in temporary memory and cognitive problems.

To further explore whether stressful life experiences can be linked to developing long-term memory problems in women especially, Munro and her team used data collected on 909 Baltimore residents for the National Institute of Mental Health Epidemiologic Catchment Area study. That study recruited participants from 1981 to 1983 from five cities in the U.S. to determine the prevalence of psychiatric disorders.

Some 63% of the participants were women and 60% were white. Participants were an average age of 47 during their mid-life check-in in the 90s.

After enrollment, participants returned to trial sites for interviews and checkups three additional times: once in 1982, once between 1993 and 1996, and once between 2003 and 2004.

During the third visit, participants were asked if they experienced a traumatic event in the past year such as combat, rape, a mugging, some other physical attack, watching someone else attacked or killed, receiving a threat, or living through a natural disaster. Some 22% of men and 23% of women reported at least one traumatic event within the past year before their visit.

They also were asked about stressful life experiences such as a marriage, divorce, death of a loved one, job loss, severe injury or sickness, a child moving out, retirement, or birth of a child. About 47% of men and 50% of women reported having at least one stressful life experience in the year before their visit.

At the third and fourth visits, the researchers tested the participants using a standardized learning and memory test developed by Iowa researchers. The test included having participants recall 20 words spoken aloud by the testers immediately after they heard them, and again 20 minutes later.

At the third visit, participants could recall on average eight words immediately and six words later. Participants also had to identify the words spoken to them among a written list of 40 words. During the third visit, participants correctly identified on average 15 words. By the fourth visit, participants recalled an average of seven words immediately, six words after a delay, and correctly recognized almost 14 words.

The researchers measured any decreases in performance on the tests between the third and fourth visits, and then compared those decreases with participants' reports of stressful life experiences or traumatic events to see if there was an association.

Munro's team found that having a greater number of stressful life experiences over the last year in midlife in women was linked to a greater decline in recalling words later and recognizing those words. Women who experienced no stressful life experiences within the past year at the third visit were able to remember on average 0.5 fewer words when given the same memory test at the fourth visit. Women with one or more stressful life experiences, however, recalled on average one fewer word at the fourth visit than they had at the third visit. The ability to recognize words declined by an average of 1.7 words for women with at least one stressor at the third visit compared with a 1.2-word decline for women without stressors at midlife.

They didn't see the same trend in women who had traumatic events. Munro says that this finding suggests that ongoing stress, such as that experienced during a divorce, may have more of a negative impact on brain functioning than distinct traumatic events. This makes sense, Munro believes, because what we call "chronic stress" can impair the body's ability to respond to stress in a healthy manner.

The researchers did not see an association in men between a drop in word recall or recognition and experiencing either stressful life

experiences or traumatic events in midlife.

Stress much earlier in life also wasn't predictive of cognitive decline later in either men or women.

"A normal stress response causes a temporary increase in stress hormones like cortisol, and when it's over, levels return to baseline and you recover. But with repeated stress, or with enhanced sensitivity to stress, your body mounts an increased and sustained hormone response that takes longer to recover," says Munro. "We know if stress hormone levels increase and remain high, this isn't good for the brain's hippocampus—the seat of memory."

The researchers say that stress reduction hasn't gotten a whole lot of attention compared with other factors that may contribute to dementia or Alzheimer's, and that it might be worth exploring stress management techniques as a way to delay or prevent disease.

Munro adds that there are medications being developed to combat how our brains handle stress, and that these may be used in conjunction with other behavioral stress coping techniques to reduce the impact of stress on aging minds.

Alzheimer's Disease International reports that 44 million people worldwide live with Alzheimer's disease.

More information: Cynthia A. Munro et al. Stressful life events and cognitive decline: Sex differences in the Baltimore Epidemiologic Catchment Area Follow-Up Study, *International Journal of Geriatric Psychiatry* (2019). DOI: 10.1002/gps.5102