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Twins Comparison Suggests Genetic Risk for Dementia

On average, twins of people who have been diagnosed with dementia score lower on cognitive tests than do the twins of people without dementia, new research has found. The study, which included more than 100 Swedish twins age 65 and older, also found that, on average, identical twins of people with dementia have poorer cognitive skills than do fraternal (non-identical) twins of people with dementia.

The researchers suggest that these differences in thinking skills reflect a genetic risk for dementia. However, they emphasize that cognitive changes and elevated genetic risk do not always predict that twins or siblings of people with dementia will eventually develop dementia themselves.

The research, reported in the December 2005 issue of the *Journal of Geriatric Psychiatry and Neurology*, was led by Margaret Gatz, Ph.D., of the University of Southern California and the Karolinska Institute in Sweden. The study was funded by the National Institute on Aging (NIA), a component of the National Institutes of Health, U.S. Department of Health and Human Services, and a Zenith Award from the Alzheimer's Association. The University of Southern California Alzheimer's Disease Center is one of more than 30 Alzheimer's Disease Centers nationwide supported by the NIA.

"This research is intriguing because it associates genetic risk for dementia with twins' cognitive deficits, even in the absence of dementia," says Neil Buckholtz, Ph.D., chief of the Dementias of Aging Branch of NIA's Neuroscience and Neuropsychology of Aging Program. "The differences in cognitive deficits between identical and fraternal twins are also important, suggesting that the twins who were more similar genetically had the greater risk."

The study included 112 members of the Swedish Twin Registry who were at least 65 years old in 1998. The registry, established in 1961, includes all twins born in Sweden. Of the study participants, 23 were identical twins and 62 were fraternal twins whose co-twins had dementia but who did not have dementia themselves. A comparison group included 27 non-demented twins whose co-twins did not have dementia. The comparison group was similar to the other participants in terms of age, gender, and level of education.

All of the study participants took a series of neuropsychological tests that assessed their attention, memory, verbal recall, verbal fluency, ability to copy simple drawings, comprehension, and other cognitive skills. The test results for twins of people with dementia were weighed against those of the comparison group.

Twins whose twin siblings had dementia had significantly lower overall scores on the cognitive-skills tests than those of the comparison group. The twins of demented co-twins and the comparison group differed most on the tests of memory and "executive functioning," such as verbal fluency and remembering patterns that include symbols and numbers. Gatz and her colleagues say this finding suggests that the twins of people with dementia are at higher risk for developing dementia in the future, although they had already lived without dementia for an average of nearly 8 years beyond their co-twins' dementia onset.

"Identical twins of dementia cases had a strikingly poorer cognitive performance profile," Gatz notes. "It could be that these twins are more likely to progress to dementia, but we don't know that. We might be seeing a difference in performance that could already have persisted for a long time without getting worse or it could be a signal that the currently non-demented twin is at greater risk for progressing."

Gatz and her co-authors point out, however, that the study included only a "modest number" of twins. They also did not gather long-term data that would show changes or stability in cognitive performance over time or whether participants would develop dementia in the future.

"While there may be a genetic risk for dementia, it is important to recognize that not everyone with a genetic risk factor will develop dementia," Buckholtz comments. "More research is needed to help us understand who will and will not develop dementia, even if they are at risk. Beyond genetics, environmental and life style factors also play a role."

The Gatz article is one of several in the December 2005 *Journal of Geriatric Psychiatry and Neurology* focusing on children of Alzheimer's parents (<http://jgpn.sagepub.com>). The papers, including a number reporting on studies funded by the NIA, are based on presentations at a workshop held in conjunction with the American Association for Geriatric Psychiatry Annual Conference in March 2005.

The article "Performance on Neurocognitive Tests by Co-twins to Dementia Cases Compared to Normal Control Twins" can be found on the *Journal of Geriatric Psychiatry and Neurology* web site at <http://jgpn.sagepub.com>. Media may receive a free copy of the article by contacting Judy Erickson of SAGE Publications at media.inquiries@sagepub.com.

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