

Cognitive Impairment Is More Common in Men

BY MARY JO M. DALES
Editorial Director

CHICAGO — Men have more mild cognitive impairment than women do, yet there is no gender difference in the prevalence of dementia, according to the results of one of the first studies to measure mild cognitive impairment prospectively in a population-based setting.

The findings, reported by Dr. Rosebud O. Roberts at the annual meeting of the American Academy of Neurology, suggest that dementia progresses either faster in women or slower in men.

For the ongoing study, called the Mayo Clinic Study of Aging, mild cognitive impairment (MCI) was evaluated in a population sample from Olmstead County, Minn. The 70- to 79-year-old group included 490 women and 596 men. The 80- to 89-year-old group included 512 women and 452 men. For both age groups, there were 1,002 women and 1,048 men.

A nurse, physician, or neuropsychologist evaluated each individual using face-to-face measures. Subjects were evaluated in four domains—memory, executive function, language, and visual/spatial skills. MCI was defined as impairment in one or more domains or an overall mild decline across cognitive abilities that is greater than would be expected for an individual's age or education but is insufficient to interfere with social and occupational functioning.

Based on these evaluations, 74% of the group had normal cognition, 16% had MCI, and 10% had dementia. Of the nearly 2,000 study participants without dementia, 51% were male, 47% had less than 12 years of education, 52% were 80-89 years old, and 61% were married.

Subjects were studied prospectively beginning in October 2004 and follow-ups will continue through 2010. This differs from most other studies of MCI, which had the limitations of applying MCI criteria to previously collected data or were conducted in study samples, such as those attending memory clinics, who might not be representative of the general population.

In men, the prevalence of mild cognitive impairment steadily increased from about 10% at age 70 and suddenly spiked after age 85 to affect 40%. In women, the rate rose more slowly and the prevalence was far lower, peaking at less than 20% at age 85.

Even after the data were corrected for age plus education, marital status, and disease burden, women had less cognitive impairment but comparable rates of dementia, compared with men, Dr. Roberts said.

"We found the overall prevalence of mild cognitive impairment is quite high—over 16%," said Dr. Roberts. "But perhaps the more surprising finding is the higher prevalence of MCI in men with the comparable prevalence of dementia for men and women." Several possible explanations for this disparity include a prevalence of risk factors in middle age vs. later life, the progression rate from MCI to dementia, and death among persons with MCI.

Dr. Roberts said that she and her coinvestigators are in the process of adding another 1,000 participants to continue the follow-up study. The study was supported by the National Institutes of Health and the Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program. ■

Risk Factors for Progression From MCI to Dementia Vary by Gender

BY HEIDI SPLETE
Senior Writer

Risk factors for mild cognitive impairment and progression from mild cognitive impairment to dementia are not the same for men and women.

Identifying the risk factors that cause mild cognitive impairment (MCI) to progress to dementia can help determine which patients might benefit from treatment, Sylvaine Artero of the Institut National de la Santé et de la Recherche Médicale (INSERM) U888, Montpellier (France), and colleagues reported. Previous studies have addressed the risk factors for progression from MCI to Alzheimer's disease and dementia, but most of those have not involved a general population and have not addressed gender-specific factors.

To determine the gender-specific factors that predict progression of MCI to dementia, the investigators recruited 6,892 community-dwelling adults aged 65 years and older and followed them for 4 years (average age 74 years; half were women). The study was based on a large multicenter prospective study on brain aging sponsored in part by Sanofi-Synthelabo.

A total of 2,882 participants (42%) met the criteria for MCI at baseline. Over the next 4 years, 189 were diagnosed with dementia, 1,626 maintained MCI, and 1,067 returned to a normal level of function (*J. Neurol. Neurosurg. Psychiatry* 2008 May 1 [doi:10.1136/jnnp.2007.136903]).

Overall, 8% of men with MCI developed dementia, vs. 6% of the women, but women were significantly less likely than men to return to normal cognitive function (36% vs. 39%) and significantly more likely to maintain a diagnosed cognitive disorder over the 4 years (58% vs. 53%).

In a multivariate analysis, older age significantly predicted progression to dementia in men and women.

In men, progression from MCI to dementia was more than three times as likely if they had the APOEε4 allele, and more than twice as likely in those with a history of stroke, a low level of education, or difficulty with daily activities as measured by the Instrumental Activities of Daily Living scale (IADL). In women, progression from MCI to dementia was more than three times as likely if they had IADL deficits and more than twice as likely if they had the APOEε4 allele, a low level of education, or subclinical depression. And the odds of progressing to dementia were almost twice as high in women who took anticholinergic inhibitors (odds ratio 1.8).

Predictors of progression from MCI to dementia in both men and women in a less rigorous, univariate analysis included the APOEε4 genotype, hypertension, diabetes, age, a low level of education, low intelligence, subclinical depression, stroke, social isolation, and difficulty with at least IADL.

"MCI cases in the general population can be differentiated by a much larger number of sociodemographic and clinical factors than previously observed," the investigators wrote. "These findings support the notion that MCI is a common end point to multiple etiological pathways which are not the same for men and women."

The study was limited by a lack of analysis of MCI subtypes and by a short follow-up, which may account for the relatively low dementia rate, the investigators said. However, clinicians may be able to use the diverse risk factor data to develop gender-specific clinical interventions, they noted.

The investigators said they had no financial conflicts to disclose. ■

More NIH, NSF Funding for Alzheimer's Research Urged

BY MICHELE G. SULLIVAN
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WASHINGTON — A firm federal commitment to increased biomedical-research funding is the best defense against the wave of Alzheimer's disease predicted to hit over the next 40 years, according to Newt Gingrich, former Speaker of the U.S. House of Representatives.

Addressing a hearing called by the Senate Special Committee on Aging, Mr. Gingrich urged annual overall funding increases of "at least" 7% after inflation for the National Institutes of Health.

He urged similarly broad financial support for the National Science Foundation (NSF), which sponsors research in math, physics, and chemistry that, Mr. Gingrich said, provides the foundation for both the drugs and imaging systems necessary to fight Alzheimer's. "The biggest mistake I made as Speaker was not tripling the National Science Foundation budget and, as a result, we are not getting the investments we need [in these areas]," he said. "Most of the research that underlies the imaging technology we have today, which allows us to have real-time images of a living brain, was developed at the NSF."

Mr. Gingrich addressed the Senate committee in his role as the founder and a member of the Alzheimer's Study Group, a bipartisan think tank urging a national strategic plan to deal with the projected surge in Alzheimer's dis-

ease. Studies indicate worldwide prevalence could quadruple by 2050, reaching 107 million people. In the United States, prevalence could rise from the current 4.5 million to more than 13 million during the same period. Such an increase would devastate the country's health care system and seriously harm the economy, Mr. Gingrich told the committee.

By 2050, federal government spending on care for Alzheimer's patients could dwarf the current annual bill of \$150 million. "Federal spending on Alzheimer's [care] will increase to more than \$1 trillion per year by 2050, in today's dollars—that is more than one-tenth of America's current economy."

Retired U.S. Supreme Court Justice Sandra Day O'Connor, whose husband, John O'Connor, suffers from advanced Alzheimer's, also urged the committee to support research. While a cure would be the "Holy Grail," she said, even a drug that could delay the onset of Alzheimer's



Retired Supreme Court Justice O'Connor and former Speaker of the House Gingrich testified at the Senate hearing.

would reap huge savings.

The government could also step up the pace of research with legislation encouraging private investment, Mr. Gingrich said. "I would strongly urge you to amend the Orphan Drug Act to include all brain research as orphan drug activity."

The downside of following the orphan-drug path would be longer-than-normal patents on any drugs developed, Mr. Gingrich said. But the benefit to patients would be worth the increase in costs resulting from drugs being slow to go generic, he asserted.

Sen. Herb Kohl (D-Wis.), committee chairman, called the hearing to support a bill that would double the funding specifically for Alzheimer's research at the National Institutes of Health to \$1.3 billion. The Alzheimer's Breakthrough Act was introduced last year. It passed through the Senate Committee on Health, Education, Labor, and Pensions last July and made the Senate Legislative Calendar in August but hasn't received further action since then. ■

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