Cognitive function in the oldest old: women perform better than men

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Abstract

***Objective*—Limited formal education is associated with poor cognitive function. This could explain sex differences in cognitive function in the oldest old. Whether limited formal education explains differences in cognitive function between elderly women and men was explored.**

***Methods*—The Leiden 85-plus Study is a population based study investigating all 85 year old inhabitants of Leiden with an overall response rate of 87%. A sample of 599 participants were visited at their place of residence. The mini mental state examination was completed by all participants. Cognitive speed and memory were determined with four neuropsychological tests in participants with a mini mental state examination score higher than 18 points.**

***Results*—The proportion of women with limited formal education was significantly higher than that of men (70% *v* 53%, p=0.001), but women had better scores for cognitive speed and memory than men (p<0.05). After adjustment for differences in limited formal education and the presence of depressive symptoms, the odds ratio for women to have a higher cognitive speed than men was 1.7 (95% CI; 1.0 to 2.6), and for them to have a better memory the odds ratio was 1.8 (95%CI; 1.2 to 2.7).**

***Conclusion*—Women have a better cognitive function than men, despite their lower level of formal education. Limited formal education alone, therefore, cannot explain the differences in cognitive function in women and men. These findings support the alternative hypothesis that biological differences, such as atherosclerosis, between women and men account for the sex differences in cognitive decline.**

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Keywords: elderly people; cognition; sex; education; depression

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The impressive body of knowledge on cognitive function that has been accumulated leaves many questions on the effect of sex on cognitive function unresolved. One explanation for a possible effect of sex on cognitive function could be that more elderly women have received a limited formal education than men. A limited formal education is associated with less cognitive function.[1 2] The "brain reserve capacity theory" argues that subjects with less cognitive function—that is, less brain reserve capacity—are more likely to surpass the threshold beyond which cognitive decline becomes clinically apparent.[1 2] An alternative explanation could be that different biological mechanisms cause differences on cognitive function in elderly men and women.

By measuring cognitive speed and memory, cognitive function in elderly persons can reliably be assessed. Cognitive speed, consisting of attention span and processing speed, is the most sensitive measure because age related cognitive decline first manifests itself by a decline in attention span and processing speed.[3 4] In old persons memory remains relatively intact until late stages of cognitive decline, whereas cognitive speed declines more rapidly.[4]

We measured cognitive speed and memory in a population based sample of women and men aged 85 years. Our aim was to explore whether there is an effect of sex on cognitive function and whether differences in formal education explain differences between elderly women and men. If this hypothesis is true we would expect women to have a poorer cognitive function than men because of the limited formal education they have received.

Methods

SUBJECTS AND PROCEDURES

The Leiden 85-plus Study is a population based study of inhabitants of Leiden, The Netherlands. Since 1997, all members of the 1912 to 1914 birth cohort were enrolled in the study in the month of their 85th birthday. Those who were eligible for the study were informed about the study by mail. Then they were contacted by telephone, or were visited at home to ask for informed consent. When the subjects were severely cognitively impaired, informed consent was obtained from a guardian. The study was approved by the medical ethics committee of the Leiden University Medical Centre.

Sociodemographic characteristics and living arrangements were obtained for all subjects eligible to participate in the study. The mini mental state examination[5] was administered to screen for cognitive impairment. Subjects were classified as severely cognitive impaired defined by a mini mental state examination score of 18 points or lower.[6] Education was divided into two levels: a lower education level, including participants without schooling or with primary school education only (with a maximum of 6 years of schooling), and those with a higher education level (equivalent to more than 6 years of schooling). Because depression could lead to cognitive impairment, we used the geri-

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atric depression scale (GDS-15)[7] to adjust for the effect of depressive symptoms on cognitive function. A score of four points or above on the geriatric depression scale indicates that the presence of depression is likely.

To further investigate the various domains of cognitive function we used four neuropsychological tests that are widely used in observational studies in and outside the Netherlands. These tests proved to have clinical relevance.[8] Cognitive speed was measured with two neuropsychological tests, the abbreviated 40 item version Stroop test (attention)[9 10] and the letter digit coding test (processing speed).[11] For data analysis we made use of the third Stroop card showing colour words printed in ink of different colours. Memory was measured with the 12 word learning test,[12 13] testing immediate and delayed recall. All neuropsychological tests were given by the same trained research nurse, who gave her impression whether the tests went well and whether the test scores could be trusted to reflect the subject's ability to perform the test at that time.

The geriatric depression scale and the neuropsychological tests were not administered in subjects with a mini mental state examination score of 18 points or lower, because in these subjects neither depressive symptoms, nor cognitive speed or memory can be accurately assessed.[6 11]

DATA ANALYSIS

Data are presented as medians and interquartile ranges. Groups were compared with non-parametric tests (χ^2 and Mann-Whitney test) that do not assume an underlying distribution of the data, as the test scores on the mini mental state examination and the delayed word learning test were skewed to the left. Confidence intervals for differences between medians were calculated assuming that the data in groups were both skewed in a similar direction.[14] Univariate odds ratios and 95% confidence intervals (95% CIs) were obtained by cross tabulation.

We compared elderly persons with a good cognitive speed with those who had a poor cognitive speed, and we compared elderly persons with a good memory with those who had a poor memory, using dichotomous variables, good and poor cognitive speed, and good and poor memory. Good cognitive speed was defined as a score below the median on the Stroop test and a score above the median on the letter digit coding test. Poor cognitive speed was defined as a score above the median on the Stroop or a score below the median on the letter digit test. Good memory was defined as a score above the median on both the immediate recall test and the delayed recall test. Poor memory was defined as a score below the median on either the immediate recall test or the delayed recall test. Subjects who for cognitive reasons were unable to perform the test were classified as having a poor test performance. Subjects who for other reasons were unable to complete the tests were excluded from the analyses.

Multivariate odds ratios were obtained by logistic regression analysis, adjusting for unequal distributions of the number of depressive symptoms and level of education, between men and women. In all analyses speed and memory, as dichotomised variables, were the dependent variables. Sex, level of education, and the presence of depressive symptoms were the independent variables.

Results

Between September first 1997 and September first 1999, 705 inhabitants of Leiden reached the age of 85 years and were eligible to participate in the study. Fourteen inhabitants died before they could be enrolled. The response rate was 87% and a total of 599 subjects (397 women, 202 men) participated. There were no significant differences between the 92 non-respondents and the 599 respondents for various demographic characteristics apart from a slightly skewed sex ratio (72 women refused whereas 61 was expected, p=0.02)

Table 1 shows the demographic and clinical characteristics of the participants. Women were significantly more institutionalised (p=0.01), more often widowed (p=0.001), and had a lower formal education level than men (p=0.001). The median score on the mini mental state examination was 26 points and similar in women (interquartile range 21 to 28) and men (interquartile range 23 to 28). Significantly more women than men (20% *v* 9%) had severe cognitive impairment, defined as a mini mental state examination score of 18 points or lower. The distribution of depressive symptoms was similar in women and men.

Three hundred and sixteen women and 184 men had a mini mental state examination higher than 18 points or more and were further characterised for cognitive function using the neuro psychological tests. In 27 women (8.5%) and 27 men (14.7%) the neuropsychological tests to measure cognitive speed and memory

Table 1 Demographic and clinical characteristics of participants in the Leiden 85-plus Study

Characteristic	*Women (%) (n=397)*	*Men (%) (n=202)*
Living arrangements*		
Independent	312 (79)	177 (88)
Institutionalised†	85 (21)	25 (12)
Marital status*		
Married	70 (18)	128 (63)
Unmarried	28 (7)	10 (5)
Widowed	283 (71)	62 (31)
Divorced	16 (4)	2 (1)
Education*		
Low level	279 (70)	107 (53)
High level	114 (29)	93 (46)
Missing	4 (1)	2 (1)
MMSE score*		
19–30 points	316 (80)	184 (91)
0–18 points	81 (20)	18 (9)
Depressive symptoms		
GDS≤3 points	241 (61)	140 (69)
GDS≥4 points	75 (19)	44 (22)
GDS not administered‡	81 (20)	18 (9)

MMSE=mini mental state examination; GDS=geriatric depression scale.
*χ^2 p<0.05.
†Institutionalised were those living in a home for elderly people or those living in a nursing home.
‡GDS not administered in subjects with an MMSE score of 18 or lower.

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Table 2 Effect of various determinants on cognitive speed

	Stroop (s)	*Letter digit test (No of letters)*
Sex:		
Women (n=289)	71.8 (58.2-95.5)	16.0 (12.5-21.0)
Men (n=157)	79.1 (64.8-104.2)	16.0 (12.0-22.0)
Median difference (95% CI)	−7.3 (−11.7 to −1.3)*	0.0 (−2.0 to 1.0)
Education:		
High (n=178)	65.3 (54.9-86.4)	19.5 (15.0-25.0)
Low (n=268)	81.7 (62.7-104.0)	14.0 (10.0-18.0)
Median difference (95% CI)	−16.4 (−17.1 to −7.3)*	5.5 (5.0 to 7.0)*
Depression:		
No (n=349)	72.3 (57.7-92.8)	17.0 (13.0-22.0)
Yes (n=97)	85.9 (65.1-115.8)	14.0 (9.0-18.0)
Median difference (95% CI)	−13.6 (−20.8 to −7.3)*	3.0 (2.0 to 5.0)*

Values are median scores and interquartile ranges or 95% CI.
*p<0.05.

Table 3 Effect of various determinants on memory

	Immediate word learning test (No of words)	*Delayed word learning test (No of words)*
Sex:		
Women (n=289)	26.0 (21.0-29.0)	9.0 (8.0-11.0)
Men (n=157)	23.0 (20.0-27.0)	9.0 (7.0-10.0)
Median difference (95% CI)	3.0 (1.0 to 3.0)*	0.0 (0.0 to 1.0)
Education:		
High (n=178)	25.0 (21.0-29.0)	9.0 (8.0-11.0)
Low (n=268)	25.0 (21.0-28.0)	9.0 (7.0-11.0)
Median difference (95% CI)	0.0 (0.0 to 2.0)	0.0 (0.0 to 1.0)
Depression		
No (n=349)	26.0 (22.0-29.0)	9.0 (8.0-11.0)
Yes (n=97)	22.0 (18.0-26.5)	8.0 (6.0-10.0)
Median difference (95% CI)	4.0 (1.0 to 4.0)*	1.0 (1.0 to 2.0)*

Values are median scores and interquartile ranges or 95% CI.
*p<0.05.

could not be completed. 18 subjects did not complete the tests because of visual impairment, 20 subjects refused to execute the neuropsychological tests, and 16 subjects did not understand the instructions as given by the research nurse, due to cognitive impairment. There were no demographic or clinical differences between the participants who were able and those who were unable to complete the neuropsychological tests (data not shown).

Table 2 presents the data on cognitive speed for women and men. Women completed the Stroop test more rapidly than men (p=0.01). The median test score on the letter digit test was similar for women and men. Table 3 presents data on memory. Women remembered more words than men on the immediate word learning test (p=0.001). Women had the same test score as men on the delayed word learning test. Participants with a higher level of education had significantly higher scores on the tests measuring cognitive speed (p<0.001). Participants without depressive symptoms scored significantly better on all tests (p<0.001). The effects of formal education and depression on cognitive function were similar in women and men (data not shown).

To further explore the sex differences in cognitive function we categorised participants as having a good or poor cognitive function based on test scores dichotomised around the median. Good cognitive speed was found in 33% of the women and 28% of the men. Forty one per cent of the women and 29% of the men had a good memory. Table 4 shows the crude and adjusted odds ratios for good cognitive speed and memory in men versus women. Odds ratios were obtained in participants with a mini mental state examination score higher than 18 points. The differences between women and men became more apparent and statistically significant after adjustment for unequal distributions of depressive symptoms and formal education. Marital status could not explain the differences between the sexes. Similar odds ratios were obtained when the sample was further restricted to participants with mini mental state examination scores between 28 and 30 points (data not shown). When we evaluated all participants with a mini mental examination score between 0 and 30 points, attributing a poor cognitive speed and memory to those who for cognitive reasons were unable to perform the neuropsychological tests, we obtained similar crude odds ratios.

Table 4 Odds ratios for good cognitive speed and good memory in women versus men

Test	*Crude odds ratio (95% CI)*	*Adjusted odds ratio* (95% CI)*
Cognitive speed	1.3 (0.8 to 1.9)	1.7 (1.0 to 2.6)
Memory	1.6 (1.1 to 2.5)	1.8 (1.2 to 2.7)

Odds ratios obtained in participants with a mini mental state examination score>18 points.
*Adjusted for the level of education and the presence of depressive symptoms.

Discussion

The aim of the present study was to explore whether there is an effect of sex on cognitive function and whether a limited formal education explains differences in cognitive function between elderly women and men. We found that women have a better cognitive function than men, despite their lower level of formal education. This effect is far greater than the sex differences that are generally reported at an earlier age.[15] We therefore conclude that limited formal education alone cannot explain the differences in cognitive function in men and women. These findings support our alternative hypothesis that biological differences between men and women could account for the sex differences in cognitive impairment.

Previous studies have described associations between limited formal education, poor cognitive function, and susceptibility to develop dementia.[2] Within the Leiden 85-plus Study, participants with low levels of education also had poorer test scores on the neuropsychological tests. We have earlier reported that elderly persons with poor cognitive function are characterised by an accelerated decline in cognitive function.[16] In line with the "brain reserve theory" these persons are thus more likely to develop dementia. However, the brain reserve theory cannot explain the sex differences in cognitive decline as elderly women have better preserved cognitive function than men.

The neuropsychological tests that were used in the present study could not be administered to participants with severe cognitive impairment. To ascertain that our findings also hold when the population is studied as a whole, we attributed a poor cognitive speed or memory to those who for cognitive reasons were unable to perform the neuropsychological tests. The results were not affected. We also studied the

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subgroup of participants who were clinically free from cognitive impairment—that is, mini mental state examination scores from 28 to 30 points. We again found that women had a better cognitive speed and memory.

It is tempting to speculate that biological mechanisms, such as atherosclerosis, could account for the sex differences in cognitive decline. Cerebrovascular disease, a late stage of systemic atherosclerosis, is highly prevalent among elderly persons. Several studies have suggested that atherosclerosis causing subclinical, ischaemic events in the brain contribute to cognitive decline at old age.[17–20] In this respect it is noteworthy that the accelerated increase in cardiovascular disease at old age starts some 10 years later in women than in men. This delay is reflected by the difference in life expectancy between men and women.[21] The greater life expectancy for women indicates that in comparison with men, elderly women of the same age are relatively free from cardiovascular disease.[22] We hypothesise that the relative absence of cardiovascular disease may explain the better cognitive functioning of old women.

Several population based studies have shown that the prevalence of dementia in women older than 80 is higher than that in men.[23–25] The higher prevalence of dementia can be explained by the finding that the mortality in patients with dementia is lower in women than that in men.[26] The lower mortality in women who have dementia, explains why we found a higher proportion of women with severe cognitive impairment among the oldest.

In conclusion, our study shows that despite a lower level of education women have better cognitive function than men. Differences in the level of education in women and men cannot explain the differences in cognitive function. The better cognitive function in women is more likely to be explained by a biological mechanism, such as atherosclerosis.

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