

Brief Report**Prevalence of Memory Loss Complaints and Other Symptoms Associated with the Menopause Transition: A Community Survey****Gayatri Devi, MD¹⁻³; Katherine Hahn¹; Stephen Massimi, BA¹; and Emiliya Zhivotovskaya¹***¹New York Memory and Healthy Aging Services, New York, New York; ²Departments of Medicine (Neurology) and Psychiatry, Lenox Hill Hospital, New York, New York; and ³Departments of Neurology and Psychiatry, New York University School of Medicine, New York, New York***ABSTRACT**

Background: Complaints of memory loss are increasingly noted as part of the constellation of symptoms experienced in the menopause transition. Studies evaluating such complaints in this population have yielded varying results.

Objective: The aim of this study was to determine if complaints of memory loss are a component of the menopause transition and a part of the menopausal symptom complex in a population of women not selected for menopausal symptoms.

Methods: Faculty members of a Long Island, New York, school district were asked to participate in a survey of menopausal symptoms. Demographic data were analyzed using χ^2 statistics. The presence or absence of memory complaints, hot flashes/night sweats, vaginal dryness, depression, reduced libido, and incontinence were analyzed as dichotomous variables in a logistic regression analysis after adjusting for demographic differences.

Results: Seventy-two percent (375/521) of the faculty members in the school district were eligible; of these, 217 (58%) completed the survey. After excluding pregnant women, those with hysterectomies or other nonmenopausal causes of amenorrhea, and those aged <30 or >60 years, 151 women were included in the analysis. Of these, 103 (68%) were experiencing natural menopause or perimenopause and 48 (32%) had no changes in menstrual cycle (the comparison group). The menopausal women were significantly older than the women in the comparison group (mean [SD] 51.2 [5.0] years vs 39.6 [7.2] years; $P < 0.001$), and they were more likely to be white than the women in the comparison group ($P < 0.001$). Menopausal women were several-fold more likely to complain of memory loss (odds ratio [OR], 3.2; 95% CI, 1.2–8.8; $P < 0.02$), hot flashes/night sweats (OR, 4.3; 95% CI, 1.4–13.3; $P < 0.01$), and reduced libido (OR, 4.5; 95% CI, 1.3–15.7; $P < 0.02$) than were women in the comparison group, after adjusting for differences in age and race. There were no significant differences in the prevalence of depression, vaginal dryness, or incontinence.

Conclusions: In our exploratory survey, complaints of memory loss were a part of the symptom complex of the menopause transition, as were hot flashes and reduced libido. Longitudinal follow-up of women with these symptoms may be helpful in understanding the menopause transition in women. (*Gen Med.* 2005;2:255–264) Copyright © 2005 Excerpta Medica, Inc.

Key words: memory complaints, night sweats, menopause, symptoms, prevalence.

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INTRODUCTION

Complaints of memory loss and cognitive complaints are increasingly noted as components of the perimenopausal and menopausal symptom complex and the menopause transition. However, data from research in this area are variable. Some studies found prevalence rates for complaints of memory loss to be as high as 70%, whereas others observed no such increase.^{1,2} Inherent difficulties in methodology may be responsible for these differing results. Variables such as the definition of perimenopause and menopause, the characteristics of the control or comparison group, surgical versus natural menopause, community- versus clinic-based populations, and the methods used to collect and analyze the cognitive data all varied from study to study. The roles of stress and depression in the etiology of memory loss have also been examined.³

Several studies used surveys of self-reported complaints among perimenopausal and menopausal women in varied populations. In one study, 477 pre-, peri-, and postmenopausal women enrolled in the Manitoba Project on Women were interviewed biannually for 3 years.⁴ Complaints of hot flashes increased from 39% to 46% and complaints of forgetfulness increased from 31% to 35% during this period. However, because symptoms were grouped into clusters, the statistical significance of individual symptoms was not analyzed. In a study of Taiwanese women culled from a centralized government database, the prevalence of memory complaints was found to be as high as 55% among menopausal women.⁵ Mitchell and Woods⁶ observed that among 230 women with a mean (SD) age of 46.7 (4.4) years, 62% complained of a change in memory. These rates rose to 70% among 88 women (mean age 52.6 [4.5] years) surveyed in a menopause clinic in Italy.¹

Interestingly, a 1997 Gallup poll of 750 telephone interviews of randomly selected women aged 45 to 60 years found that although women (up to 63%) were willing to attribute symptoms of depression and irritability to the menopause transition, only 33% believed that memory complaints are linked to menopause.⁷ How well memory complaints translate into objective memory

impairment has not been studied in this population. However, several studies in other groups, including persons with depression, mild cognitive impairment, and dementia, have shown a correlation between perceived memory loss and objective evidence of cognitive loss and, in some cases, eventual progression to dementia.⁸⁻¹⁰

In a pilot survey of 60 perimenopausal and menopausal women, we found a 78% prevalence of self-reported memory complaints.¹¹ As a follow-up to the pilot survey, our larger study was intended to investigate the prevalence of menopausal symptoms in a population of women not selected for menopausal symptoms. Our aim was to determine if memory complaints were part of the constellation of symptoms experienced by women in the menopause transition compared with a group of nonmenopausal women in a community setting. We hypothesized that perimenopausal and menopausal women would have a significantly higher prevalence of memory complaints than would nonmenopausal women.

SUBJECTS AND METHODS

All faculty members of a Long Island, New York, school district were solicited to participate in this study. A high school student (K.H.) presented the survey at a district faculty meeting. By filling out the survey, the woman involved was presumed to give informed consent. The institutional review board of the school system community approved this manner of implied consent. The population was chosen to provide a group of women who were not selected for illness or gynecologic or menopausal complaints. Women faculty members were asked to complete the survey personally, and male faculty members were asked to present the survey to their spouse or female partner. Follow-up by personal contact and mailed appeals was used to maximize the response rate.

The New York Memory and Healthy Aging Services generated this survey, which requires ~10 minutes to complete (see **Appendix**). The survey queried demographic characteristics and menopausal symptoms. Participants were asked to respond "yes" or

“no” to questions about the presence of hot flashes/night sweats, memory loss, vaginal dryness/irritation, depression/anxiety, reduced sexual drive, and incontinence. Symptom severity was not queried. We determined whether the surveyed women were nonmenopausal, perimenopausal, or menopausal by querying their age, whether the nature of their menstrual cycles had changed, and what they believed caused any such change.

Demographic characteristics (age, education, and race) for all eligible female faculty were available through a centralized data bank, so that the differences between survey participants and nonparticipants could be compared. Demographic data were not available for eligible spouses and significant others of male faculty members who chose not to participate.

The survey respondents were divided into 2 groups for analysis. One group comprised women who reported a change in their menstrual cycle that they attributed to either natural menopause or perimenopause (hereafter referred to as [peri]menopause in our study). Women who reported no changes in their menstrual cycles composed the nonmenopausal comparison group. All women who attributed a change in their menstrual cycle to pregnancy, hysterectomy, chemotherapy, or other nonmenopausal reasons were excluded from the study. We also excluded women aged <30 or >60 years to include most of the women in the menopause transition while excluding those with possible early symptoms of dementia.

Statistical Analysis

Demographic data were analyzed using 1-way analysis of variance for the normally distributed continuous variables and the Pearson χ^2 test for categorical data. First, differences between survey respondents and nonrespondents were assessed. Then, differences in demographic characteristics between naturally (peri)menopausal women and the comparison group were examined. Each (peri)menopausal symptom was evaluated as a categorical variable using logistic regression analysis (odds ratios [ORs] and CIs were determined), both before and after adjusting for differences in demographic characteristics between the (peri)menopausal and comparison women. All data were examined using the Statistical Package for Social Sciences, version 10 (SPSS Inc., Chicago, Illinois).

RESULTS

Seventy-two percent (375/521) of the faculty members in the school district were eligible for the study. Of these, 217 (58%) completed the survey (Table I). The mean age of the women who did not complete the survey was significantly younger than that of the women who completed it (43.0 [11.0] years vs 47.7 [9.5] years; $P < 0.001$). Compared with respondents, significantly more of the survey nonrespondents were white (100% [158] vs 93% [201]; $P < 0.001$). There was no significant difference in educational level between survey respondents and nonrespondents.

Table I. Demographic characteristics of survey respondents and nonrespondents.

Characteristic	Respondents (n = 217)	Nonrespondents (n = 158)	P
Age, mean (SD), y	47.7 (9.5)	43.0 (11.0)	<0.001
Race, no. (%)			
White	201 (93)	158 (100)	<0.001
Other	16 (7)		
Educational level, no. (%)			
Graduate	111 (51)	69 (44)	
Undergraduate	74 (34)	53 (34)	
High school	32 (15)	36 (23)	<0.1

After excluding pregnant women, women who had hysterectomies or various other nonmenopausal causes of amenorrhea, and those aged <30 or >60 years, 151 of the survey respondents were included in our analysis of symptoms of the menopause transition. Sixty-eight percent ($n = 103$) of the women were placed in the natural (peri)menopause group and 32% ($n = 48$) of the women were placed in the comparison group (Table II). (Peri)menopausal women were significantly older than the women with regular menstrual cycles (51.2 [5.0] years vs 39.6 [7.2] years; $P < 0.001$) and significantly more likely to be white (101 [98%] vs 40 [83%]; $P < 0.001$). The 2 groups were similar in educational level. After adjusting for age and race, we found that (peri)menopausal women were ~3 times more likely to complain of memory loss than were women in the comparison group (64% [66] vs 25% [12]; OR, 3.2; 95% CI, 1.2–8.8; $P < 0.02$). (Peri)menopausal women were also ~4 times more likely to complain of night sweats/hot flashes (52% [54] vs 15% [7]; OR, 4.3; 95% CI, 1.4–13.3; $P < 0.01$) and were ~4 times more likely to complain of reduced libido (39% [40] vs 13% [6]; OR, 4.5; 95% CI, 1.3–15.7; $P < 0.02$). There were no sig-

nificant differences in complaints of depression, vaginal dryness, and incontinence between the 2 groups.

DISCUSSION

In our exploratory survey of a group of community-dwelling women not selected for symptoms of the menopause transition, we found significant increases in complaints of memory loss, reduced libido, and hot flashes/night sweats in a group of (peri)menopausal women compared with a group of normally menstruating women. In our group of 103 (peri)menopausal women, 64% complained of memory loss, 52% hot flashes/night sweats, and 39% of reduced libido, compared with 25%, 15%, and 13%, respectively, in the nonmenopausal group.

Our findings on the prevalence of hot flashes/night sweats are similar to those of a large survey of 850 women in which 55% of peri- and postmenopausal women complained of hot flashes/night sweats compared with 15% of normally menstruating women. These findings are also supported by the findings in other studies.^{11,12} In one study of 230 perimenopausal

Table II. Demographic and clinical characteristics of (peri)menopausal and nonmenopausal women.

Characteristic	(Peri)menopausal Women ($n = 103$)	Nonmenopausal Women ($n = 48$)	<i>P</i>	Odds Ratio (95% CI)*
Age, mean (SD), y	51.2 (5.0)	39.6 (7.2)	<0.001	–
Race, no. (%)				
White	101 (98)	40 (83)	<0.001	–
Other	2 (2)	8 (17)		
Educational level, no. (%)				
Graduate	58 (56)	25 (52)		
Undergraduate	35 (34)	17 (35)		–
High school	10 (10)	6 (13)	<0.8	
Symptoms, no. (%)				
Memory loss	66 (64)	12 (25)	<0.02	3.2 (1.2–8.8)
Hot flashes/night sweats	54 (52)	7 (15)	<0.01	4.3 (1.4–13.3)
Reduced libido	40 (39)	6 (13)	<0.02	4.5 (1.3–15.7)
Depression	32 (31)	8 (17)	<0.17	2.2 (0.7–7.4)
Incontinence	33 (32)	3 (6)	<0.62	1.4 (0.3–6.2)
Vaginal dryness	29 (28)	4 (8)	<0.11	3.1 (0.8–12.4)

*Adjusted for age and race.

community-dwelling women, 62% reported memory loss,¹¹ as did 55% of menopausal Taiwanese women,⁴ and 70% of 88 Italian women attending a menopause clinic.¹

A study of 495 Taiwanese women used objective cognitive tests (eg, the Auditory Verbal Learning Test, the Trail-Making Test, and tests for visual memory, verbal fluency, and digit span) to measure changes in memory during 2 time periods 18 months apart.¹³ The authors found a significant decline in visual memory among perimenopausal compared with premenopausal groups ($P < 0.01$), but no differences in other cognitive functions.

However, our findings of increased memory complaints among (peri)menopausal women compared with normally menstruating women were not supported by Ford et al,² who found no correlation between the menopause transition and an overall subjective memory questionnaire score in a cross-sectional study of 202 women. One reason for differences in results may be varying criteria used for menopausal staging. The Study of Women's Health Across the Nation and the Stages of Reproductive Aging Workshop divide the menopause transition into premenopause, early transition, late transition, and postmenopause; yet another system adds a late premenopausal stage.¹⁴ Laboratory measures have also been used to identify menopausal stage.^{14,15} Our study separated participants into nonmenopausal and (peri)menopausal groups based on whether or not the women experienced a change in menstrual cycle not related to a cause such as pregnancy.

Increased memory loss and other cognitive deficits during menopause may be explained in several ways. Estrogen-influenced neurons are involved in the regulation of memory and mood, in addition to other tasks. Estrogen may affect language, spatial tasks, and memory tasks. Estrogen alters brain function through promotion of neuronal networking by increasing the sprouting of dendrites and dendritic spines.¹⁶ It also increases brain levels of acetylcholine, and promotes individual nerve cell growth by free-radical scavenging, reducing inflammation, and increasing brain blood flow and glucose utilization.¹⁷

The question of whether estrogen replacement ameliorates memory loss and other cognitive symptoms has been examined. In a study of 88 women (mean age, 52.6 years) treated at the menopause service of a hospital, 70% of participants complained of memory loss and 37% complained of hot flashes. Half of the women were in a group that was receiving hormone replacement therapy (HRT); those women had lower rates of complaints of both memory loss and hot flashes, although statistical significance was not assessed.¹ However, the Melbourne Women's Midlife Health found a nonsignificant positive trend between duration of HRT and delayed recall, and no significant effect on memory due to menopausal status or HRT ($F = 0.356$ and $F = 0.367$, respectively).¹⁸

In an extensive review of estrogen therapy in postmenopausal women, Yaffe et al¹⁹ noted that in 5 observational studies and 8 trials, cognition improved in perimenopausal but not in asymptomatic women. Memory and cognitive decline in perimenopausal women may be associated with reduced levels of hormones and neurotransmitters, among other factors. The menopausal years, commonly the mid-40s through the mid-50s, coincide with loss of hippocampal neurons at the rate of ~5% per decade beginning at 45 years of age.²⁰ It is tempting to speculate that declining estrogen levels at this time may in some way increase the vulnerability of hippocampal neurons to toxicity and cell death, ultimately leading to clinical symptoms of cognitive loss. However, the Women's Health Initiative Memory Study found that estrogen in combination with progestin might slightly increase the risk of cognitive decline and dementia in postmenopausal women aged >65 years.^{21,22} There may be several reasons for these results, including the use of a conjugated equine estrogen rather than the more bioavailable estradiol, possible attenuation of the effects of estrogen by progestin, the older age of the women studied, and the use of the modified Mini-Mental Status Examination (MMSE) as the method for determining cognitive dysfunction. However, the MMSE may not be the most sensitive indicator of cognitive dysfunction in functional patients.²²

Our study had several limitations. The survey did not question the participant's perceived origin of memory loss or emotional well-being. Although our data were obtained through self-reported surveys and it remains unclear how well reported menopausal symptoms correlate with the actual existence of symptoms, studies have found a positive association between subjective memory complaints and objective evidence of memory impairment.²³

Owing to the small sample size, this study may not be entirely reflective of a broader population of women. The higher prevalence of older women may have led to overrepresentation of perceived memory loss. Moreover, participants who chose to complete the survey may have had more symptoms than did those who decided not to participate. Overreporting of symptoms may have resulted from a general desire to discuss one's health issues when an opportunity is provided. On the other hand, there may have been an underreporting bias that may have understated the prevalence of memory loss; specifically, respondents may not have reported memory complaints because of denial or the possible perceived negative connotation attached to such complaints while employed as educators.²⁴

CONCLUSIONS

This preliminary study suggests that complaints of memory loss may be associated with (peri)-menopause, with prevalence similar to that of hot flashes/night sweats. Further research in this area may be beneficial to understanding the cognitive changes associated with aging in women.

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Address correspondence to: Gayatri Devi, MD, 65 East 76th Street, New York, NY 10021. E-mail: gd@nymemory.org

Appendix. Menopause Survey.

The survey will take approximately 10 minutes to complete.

1. When is your date of birth? ___/___/___
2. How many years of education have you received?
 - Less than 8 years
 - 8–12 years (through high school)
 - 12–16 years (college)
 - More than 16 years (graduate/medical/law)
3. What is your race?

<input type="checkbox"/> African-American	<input type="checkbox"/> Hispanic	<input type="checkbox"/> White
<input type="checkbox"/> Asian	<input type="checkbox"/> Native American	<input type="checkbox"/> Other
4. How did you hear about this survey?
 - From the presentation
 - From my spouse/significant other
 - Other
5. How old were you when you started having your periods?
_____ years
6. Have your periods changed in flow, cycle, or stopped? ___ Yes ___ No
(If NO, skip to question #10.)
7. How old were you when your periods changed in flow or cycle?
_____ years
8. If you no longer have periods, how old were you when they stopped completely?
_____ years
9. What do you think caused the change in your periods?
 - Beginning of natural menopause
 - Hysterectomy
 - Chemotherapy
 - Other (please specify): _____
10. Are you experiencing any of the following symptoms?

<input type="checkbox"/> Cold sweats/hot flashes	<input type="checkbox"/> Memory loss
<input type="checkbox"/> Vaginal dryness/irritation	<input type="checkbox"/> Depression/anxiety
<input type="checkbox"/> Reduced sexual drive	<input type="checkbox"/> Bladder/urinary problems
<input type="checkbox"/> Other (please specify): _____	
11. Are you or have you ever been on hormone replacement therapy? ___ Yes ___ No
(If NO, skip to question #19.)
12. What is the name and dose of the hormone replacement you are now taking or that you last took?

13. About how long have you or had you been on this preparation?
_____ years
14. Is the hormone replacement therapy a

<input type="checkbox"/> Skin patch	<input type="checkbox"/> Pill	<input type="checkbox"/> Vaginal cream/suppository
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15. Approximately how long have you been on hormone replacement all together?
_____ years
16. How long do you plan to be on hormone replacement?
_____ years
17. Do you or did you have any side effects from hormone replacement?

<input type="checkbox"/> Vaginal bleeding/spotting	<input type="checkbox"/> Headaches
<input type="checkbox"/> Depression	<input type="checkbox"/> Skin rash/breakout
<input type="checkbox"/> Sleepiness	<input type="checkbox"/> Blood clots
<input type="checkbox"/> Breast tenderness	<input type="checkbox"/> Other (please specify): _____

(continued)

Appendix. (Continued)

18. Please rate, from 1 to 3, the top 3 reasons you are on hormone replacement therapy, with 1 being the most important reason:
- Treatment of hot flashes
 - Treatment of bladder or urinary problems
 - Treatment of sexual dysfunction
 - Treatment of mood and anxiety problems
 - Treatment of memory and language problems
 - Prevention of osteoporosis and fractures
 - Prevention of heart disease and stroke
 - Prevention of Alzheimer's disease
 - Other (please specify): _____
19. If you are not now on hormone replacement, why did you decide to not go on, or to stop hormone replacement?
- Have not reached menopause yet
 - No symptoms, although I am menopausal
 - Fear of breast cancer
 - Have not thought about hormone replacement
 - Bad side effects on hormone replacement in the past
 - Do not wish to introduce chemicals into the body
 - Other (please specify): _____
20. Where do you think prescription hormone replacements come from?
- Plants (wild yam and soy)
 - Urine of pregnant mares
 - Synthetic chemicals
 - Other (please specify): _____
21. A. Are you taking any of these over-the-counter menopause treatments?
- Black cohosh
 - Dong quoi
 - Soy products
 - Progesterone creams
 - Other (please specify): _____
- B. Are you taking any of these other over-the-counter supplements?
- Gingko biloba
 - Vitamin E
 - Valerian
 - St. John's wort
 - Melatonin
 - Primrose oil
 - SAM-e
 - Other (please specify): _____
22. Are you currently on birth control pills? Yes No
23. Were you ever on birth control pills? Yes No
24. What is the total length of time you have been on birth control pills?
_____ years
25. If there is a history of breast cancer in your family, who was affected?
- Mother
 - Sister
 - Father or brother
 - Second-degree relative (aunt, grandparent, cousin)
26. If you have a history of breast disease, what type was it?
- Benign
 - Malignant
 - No history of breast disease
27. Have you ever had a breast biopsy? Yes No
28. How many times have you lost consciousness because of a blow to the head?
- Never
 - Once
 - Two or more times
29. Have you noticed changes in your thinking? Yes No
(If NO, skip to question #38.)
30. Do you have trouble with your memory? Yes No

(continued)

Appendix. (Continued)

31. Do you have trouble finding words? Yes No
32. Has your ability to do mental mathematics changed? Yes No
33. Do you have trouble remembering recent events? Yes No
34. Do you have trouble recalling lists? Yes No
35. Has anyone else noticed these difficulties about you? Yes No
36. Have these difficulties interfered with your ability to function? Yes No
37. How do you rate your mental capacity now versus your performance before you began to have menopausal symptoms?
- | | | | |
|--|------------------------------------|------------------------------------|------------------------------|
| Has your mental capacity | <input type="checkbox"/> Improved? | <input type="checkbox"/> Worsened? | |
| By what proportion has your mental capacity changed? | | | |
| <input type="checkbox"/> 10% | <input type="checkbox"/> 20% | <input type="checkbox"/> 30% | <input type="checkbox"/> 40% |
| <input type="checkbox"/> 50% | <input type="checkbox"/> 60% | <input type="checkbox"/> 70% | <input type="checkbox"/> 80% |
| <input type="checkbox"/> 90% | <input type="checkbox"/> 100% | | |
38. Do you feel depressed? Yes No
39. If you are not depressed, have you lost pleasure doing things that gave you enjoyment? Yes No
If you answered YES to EITHER question #38 or #39, continue to #40.
If you answered NO to BOTH questions #38 & #39, skip to question #48.
40. Do you have trouble sleeping or do you sleep too much? Yes No
41. Have you recently gained or lost weight? Yes No
42. Do you have trouble concentrating? Yes No
43. Do you feel tired all the time? Yes No
44. Do you have feelings of guilt? Yes No
45. Do you feel more irritable than usual? Yes No
46. Do you feel suicidal? Yes No
47. Does your mind ever play tricks on you? (Do you hear or see things when no one is around?) Yes No
48. Do any of these areas cause stress in your life?
- | | |
|--|--|
| <input type="checkbox"/> Career | <input type="checkbox"/> Significant other |
| <input type="checkbox"/> Children | <input type="checkbox"/> Friends |
| <input type="checkbox"/> Other (please specify): _____ | |
49. If you knew that prescription hormone replacement was plant-based, would you choose:
- | |
|---|
| <input type="checkbox"/> Over-the-counter hormone replacement |
| <input type="checkbox"/> Prescription hormone replacement |
| <input type="checkbox"/> Don't care either way |
50. Would you mind if we contacted you? If not, please enclose your e-mail address or your telephone number to participate further in the survey.
- _____
- _____