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Physical activity and risk of vasomotor symptoms in women with and without a history of depression: results from the Harvard Study of Moods and Cycles

Rebecca C. Thurston, PhD,[1] Hadine Joffe, MD, MSc,[2] Claudio N. Soares, MD, PhD,[3] and Bernard L. Harlow, PhD[4]

ABSTRACT

Objective: To examine whether physical activity was associated with decreased risk of vasomotor symptoms in a prospective study of women transitioning through menopause.

Design: Hypotheses were evaluated in the Harvard Study of Moods and Cycles, a longitudinal study of women with and without a history of major depression (N = 523). Ordinal logistic regression models were utilized to assess the odds of vasomotor symptoms (none, mild, moderate/severe; Greene Climacteric Scale) associated with physical activity (quartiles of metabolic equivalent-hours per week) at study enrollment and over a 3- to 5-year follow-up period.

Results: No significant associations between physical activity and vasomotor symptoms were observed for the sample as a whole. However, exploratory analyses stratified by depression history revealed that among the 157 women with a lifetime history of major depression, high (odds ratio [OR] = 0.28, 95% CI: 0.09-0.83) or moderately high (OR = 0.33, 95% CI: 0.11-0.99) physical activity proximal to the vasomotor assessment, as well as consistently high (OR = 0.27, 95% CI: 0.10-0.75) or increasing (OR = 0.33, 95% CI: 0.12-0.92) physical activity over the duration of the 3- to 5-year follow-up period was associated with decreased vasomotor symptoms relative to sedentary behavior. No significant associations were observed for women without a history of depression.

Conclusions: Physical activity may be associated with decreased risk of vasomotor symptoms among women with a history of major depression.

Key Words: Hot flashes – Hot flushes – Menopause – Physical activity – Exercise – Vasomotor symptoms.

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From the [1]Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA; [2]Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA; [3]Department of Psychiatry and Behavioral Neurosciences, McMaster University, Hamilton, Ontario, Canada; and [4]Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

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Address correspondence to: Rebecca C. Thurston, PhD, Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213. E-mail: thurstonrc@upmc.edu.

The majority of American women report vasomotor symptoms during the menopausal transition, with estimates ranging from 58% to 93%.[1] Vasomotor symptoms are sensations of intense heat on the upper torso, head, and neck that are often accompanied by profuse sweating and flushing.[1] The incidence and frequency of vasomotor symptoms are highest in the several years directly preceding and following the final menstrual period.[2] They are associated with increased depressive symptoms[3,4] and are a leading reason women seek medical care at midlife.[5] Because hormone therapy

(HT) has been associated with increased risk of chronic disease,[6] attention is increasingly directed toward managing vasomotor symptoms via behavioral approaches, including physical activity.[7] Unfortunately, due to inconsistencies in the published literature, it is unclear to what extent behavioral changes affect vasomotor symptoms.

In a recent position statement on the treatment of vasomotor symptoms, The North American Menopause Society recommended physical activity as a first step in managing vasomotor symptoms.[7] Several cross-sectional studies have reported a lower prevalence or severity of vasomotor symptoms among physically active women,[8-10] although other studies have found no association,[11-14] or associations that do not persist when controlling for potential confounders.[15-17] Moreover, the cross-sectional nature of this research limits understanding of the causal nature of these associations.[18] The few small randomized trials conducted have produced mixed findings.[19-22] However, their small size[19,20] and low numbers of symptomatic women[21] or women not taking HT[22] limit conclusions. One prospective study of Australian women transitioning through menopause has suggested a slightly decreased risk of hot flashes among more physically active women,[23] although this study included a very limited assessment of physical activity. Thus, some research suggests a potential protective effect of physical activity in reducing hot flashes, although the contradictory nature of these findings limits conclusions.

Important subgroup differences may contribute further to the heterogeneity of findings. Although existing research has generally considered women together or stratified on reproductive factors,[23] certain other individual differences may show important associations with vasomotor symptoms, physical activity, and physiological systems related to both. Women with high vasomotor symptoms often show elevated depressive symptoms.[3,4] Moreover, physical activity can be an effective treatment for major depression.[24] Common central nervous system processes are implicated in vasomotor symptoms[25-27] and depression[28-30] and are often altered among those with a history of current depression.[30] Thus, past or present depression status may be important to consider in associations between physical activity and vasomotor symptoms.

To investigate prospectively the association between physical activity and vasomotor symptoms, we used data from the Harvard Study of Moods and Cycles, a longitudinal population-based study of late reproductive–age women with and without a history of major depressive disorder. We hypothesized that women who are more physically active in their late reproductive years would have decreased risk of vasomotor symptoms. In an exploratory fashion, we examined associations stratified by depression history.

METHODS

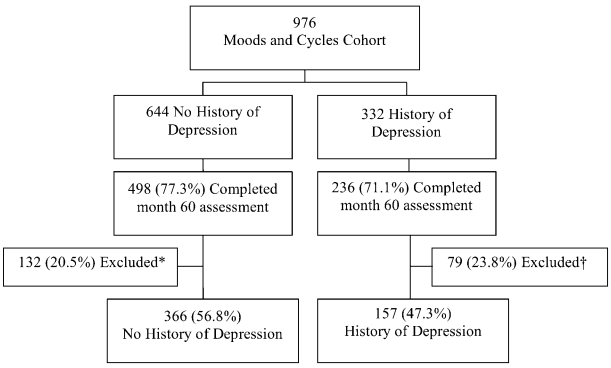
Target population

The target population was derived from a population-based sample of women between the ages of 36 and 44 selected from seven Boston metropolitan area communities. Massachusetts Town Books (annual publication listing residents by name, age, and address according to voter precincts) were used to identify all women in this age range with a verified address and telephone number. A one-page optically scannable questionnaire was mailed to screen for women menstruating in the past 60 days, and women with and without a history of depression and/or current elevated depressive symptoms.[31] Questionnaires were completed by 72% (n = 4,161) of women contacted. Details pertaining to this population screening can be found elsewhere.[32]

Harvard Study of Moods and Cycles cohort

The Harvard Study of Moods and Cycles cohort was composed of 332 women with and 644 women without a lifetime history of major depression. It was derived from and representative of the 4,161 women comprising the target population. Details pertaining to this sampling method can be found elsewhere.[33] Lifetime history of depression was confirmed based on in-person Structured Clinical Interviews for DSM-IV Depression (SCID).[34] Physical activity (see below), demographic and menstrual cycle characteristics, reproductive and medical history, medication use, and depression status were assessed at baseline via in-person interviews and by telephone every 6 months over a 36-month follow-up period. A self-administered questionnaire (month 60 assessment) that included the vasomotor symptom assessment (see below) was mailed an average of 37 months (range, 26.2-80.2) after the month 36 interview.

The present sample was restricted to 734 women (498 with no depression history, 236 with a depression history) that returned the month 60 questionnaire (Fig. 1). We further excluded 211 women due to (1) use of medications at the month 60 assessment likely to alter the presence of hot flashes (HT, oral contraceptives, tamoxifen, gabapentin, phenobarbital, luprolide, clonidine, aromatase inhibitors), (2) surgical



* = 4 no menstrual cycle at month 60 follow-up due to breast-feeding; 11 bilateral oophorectomy; 15 hysterectomy; 18 one or part ovary removed; 5 amenorrhea due to chemotherapy; use of the following medication at month 60 follow-up assessment: 94 HT or oral contraceptives, 5 tamoxifen, 2 gabapentin, 1 phenobarbitol, 3 lupron, 1 clonidine; 1 leukemia; 28 women represented in more than one category.
† = 6 no menstrual cycle at month 60 follow-up due to breast-feeding; 4 bilateral oophorectomy; 3 hysterectomy; 8 one or part ovary removed; 1 amenorrhea due to chemotherapy; use of the following medication at month 60 follow-up assessment: 59 HT or oral contraceptives, 4 tamoxifen, 9 gabapentin, 4 lupron; 19 women represented in more than one category.

FIG. 1. The Harvard Study of Moods and Cycles, United States, 1995-1999.

menopause or inability to characterize menopause status based on menstrual cycle characteristics (i.e., amenorrhea secondary to breast-feeding, long-term oral contraceptive use, removal of one or both ovaries, or chemotherapy), or (3) reporting a medical condition that may produce hot flash sensations (ie, leukemia). The final sample for analysis included 157 women with and 366 women without a lifetime history of major depression. Forty percent (n = 62) of women with a baseline history of major depression experienced a recurrent depressive episode, and 5% (n = 20) of women with no baseline history of major depression experienced a new depressive episode over the 36-month follow-up period.

Measures

Physical activity

Physical activity was assessed at baseline and at each of the six follow-up interviews (months 6 through 36). At baseline, participants reported up to four leisure time physical activities in which they regularly engaged, including the frequency (months/year) and weekly duration (h/w) performing each activity. At months 6 through 36, participants reported up to two leisure time physical activities and the current weekly duration engaging in each activity.

For these analyses, four physical activity indices were calculated: (1) physical activity level metabolic equivalent MET hours/week at study enrollment averaged over the year, (2) physical activity level (MET h/wk) at month 36, (3) average physical activity level (MET h/wk) from baseline through month 36, and (4) trajectory of physical activity (low, medium, high, increasing, decreasing) from baseline through month 36. To calculate these indices, each activity was assigned a MET value[35] and was multiplied by the weekly activity duration to yield a MET hours per week for each activity. For the baseline assessment, this value was adjusted by the proportion of the year performing the activity (number of months performing the activity/12). MET hours per week across activities within a follow-up were summed to yield total MET hours per week per follow-up. To yield the average MET hours per week over the study, MET hours per week across follow-up assessments were summed and divided by the number of completed assessments. Baseline, month 36, and average MET hours per week were categorized into four groups based on the distribution of activity at month 36, the activity assessment most proximal to the vasomotor symptom assessment.

The trajectory of activity over the study was calculated by tertiling the MET hours per week at each follow-up and assigning a value of 0, 1, or 2 for each tertile (0 = low, 1 = medium, 2 = high). An average tertile was derived for the first half of the study (baseline, months 6, 12, 18) by summing the tertile groups (0, 1, 2) across the four assessments and dividing by the number of assessments represented. Averages were rounded to the nearest whole number. Activity for the second half of the study (months 24, 30, 36) was calculated using the same methods. Participants remaining in the low tertile in both the first and second half of the study were classified as low, those remaining in the medium tertile were classified as medium, and those remaining in the high tertile were classified as high. Participants moving to a higher physical activity tertile from the first to the second half of the study were classified as increasing, and those moving to a lower physical activity tertile were classified as decreasing activity.

Vasomotor symptoms

Vasomotor symptoms were assessed using the Greene Climacteric Scale,[36] a widely used and psychometrically well-characterized self-report measure of menopausal symptoms. Symptoms are recalled over the past week and are rated on a 4-point scale from not at all (0) to severe (3) with respect to the extent of bother associated with each symptom. Two questions pertaining to hot flashes and night sweats were summed to comprise the vasomotor subscale

(range = 0-6). Due to small numbers of women reporting moderate to severe symptoms, vasomotor subscale scores were categorized into none (0), mild (1), and moderate to severe (2-6) symptoms.

Depression

The SCID[34] was administered at the baseline in-person interview to determine lifetime history of major depression and at each follow-up telephone interview (months 6-36) to determine recurrent or new-onset of major depressive episodes. At month 60, depressive symptoms were obtained via the Center for Epidemiologic Studies Depression Scale (CES-D).[31] Only SCID assessments were used to quantify past or present major depression.

Menopause status

At each follow-up, women were classified as perimenopausal if reporting one of the following within the previous 6 months: change in menstrual cycle length of longer than 7 days relative to baseline, change in menstrual flow amount (more than two flow categories, eg, from light or moderately light to moderately heavy or heavy) or duration (change of more than two flow days), or amenorrhea for more than 3 months.

Data analysis

Differences in the study population by baseline physical activity levels were evaluated using analysis of variance and chi-square tests. Ordinal logistic regression was utilized to estimate associations between the four physical activity indices, considered separately, and vasomotor symptoms. Both continuous and categorical forms of the physical activity indices were considered. Models were estimated adjusting for age, and subsequently for covariates educational attainment, body mass index (BMI), selective serotonin or serotonin-norepinephrine reuptake inhibitor (SSRI/SNRI) antidepressant use, smoking, parity, baseline depression history, and menopausal stage. After consideration of the sample as a whole, models were stratified by baseline lifetime depression history and were conducted adjusting for the same covariates listed above. Twenty women with no lifetime history of depression at baseline had a major depressive episode during the course of the study, the onset of which appeared to coincide with the onset of perimenopause (data not shown). Because mood disturbance during perimenopause may be causally related to menopausal vasomotor symptoms,[3,4,37] these women were eliminated from stratified analyses. Odds ratios and CIs were estimated via the profile likelihood method. The proportional odds assumption was evaluated in all logistic regression models. Alpha was set at 0.05. Analyses were conducted with SAS version 8.2 (SAS Institute, Cary, NC).

RESULTS

Sample characteristics

More than 35% of women reported no leisure time physical activity at baseline and at the month 36 assessment (Table 1). However, among women reporting activity, they were quite active, with 23% reporting up to moderate (>0-16 MET h/wk, eg, <30 min of brisk walking daily), 18% reporting moderate to high (>16-26 MET h/wk, eg, 30-55 min brisk walking daily), and 24% reporting very high levels of activity (>26 MET h/wk, eg, >55 min brisk walking or 30 min of jogging daily).

As illustrated in Table 2, study participants were mainly white and highly educated. They were an average (SD) of 40.7 (2.5) years old at the baseline examination, and the majority (66.9%) had transitioned to perimenopause by the end of the study. Physical activity varied significantly by education, martial status, and parity, but did not vary by age, race, antidepressant use, transition to the perimenopause, depression history, or smoking status.

TABLE 1. *Distribution of physical activity (average MET h/wk) of participants in the Harvard Study of Moods and Cycles, United States, 1995-1999*

Baseline	
0	185 (35.4)
>0-16	120 (22.9)
>16-26	94 (18.0)
>26	124 (23.7)
Month 36 assessment	
0	156 (36.9)
>0-16	90 (21.3)
>16-26	87 (20.6)
>26	90 (21.3)
Average over study	
0	51 (9.8)
>0-16	255 (48.8)
>16-26	107 (20.5)
>26	110 (21.0)
Trajectory[a]	
Low (≤6)	107 (20.9)
Medium (>6 to ≤19)	84 (16.4)
High (>19)	138 (26.9)
Increasing[b]	107 (20.9)
Decreasing[c]	77 (15.0)

[a]Trajectory of physical activity patterns between the first half (baseline, months 6, 12, 18) to the second half (months 24, 30, 36) of the study.
[b]Moving to a higher average physical activity tertile group from first half (baseline, months 6, 12, 18) to the second half (months 24, 30, 36) of the study.
[c]Moving to a lower average physical activity tertile group from first half (baseline, months 6, 12, 18) to the second half (months 24, 30, 36) of the study.

TABLE 2. *Demographic characteristics of participants in the Harvard Study of Moods and Cycles by baseline physical activity United States, 1995-1999*

	Physical activity (average MET h/wk)[a] (%)			
	0 (n = 185)	<0-16 (n = 120)	<16-26 (n = 94)	>26 (n = 124)
Race				
White	94.1	95.0	96.8	96.8
African American	2.2	0.8	1.1	1.6
Other[b]	2.7	4.2	2.1	1.6
Education[c]				
High school	13.5	12.5	2.1	5.6
Some college/ vocational school	13.5	16.6	16.0	10.5
College	29.7	29.2	34.0	50.8
Graduate school	43.3	41.7	47.9	33.1
Marital status[c]				
Married	83.8	70.0	68.1	69.4
Single	9.2	16.7	21.3	21.8
Divorced/widowed	7.0	13.3	10.6	8.8
Parity (month 60 assessment)[c]				
0	20.5	27.5	33.0	45.2
1	17.8	17.5	17.0	8.9
2	39.5	35.0	34.0	27.4
≥3	22.1	29.0	16.0	18.5
BMI (kg/m^2; month 60 assessment)[d]				
Normal (<25)	52.4	60.0	66.8	64.5
Overweight (25-29.9)	23.8	22.5	22.3	25.8
Obese (>30)	23.8	17.5	14.9	9.7
Current cigarette smoker	47.0	41.7	37.2	44.4
History of depression	30.8	24.2	37.2	29.0
Antidepressant use (SSRI or SNRI)	22.2	20.0	19.2	14.5
Transition to perimenopause (by month 60 assessment)	66.7	66.7	73.4	62.7

BMI, body mass index; SSRI, selective serotonin reuptake inhibitor; SNRI, selective norepinephrine reuptake inhibitor.
[a]Physical activity quartile categorization is based on distribution at the month 36 assessment.
[b]Asian American, Latina, Native American.
[c]$P < 0.01$.
[d]$P < 0.10$.

Physical activity and vasomotor symptoms

Participants reported relatively low levels of vasomotor symptoms, with 68% (n = 353) reporting no vasomotor symptoms, 14% (n = 71) reporting mild, and 18% (n = 93) reporting moderate to severe vasomotor symptoms at month 60. Physical activity at baseline, at month 36, and throughout the study was not significantly associated with vasomotor symptoms in age-adjusted or fully adjusted models (Table 3).

In analyses stratified by baseline depression history, there were few significant associations between physical activity and vasomotor symptoms among women with no depression history, with the exception of some evidence of increased risk of vasomotor symptoms among women who were highly physically active at month 36. However, among women with a history of depression, increased physical activity was associated with decreased vasomotor symptoms. This effect was particularly pronounced for physical activity levels most proximal to the vasomotor symptom assessment. Women with a history of depression who maintained high levels of physical activity or who increased their physical activity during the study were at decreased risk of vasomotor symptoms compared to women with a history of depression who maintained low physical activity levels throughout the study (Table 4). Results were similar utilizing a continuous index of physical activity or without adjustment for antidepressant use.

To examine whether associations between physical activity and vasomotor symptoms among women with a history of depression were accounted for by current depressive symptom levels, the CES-D score obtained concurrent in time with the vasomotor assessment (month 60) was added to the fully adjusted stratified model. In these models, among women with a history of depression, moderately high (>16-26 MET h/wk; OR = 0.26, 95% CI: 0.08-0.83) and high (>26 MET h/wk; OR = 0.31, 95% CI: 0.09-0.94) physical

TABLE 3. *Physical activity (average MET h/wk) and risk of increased vasomotor symptoms in participants in Harvard Study of Moods and Cycles, United States, 1995-1999*

	Age-adjusted		Fully adjusted[a]	
	OR[b]	95% CI	OR[b]	95% CI
Baseline				
0	1.00	—	1.00	—
>0-16	0.77	0.47-1.27	0.80	0.47-1.32
<16-26	0.71	0.41-1.23	0.76	0.43-1.34
>26	0.99	0.61-1.60	1.07	0.65-1.77
Month 36 assessment				
0	1.00	—	1.00	—
>0-16	0.86	0.49-1.51	0.94	0.52-1.66
<16-26	0.82	0.45-1.46	0.85	0.46-1.54
>26	1.07	0.61-1.85	1.19	0.67-2.11
Average				
0	1.00	—	1.00	—
>0-16	0.64	0.35-1.21	0.69	0.37-1.31
<16-26	0.54	0.27-1.09	0.58	0.28-1.22
>26	0.72	0.36-1.43	0.88	0.43-1.84
Trajectory				
Low (≤6)	1.00	—	1.00	—
Medium (>6-≤19)	0.69	0.38-1.25	0.76	0.41-1.41
High (>19)	0.59	0.34-1.02	0.68	0.39-1.21
Increasing	0.66	0.37-1.16	0.69	0.39-1.34
Decreasing	0.75	0.40-1.39	0.76	0.40-1.44

OR, odds ratio.
[a]Fully adjusted models: education, age, body mass index, selective serotonin/norepinephrine reuptake inhibitor antidepressant use, menopausal stage, parity, smoking, depression history.
[b]Odds of increased vasomotor symptom category associated with physical activity in ordinal logistic regression models.

TABLE 4. *Vasomotor symptoms associated with physical activity (metabolic equivalent hours per week), stratified by history of depression in participants in the Harvard Study of Moods and Cycles, United States, 1995-1999*

	No depression history (n = 346)			Depression history (n = 157)		
	Age-adjusted	Fully adjusted[a]		Age-adjusted	Fully adjusted[a]	
	OR[b]	OR[b]	95% CI	OR[b]	OR[b]	95% CI
Baseline						
0	1.00	1.00	—	1.00	1.00	—
>0-16	0.69	0.68	0.34-1.30	1.35	1.22	0.50-2.96
<16-26	0.97	1.07	0.52-2.17	0.37	0.37	0.13-0.99
>26	0.92	1.13	0.57-2.22	1.12	1.03	0.44-2.40
Month 36 assessment						
0	1.00	1.00	—	1.00	1.00	—
>0-16	1.40	1.58	0.75-3.31	0.35	0.40	0.13-1.15
<16-26	1.31	1.39	0.64-2.96	0.37	0.33	0.11-0.99
>26	2.09	2.56	1.24-5.36	0.28	0.29	0.09-0.83
Average						
0	1.00	1.00	—	1.00	1.00	—
>0-16	1.07	1.10	0.46-2.85	0.35	0.41	0.14-1.18
<16-26	0.77	0.92	0.33-2.70	0.26	0.30	0.09-0.97
>26	1.24	1.52	0.57-4.33	0.34	0.41	0.11-1.45
Trajectory						
Low (≤6)	1.00	1.00	—	1.00	1.00	—
Medium (>6-≤19)	0.96	1.08	0.49-2.41	0.45	0.45	0.15-1.28
High (>19)	0.84	1.08	0.51-2.33	0.29	0.27	0.10-0.75
Increasing	1.01	1.05	0.49-2.23	0.27	0.33	0.12-0.92
Decreasing	0.68	0.68	0.28-1.63	0.62	0.76	0.27-2.12

OR, odds ratio.
[a]Fully adjusted models: education, age, body mass index, selective serotonin/norepinephrine reuptake inhibitor antidepressant use, menopausal stage, parity, smoking.
[b]Odds of increased vasomotor symptom category associated with physical activity in ordinal logistic regression models.

activity at month 36 remained associated with significantly decreased vasomotor symptoms. Consistently high (OR = 0.30, 95% CI: 0.10-0.87) and increasing (OR = 0.36, 95% CI: 0.12-1.07) physical activity over the study was associated with marginally decreased vasomotor symptoms. Findings among women without a history of depression remained largely unchanged and not significant. Thus, associations between vasomotor symptoms and physical activity were not accounted for by current depressive symptoms among women with a history of depression.

DISCUSSION

Our findings suggest that among women with no history of depression, leisure time physical activity levels were largely unrelated to subsequent vasomotor symptom severity. However, among women with a history of depression, higher levels of leisure time physical activity were associated with decreased risk of vasomotor symptoms during perimenopause. This effect seemed to be strongest for physical activity most proximal to the vasomotor symptom assessment and for women increasing physical activity levels throughout the late reproductive/early perimenopausal years.

Previous investigations of associations between physical activity and vasomotor symptoms have shown mixed results. The vast majority of this research has been cross-sectional and thus has important limitations.[18] Some of this research has shown decreased vasomotor symptoms among women with high levels of physical activity,[8-10] whereas others have not,[11-14] or only in univariate analyses.[15-17] Some evidence suggests increased risk of vasomotor symptoms after acute exercise but decreased frequency of symptoms among physically active women.[38] The one prospective study evaluating this question reported lower rates and severity of vasomotor symptom reporting of physically active women throughout the menopausal transition.[23] Several small randomized controlled trials have suggested a weak inverse,[19,20] nonexistent,[22] or slight inverse[21] association between physical activity and vasomotor symptoms, although these studies were very small in size[19,20] or included a limited number symptomatic women.[21,22] Major depression history among women participating in these studies was not characterized. To our knowledge, neither existing observational nor intervention studies of physical activity and vasomotor symptoms have evaluated associations by depression history.

There are likely to be multiple mechanisms by which physical activity may influence vasomotor symptoms and why depression history may modify these associations. Alterations in both central adrenergic and serotonergic systems may play a key in the etiology of both vasomotor symptoms[25,26,39] and major depression,[28,29] including that which has remitted.[30] Aerobic exercise has been shown to elevate mood among those with major depression,[24] possibly due to its impact on the serotonergic and adrenergic systems.[40,41] Moreover, the opiate system, modulated by exercise and with a positive impact on mood,[42] may be involved in the genesis of hot flashes.[27] Finally, models of the etiology of hot flashes indicate an important role of thermoregulatory functioning,[25] which may be altered by physical activity,[43] by medications impacting serotonergic functioning,[44] and among patients with depression.[45] However, given that vasomotor symptom physiology is not fully characterized, these links remain speculative.

The impact of physical activity on the perception and reporting of hot flashes may also account in part for observed associations. Vasomotor symptoms in this study were solely evaluated by self-report, which can diverge from physiologically measured hot flashes, particularly among women with increased negative affect.[38] By elevating mood,[24] physical activity may have influenced the reporting, but not the occurrence, of vasomotor symptoms among women with a depression history. However, most women in the present study with a history of major depression did not experience a major depressive episode during the course of the study, and only 10% met criteria for major depression at study end. Moreover, depressive symptoms did not account for associations between physical activity and vasomotor symptoms, which would be expected if the primary impact of physical activity was on symptom perception.

It is also notable that there was a relatively low rate of hot flash reporting among this sample of women (32%). These women were of a fairly high socioeconomic level and were primarily white, both associated with lower reporting of hot flashes.[10] Moreover, although there was likely some overreporting,[46] women were engaging in a level of physical activity higher than similar samples, which may have played a role in their low symptom reporting.[47] Finally, 20 women had a new onset of depression during the menopausal transition. Because new-onset depression during the menopause is likely etiologically related to vasomotor symptoms,[3,4,37] and thereby confounded with the outcome, an a priori decision was made to exclude these women from stratified analyses. Inclusion of these women left study conclusions unchanged.

Several limitations deserve mention. There may have been measurement error and misclassification in the measurement of physical activity and vasomotor symptoms. Although this study was a prospective investigation of physical activity throughout the late reproductive and early perimenopausal years, the causal direction between physical activity and vasomotor symptoms cannot be established given assessment of vasomotor symptoms at one time point. Moreover, because measurement of vasomotor symptoms and physical activity were not concurrent in time, the impact of physical activity on vasomotor symptoms at the vasomotor symptom assessment is unknown. Finally, 32% of women reported vasomotor symptoms, limiting power to detect associations.

Despite these limitations, this study has several important strengths. It is a large, population-based, longitudinal investigation of women in their late reproductive years transitioning through menopause. It is one of the few prospective investigations of associations between physical activity and vasomotor symptoms. It used a very detailed assessment of physical activity allowing calculation of energy expenditure at multiple time points throughout the study. It included a widely used, well-characterized measure of menopausal symptoms. Finally, it included large numbers of women with and without a history of depression, providing the unique opportunity to examine differential associations between physical activity and vasomotor symptoms by depression history.

CONCLUSIONS

These study results indicated that increased physical activity in the years before menopause was associated with decreased severity of vasomotor symptoms during the menopausal transition among women with a history of major depression only. This study suggests that physical activity, even initiated shortly before or during perimenopause, may be a promising nonpharmacological approach to managing vasomotor symptoms in this subgroup of women.

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