Published in final edited form as:
Menopause. 2011 December ; 18(12): 1270–1277. doi:10.1097/gme.0b013e3182230e42.

Negative Affect and Vasomotor Symptoms in the Study of Women's Health Across the Nation (SWAN) Daily Hormone Study

Carolyn J. Gibson, MPH[1,*], **Rebecca C. Thurston, PhD**[2], **Joyce T. Bromberger, PhD**[3], **Thomas Kamarck, PhD**[4], and **Karen A. Matthews, PhD**[5]

[1]Department of Psychology University of Pittsburgh Pittsburgh, PA 15213

[2]Department of Psychiatry University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania 15213

[3]Departments of Epidemiology and Psychiatry University of Pittsburgh Pittsburgh, PA 15213

[4]Department of Psychology University of Pittsburgh Pittsburgh, PA 15213

[5]Departments of Psychiatry, Psychology, and Epidemiology University of Pittsburgh School of Medicine Pittsburgh, PA 15213

Abstract

Objective—Vasomotor symptoms (VMS) are common during the menopausal transition. Negative affect is consistently associated with self-reported VMS, but interpretation of this relationship is limited by infrequent measurement and retrospective recall of VMS. Using prospective data from daily diaries, we examined the daily association between negative affect and reported VMS, as well as temporal associations between negative affect and next day VMS, and VMS and next day negative affect.

Methods—Data were derived from the third wave of the Daily Hormone Study (DHS) (n=625). DHS is a substudy of the Study of Women's Health Across the Nation (SWAN), a multi-site community-based prospective cohort study of the menopausal transition. Participants reported VMS and affect in daily diaries for 12–50 days. Multilevel mixed models were used to determine the associations between reported VMS and negative affect, adjusted by antidepressant use, age, education, menopausal status, self-reported health, and race/ethnicity drawn from annual SWAN visits.

Results—VMS were reported by 327 women (52.3%). Negative affect was positively associated with VMS (OR 1.76, 95% CI 1.43–2.17, p<.001) in cross-sectional analyses. Negative affect, adjusted by same day VMS, was not predictive of next day VMS (OR 1.11, 95% CI .85–1.35, p=.55), whereas VMS, adjusted by same day negative affect, was predictive of negative affect the next day (OR 1.27, 95% CI 1.03–1.58, p=.01).

Conclusions—Negative affect was more likely to be reported on the same day and the day after VMS. Potential mechanisms underlying this relationship include negative cognitive appraisal, sleep disruption, and unmeasured third factors.

[*]gibsoncj@upmc.edu Phone: 412-648-9697.

The authors have no conflicts of interest to disclose.

Keywords

affect; menopause; vasomotor symptoms

Introduction

Hot flashes and night sweats, or vasomotor symptoms (VMS), are reported by an estimated 70–80% of women at some point in the menopausal transition. Symptom prevalence increases with advancing menopausal stage[1], though the duration, severity, frequency[2], and perceived bother[3] of VMS are highly variable. Despite the common occurrence of these symptoms, the etiology underlying VMS and individual differences in symptom presentation is unclear.

Measures of negative affect appear to be among the strongest and most consistent correlates of VMS[2,4,5]. These associations suggest that women with more depressive symptoms, anxiety, and general negative mood are at increased risk for reporting VMS, and are more bothered by symptoms regardless of frequency[6]. However, interpretation of these associations is currently limited by typical measurement, in which the occurrence of VMS over the past several weeks is retrospectively self-reported along with current mood ratings. Mood at the time of reporting may bias recall of physiological symptoms, which may inflate the association between these factors[7]. Further, while typical assessments offer information about the global covariance of these symptoms, they cannot provide information on the antecedent-consequent relationship between these frequently occurring events.

Negative affect may precipitate VMS by impacting the subjective experience of symptoms via increased cognitive catastrophization, vigilance to somatic symptoms, or anxiety sensitivity[8]. These cognitive processes may create an environment in which symptoms are more commonly perceived and reported[3,9]. This relationship is supported by findings from studies using annual measurements of mood and VMS, which suggest that anxiety[10] and depressive symptoms[11–14], both precede and predict the onset of self-reported VMS in later years. This is also supported by a study of ambulatory mood and VMS assessment, in which self-reported VMS, not confirmed by physiologic evidence of VMS occurrence, was more likely following acute emotional arousal[7].

Alternately, VMS may have a negative impact on mood. Women often report distress and embarrassment due to VMS, particularly when they occur in public. VMS may precede negative mood by activating negative schemas and triggering feelings of lack of control, embarrassment, and shame[15], or by disturbing sleep, leading to functional impairment and negative mood[16]. This relationship is supported by studies using annual measurements of mood and VMS, in which VMS in the years preceding the onset of mood symptoms predicted the development of depressive symptoms later in the menopausal transition[17].

While both directional theories linking VMS to mood are plausible and supported largely by annually collected data, a more definitive analysis requires shorter durations between assessments. Only one study has examined the relationship between VMS and mood on a day-to-day basis. Burleson et al.[18] examined 252 contiguous daily ratings from 55 healthy middle-aged women of to determine if VMS predicted next day mood. In this sample, VMS was significantly associated with decreases in next day positive mood, but not with increases in next day negative mood. Analysis of interactions suggested that the relationship between VMS and positive mood was seen only in individuals with low or moderate depression scores at baseline. Analyses did not examine whether mood predicted next day VMS, and were further limited by the high socioeconomic status of the racially homogenous sample.

In the current study, we sought to replicate the commonly found association between negative affect and VMS in a large, multiethnic sample, using daily measures of VMS and affect as opposed to annual retrospective measures. We also examined the directional relationship between VMS and negative affect on a day-to-day basis, determining whether VMS predicts next day negative affect, and whether negative affect predicts next day VMS.

Methods

Participants

The 625 women in the present analysis were drawn from the Daily Hormone Study, a substudy of the Study of Women's Health across the Nation (SWAN). SWAN is a multiethnic, community-based natural history cohort study of 3,302 women at seven sites across the United States followed annually as they approach and traverse the menopause. The details of recruitment and enrollment have been reported elsewhere in detail[19]. Briefly, eligible women were, at baseline, aged 42–52 years, self-identified with one of five racial/ethnic groups (Caucasian, African-American, Chinese, Japanese, or Hispanic), reported at least one menstrual period in the prior 3 months, did not use sex-steroid hormones in the prior 3 months, had an intact uterus and at least one ovary, and were not currently pregnant or breastfeeding[20].

The same eligibility criteria were used for the Daily Hormone Study. Of the women in the SWAN cohort, 1,443 were screened, 1,219 were eligible, and 848 (69.6%) agreed to participate and provided a sufficiently complete cycle at the first DHS year, with 651 participating at year 3 of the DHS. Reasons for discontinuation or non-participation in DHS year 3 included current or recent (within the previous 3 months) HT use (n=65), fertility medication use (n=1), and oral contraceptive use (n=3), bilateral oopherectomy (n=7), more than one year of amenorrhea (n=7) (women were eligible in the first year of becoming postmenopausal), refusal or inability to participate in that year's DHS visit (n=40), and attrition from SWAN (n=74). Women who had a hysterectomy were eligible as long as they retained one or both ovaries. Year 3 of the DHS was chosen as the analytic sample because it is comprised of a larger percentage of perimenopausal women (81.2%) relative to earlier years, the time in which participants are likely to report VMS[1]. Participants completed daily diaries over a period of 12–50 days (mean 33.91, SD 10.85), and were excluded from analysis if they were missing daily diary data on VMS and affect on all observations (n=26). The 26 excluded women were more likely to be from the New Jersey site ($p<.01$), to be Hispanic ($p<.01$), to have a high school education or less ($p<.01$), to report fair/poor self-rated health ($p=.02$), and to have a higher BMI ($p=.02$) than the 625 women in the final analytic sample (data not shown).

Procedure

DHS enrollees rated mood and physical symptoms that had occurred within the preceding 24 hours in diaries at the end of each day. Participants were instructed to complete these diaries daily for the duration of an entire menstrual cycle ending in bleeding or 50 days, whichever came first. Women who did not have a bleeding cycle coincident with 1-year follow-up began on the next convenient day and collected for 50 days or until a menstrual cycle began. Women who had no menses for the 12 months before an annual follow-up kept a daily diary for 25 days[20]. The start date of the DHS was scheduled within 6 months of the SWAN core visit.

Measures

Diary measures of symptoms—Women rated how strongly they felt 14 mood and physical states (happy, bored, headaches, blue/down, tired, aches/pains, calm, forgetful,

mood swings, irritable, anxious, confident/in control, difficulty concentrating, feelings easily hurt) in the last 24 hours, on a 4 point scale from not at all (1) to a lot (4). They indicated whether hot flashes/night sweats, trouble sleeping, and abdominal pain/cramps (all yes/no) had occurred in the last 24 hours.

A principal components analysis with oblique rotation in SPSS[21] on the 14 items of the daily diary yielded three factors. The first component was comprised of seven items related to negative mood: mood swings, feelings easily hurt, irritable, difficulty concentrating, forgetful, anxious, and blue/down. This component explained 39.0% of the variance, and had a Cronbach's alpha of .87. The mean of these seven items each day for each participant was used to create daily and overall mean composite negative mood variables., These scores were dichotomized for analysis due to their significantly skewed distribution, with scores ≥2 indicating the presence of negative mood. Two was chosen as the cutoff because it represented a meaningful value on the likert scale, dividing endorsing symptoms “not at all” to “a little bit” or more. The second component was comprised of 3 items related to positive mood: confident/in control, happy, and calm. This factor explained 10.2% of the variance, and had a Cronbach's alpha of .77. Daily and overall mean composite positive mood variables were created from the ratings of these three items for each participant, and treated as continuous variables. The third factor was composed of 3 items related to somatic symptoms: headaches, tired, and aches/pains. This factor explained 8.0% of the variance, and had a Cronbach's alpha of .64. This factor was not considered in this analysis.

Covariates—Potential covariates were selected due to their associations with VMS and negative mood in the literature. Covariates considered were site, age, education, and race (White, African American, Chinese, Hispanic, or Japanese), drawn from baseline, and physical activity, self-rated health, body mass index (BMI), smoking, menopausal status, and antidepressant use, assessed anually and drawn for this analysis from the annual SWAN visit preceding and most proximal to DHS data collection. Education was determined using one question that asks the highest grade completed or degree attained[22], and coded as high school or less, some college, and completed college or post-college. Physical activity was assessed with the Kaiser Physical Activity Survey (KPAS)[23], an adaptation of the Baecke physical activity questionnaire[24]. Self-rated health was assessed by response to the following question: “In general, would you say your health is excellent, very good, good, fair or poor?”. Responses were categorized into four categories, with responses of “fair” and “poor” collapsed into a single category. Body mass index (BMI) was calculated using weight (kg) and height $(m)^2$ and categorized (underweight/normal: <25; overweight: 25–30; obese: >30). Smoking status (never, ever, current) was self-reported at each visit. Menopausal status was assessed annually in SWAN and was defined as indeterminant (preand perimenopasual women who used hormones in the past year), premenopausal (bleeding in the last 3 months with no cycle irregularity in the previous 12 months), early perimenopausal (bleeding in the last 3 months with some change in cycle regularity in the last 12 months), late perimenopausal (bleeding >3 months ago but within the last 12 months), postmenopausal (no bleeding in the last 12 months). Menopausal status was collapsed into three categories: premenopausal, perimenopausal (early and late perimenopausal), and postmenopausal. For this analysis, records were reviewed to reclassify women defined as indeterminant as premenopausal (n=1) or perimenopausal (n=9), based on their status at annual visits before and after the annual visit coinciding with their DHS data collection. Current antidepressant use was self-reported in response to questions about medications used currently and in the previous year during each annual SWAN visit.

Analytic plan

We assessed differences between those women who ever reported vasomotor symptoms over the observed time period and those who did not were assessed using logistic regression. We assessed associations between potential covariates and overall positive mood with linear regression. Descriptive analysis was conducted to evaluate the overall proportions of days that women experienced mood and VMS over the observed period.

We examined daily observations, nested within women, with two-level hierarchical generalized linear models (HGLM). To examine daily associations between negative affect and VMS, daily negative affect was regressed on same day VMS; in separate models, daily VMS was regressed on same day negative affect. To examine the day-to-day temporal associations between affect and VMS, we utilized lagged analysis. Specifically, negative affect at time t, adjusted by vasomotor symptoms at time t, was examined as a predictor of vasomotor symptoms at time t+1; vasomotor symptoms at time t, adjusted by negative affect at time t, was examined as a predictor of negative affect at time t+1. The daily-level intercept was regressed on woman-level covariates. A similar approach was used to evaluate the association between positive mood and VMS. Race/ethnicity, menopausal status, self-rated health, age, and education were included as covariates in final models with VMS or positive affect as the outcome; race/ethnicity, menopausal status, self-rated health, and antideprssant use were included as covariates in final models with negative affect as the outcome. We used SPSS v. 17[21] to conduct univariate analyses of overall associations, and HLM 6.08[25] to run hierarchical generalized models of daily associations between affect and VMS.

Results

Characteristics of sample

Participants represented the racial/ethnic diversity of SWAN (30.6% White, 22.9% Japanese, 19.7% Black, 19.5% Chinese, 7.4% Hispanic), and were largely perimenopausal (81.6%), and well-educated (44.8% with a college or professional degree), with an average age of 48.8 at the time of data collection. Over the observed period, 52.3% of participants (n=327) ever reported VMS (table 1). Ever reporting VMS varied by race, age, menopausal status, self-rated health, and site, and was associated with higher mean negative mood and lower mean positive mood over the course of the daily diary collection (table 1). The odds of reporting daily VMS were also increased among women with less education. Most of the variance (95%) in daily VMS reporting was seen between women, with 5% of the variance occurring within women's daily observations.

In univariate models, the odds of reporting daily negative mood were lower among older women and black (compared to white) women, and higher among perimenopausal (compared to premenopausal) women, and among women reporting antidepressant use and poorer self-rated health (data not shown). Most of the variance (96%) in daily negative mood reporting was seen between women, with 4% of the variance occurring within women's daily observations. The odds of reporting daily positive mood were increased among women with more education, in younger and black (compared to white) women, and lower among perimenopausal (compared to premenopausal) women, and among women reporting poor self-rated health. Most of the variance (64%) in positive mood reporting was seen between women, with 36% of the variance occurring within women's daily observations.

Daily Covariance of VMS and Negative Affect

VMS and negative affect were significantly associated with each other within each 24-hour period (table 2). Older age, poorer health, and perimenopausal status (compared to premenopausal status) increased the likelihood of reporting VMS on a given day, while being Chinese was associated with reduced odds of daily VMS (table 2). Similar results were found when daily negative affect was set as the outcome and VMS was the predictor (data not shown).

Negative Affect as a Predictor of Next Day VMS

Negative mood, adjusted by same day VMS, was not associated with next day VMS. In the fully adjusted model, previous day VMS, older age, poor health, and perimenopausal status was associated with increased odds of reporting next day VMS; being Chinese was negatively associated with next day VMS (table 3).

VMS as a Predictor of Next Day Negative Affect

VMS, adjusted by same day negative affect, was significantly associated with next day negative affect in unadjusted and adjusted models. In the fully adjusted model, previous day VMS, previous day negative mood, antidepressant use, poorer health, and perimenopausal status were each associated with increased odds of reporting negative mood the next day. Older women and Black women were less likely to report next day negative mood (table 4).

Secondary analyses

Negative mood was replaced with positive mood in a secondary analysis. VMS and positive affect were negatively associated with each other within each 24-hour period. No relationship was seen between positive affect and next day VMS, or between VMS and next day positive affect (data not shown).

Race/ethnicity and BMI were explored as potential moderators of the relationship between daily VMS and negative affect, VMS and next day negative affect, and negative affect and next day VMS. No significant cross-level interactions were found, indicating that race/ethnicity and BMI do not moderate these relationships (data not shown).

Because poor sleep is associated with negative mood, and self-reported sleep disruption is often attributed to night sweats[16], sleep difficulty was explored as a potential factor that might account for the association between self-reported VMS and next day negative affect. After adjusting for VMS within the same 24 hour period, as well as race/ethnicity, menopausal status, age, and antidepressant use, , self-reported trouble sleeping was significantly associated with next day negative mood, OR = 1.97 (95% CI 1.64-2.38), $p < .001$. The addition of trouble sleeping to the model reduced the significant relationship between previous day VMS and next day negative mood from OR= 1.27 (95% CI 1.03-1.58), $p < .001$ (table 4), to a trend, OR= 1.24 (95% CI .99-1.56), $p = .06$ (data not shown).

Discussion

It has been well established that measures of negative affect and VMS are associated among women during the menopausal transition. However, methodological limitations of traditional symptom measurement have limited our ability to interpret this relationship. This study utilized prospective daily diary reports of mood and VMS to expand our current understanding of the commonly found relationship between these factors by examining both the daily and day-to-day associations between them. In this sample of women in midlife,

higher average negative affect over the course of daily diary collection was associated with an increased risk of ever reporting VMS. On a day-to-day basis, higher negative affect was positively associated with VMS within each 24-hour period. This relationship was maintained regardless of whether negative affect or VMS was the predicted outcome. Our results suggest that the often-reported association between negative affect and VMS is present on a daily basis, even with the retrospective reporting bias limited by a short recall period.

The more novel aspect of the study was to determine the directionality of effect between negative affect and VMS. Negative affect was examined as a predictor of next-day VMS, while in separate models VMS was considered as a predictor of next-day negative affect. In this sample, negative affect, adjusted by same day VMS, was not associated with next day VMS. In contrast, VMS, adjusted by same day negative mood, was associated with next day negative mood. Our finding is consistent with the notion that VMS may lead to negative mood over time via activation of negative schemas about aging and the self, and perhaps to chronic poor sleep attributable to disruptive night sweats. The inclusion of a rating of sleep quality in the daily diaries allowed us to examine the latter possibility. Adding sleep quality into the model reduced the association between VMS and next day negative mood to a trend, but the amount of variance accounted for was small, with the odds ratio reduced only by .03. Given the crude sleep measure, however, it is important that sleep is assessed with a more rigorous measure in future research. Other explanatory factors also remain to be explored. It is also possible that a third factor not assessed here may contribute to the risk of both negative mood symptoms and VMS. Estrogen withdrawal may impact hypothalamic thermoregulatory centers as well as serotonergic, adrenergic, and noradrenergic systems[5], systems that may play a role in VMS and mood.

These findings are partially consistent with Burleson et al.[18], which found that VMS preceded next-day negative mood in women, with a small but significant role of sleep in explaining this relationship. However, Burleson et al.[18] saw this relationship only in women with low levels of depressive symptoms at baseline. They also found an association between VMS and decreased next day positive affect, which was not replicated in this study. The ethnic diversity and low levels of negative mood generally reported in this sample may have contributed to differences in findings.

Several commonly reported correlates of typical retrospectively measured VMS were also seen with the overall and daily reports of VMS in this prospective daily diary collection. As with past investigations, the risk of ever reporting VMS increased with age[1], poorer health[26], and perimenopausal status[1]. The risk of reporting VMS on any given day was also associated with these factors, as well as with postmenopausal status and lower educational attainment. These associations were consistent with past investigations of annually-measured VMS[1,27], and, with the exception of educational attainment, maintained when entered into models simultaneously. Some factors commonly associated with VMS did not increase risk of VMS reporting in this sample. Foremost among these were race/ethnicity and BMI. While overall and daily VMS reporting varied significantly by race/ethnicity, this effect was driven by the reduced reporting seen only in Chinese women relative to other ethnic groups. Based on past assessments of VMS reporting by race, it was expected that VMS reporting would also be higher among Black women than White women[1]. However, daily prospective reporting, with decreased retrospective bias, may better sample the true symptom experience of this population. Additionally, BMI had no association with VMS in this sample, though increased BMI is related to increased risk of VMS in numerous cross-sectional and longitudinal studies, including SWAN[28].

Some additional findings in this study deserve mention. Past studies utilizing retrospectively self-reported VMS have indicated that VMS occur on a daily basis at some point in the menopausal transition for 20–25% of women[10]. The findings of this study suggest that the majority of women who experience VMS do not have them daily; only 6.1% of symptomatic women reported VMS on every observation, while 56.7% of symptomatic women reported symptoms on just 2–30% of their daily observations. Prospective daily diary reporting may provide a more accurate representation of symptom frequency, with limited retrospective recall bias and error. The menopausal transition is also considered a vulnerable period for higher levels of depressive symptoms[29]. In this sample, prospective ratings of negative mood were very low, with most women reporting no to little endorsement of negative mood symptoms on a daily basis. In contrast, positive mood ratings were consistently relatively high, though more variable within women than negative mood ratings. This snapshot of the menopausal transition did not appear to represent a period of highly negative mood as measured with prospective daily reports in our large, multiethnic, largely perimenopausal sample. However, it should be noted that women in the DHS had to be quite compliant, and may represent a group with overall more positive mood than the larger SWAN cohort that they were drawn from.

Several limitations of this study should be noted. As previously discussed, the time at which VMS occurred within the 24-hour interval was not determined. Whether associations seen between mood and VMS were driven by hot flashes or night sweats cannot therefore be examined. Within-day frequency, severity, and bother of VMS were also not assessed, and these characteristics of VMS experience may play an important role in the relationship between daily VMS and daily mood[3]. Different relationships may also have been seen if physiologic VMS measures, rather than just self-report, had been assessed[7]. Interpretation of these findings is also limited by the low levels and limited heterogeneity of daily negative mood reported in this sample, as the negative mood reported may not be of meaningful severity. Further, 24-hour periods may not have been the appropriate timeframe in which to see effects, particularly an association between negative affect and subsequent VMS. In Thurston et al.[7], self-reported VMS not confirmed by physiologically measured evidence of VMS occurrence was more likely within 30 minutes of negative emotional arousal. Negative affect may therefore have an acute impact on the perception and reporting of VMS, which would not have been captured over this extended period. Finally, participation in DHS is demanding; in addition to annual SWAN visits, these women complied with annual completion of a month or more of daily diaries and daily urine collection. The generalizeability of this highly compliant, highly motivated sample may be limited.

This study also has considerable strengths. Foremost among these is the contribution of prospective daily measurement of mood and VMS, rather than the typical retrospective recall of symptom experience in previous weeks. This both confirms the stable relationship typically seen between these factors and elucidates the relationship between these transient and fluctuating factors on a day-to-day basis, adjusting by stable woman-level characteristics related to symptom experience. The size of the sample and length of data collection lends validity, model stability, and the ability to examine over 21,000 separate observations. The multiethnic makeup of the sample provides valuable information about symptom experience in understudied populations. Finally, the large number of symptomatic women in this sample provided novel information about day to day symptom experience in a diverse sample of women in the menopausal transition.

Conclusions

This study contributes to our knowledge about the relationship between negative affect and VMS. Assessment of temporal relationships between negative affect and reported VMS

suggests that VMS precedes elevated daily negative affect, while daily fluctuations in negative affect do not increase the likelihood of reported VMS. VMS may be impacting mood by way of sleep disturbance attributable to night sweats. Women with VMS may be at increased risk for subsequent negative mood symptoms, as well as for sleep difficulty that may have a broad impact on mood, health, and daily functioning. Health care practitioners should be aware of this potential detrimental effect of VMS experience in menopausal women, and consider addressing VMS as an appropriate route to alleviating sleep difficulty and mood symptoms as well as VMS in the menopausal transition. This study takes us one step closer toward better understanding the relationship between negative mood and VMS, which may help inform intervention strategies to improve quality of life and health in women as and after they traverse the menopause.

Acknowledgments

The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

Supported by Cardiovascular Behavioral Medicine Training Grant NIH T32 HL 007560.

Clinical Centers: University of Michigan, Ann Arbor - MaryFran Sowers, PI; Massachusetts General Hospital, Boston, MA - Joel Finkelstein, PI 1999 - present; Robert Neer, PI 1994 – 1999; Rush University, Rush University Medical Center, Chicago, IL - Howard Kravitz, PI 2009 - present; Lynda Powell, PI 1994 – 2009; University of California, Davis/Kaiser - Ellen Gold, PI; University of California, Los Angeles - Gail Greendale, PI; Albert Einstein College of Medicine, Bronx, NY - Rachel Wildman, PI 2010; Nanette Santoro, PI 2004 – 2010; University of Medicine and Dentistry - New Jersey Medical School, Newark - Gerson Weiss, PI 1994 – 2004; and the University of Pittsburgh, Pittsburgh, PA - Karen Matthews, PI.

NIH Program Office: National Institute on Aging, Bethesda, MD - Marcia Ory 1994 – 2001; Sherry Sherman 1994 - present; National Institute of Nursing Research, Bethesda, MD - Program Officers.

Central Laboratory: University of Michigan, Ann Arbor - Daniel McConnell (Central Ligand Assay Satellite Services).

Coordinating Center: University of Pittsburgh, Pittsburgh, PA - Kim Sutton-Tyrrell, PI 2001 -present; New England Research Institutes, Watertown, MA - Sonja McKinlay, PI 1995 – 2001.

Steering Committee: Susan Johnson, Current Chair Chris Gallagher, Former Chair

We thank the study staff at each site and all the women who participated in SWAN. a

References

1. Gold EB, Colvin A, Avis N, et al. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. American Journal of Public Health. 2006; 96:1226–1235. [PubMed: 16735636]
2. Woods NF, Mitchell ES, Landis C. Anxiety, hormonal changes, and vasomotor symptoms during the menopause transition. Menopause. 2005; 12:242–245. [PubMed: 15879910]
3. Thurston RC, Bromberger JT, Joffe H, et al. Beyond frequency: who is most bothered by vasomotor symptoms? Menopause. 2008; 15:841–847. [PubMed: 18521049]
4. Bromberger JT, Meyer PM, Kravitz HM, et al. Pscychologic distress and natural menopause: A multiethnic community study. American Journal of Public Health. 2001; 91:1435–1442. [PubMed: 11527777]
5. Joffe H, Hall JE, Soares CN, et al. Vasomotor symptoms are associated with depression in perimenopausal women seeking primary care. Menopause. 2002; 9:392–398. [PubMed: 12439097]

6. Thurston RC, Sutton-Tyrrell K, Everson-Rose SA, Hess R, Matthews KA. Vasomotor symptoms and subclinical cardiovascular disease: findings from the Study of Women's Health Across the Nation Heart Study. Circulation. 2008; 118:1234–1240. [PubMed: 18765392]
7. Thurston RC, Blumenthal JA, Babyak MA, Sherwood A. Emotional antecedents of hot flashes during daily life. Psychosomatic Medicine. 2005; 67:137–146. [PubMed: 15673636]
8. Keefe FJ, Lumley M, Anderson T, Lynch T, Studts JL, Carson KL. Pain and emotion: New research directions. J Clin Psychol. 2001; 57:587–607. [PubMed: 11255208]
9. Hanisch LJ, Hantsoo L, Freeman EW, Sullivan GM, Coyne JC. Vasomotor symptoms and panic attacks: a comparison of symptomatology, neurobiology, treatment, and a role for cognition. Psychological Bulletin. 2008; 134:247–269. [PubMed: 18298271]
10. Freeman EW, Sammel MD, Lin H, Gracia CR, Kapoor S, Ferdousi T. The role of anxiety and hormonal changes in menopausal vasomotor symptoms. Menopause. 2005; 12:258–266. [PubMed: 15879914]
11. Freeman EW, Sammel MD, Grisso JA, Battistini M, Garcia-Espagna B, Hollander L. Hot flashes in the late reproductive years: risk factors for African American and Caucasian women. Journal of Women's Health. 2001; 10:67–76.
12. Freeman EW, Sammel MD, Lin H. Temporal associations of hot flashes and depression in the transition to menopause. Menopause. 2009; 16:728–734. [PubMed: 19188849]
13. Guthrie JR, Dennerstein L, Taffe JR, Lehert P, Burger HG. Hot flushes during the menopause transition: A longitudinal study in Australian-born women. Menopause. 2005; 12:460–467. [PubMed: 16037762]
14. Sabia S, Fournier A, Mesrine S, Boutron-Ruault MC, Clavel-Chapelon F. Risk factors for onset of menopausal symptoms: results from a large cohort study. Maturitas. 2008; 60:108–121. [PubMed: 18513898]
15. Hunter MS, Mann E. A cognitive model of menopausal hot flushes and night sweats. Journal of Psychosomatic Research. 2010; 69:491–501. [PubMed: 20955869]
16. Joffe H, Soares CN, Petrillo LF, et al. Treatment of depression and menopause-related symptoms with the serotonin-norepinephrine reuptake inhibitor Duloxetine. Journal of Clinical Psychiatry. 2007; 68:943–950. [PubMed: 17592922]
17. Dennerstein L, Guthrie JR, Clark M, Lehert P, Henderson VW. A population-based stud of depressed mood in middle-aged, Australian-born women. Menopause. 2004; 11:563–568. [PubMed: 15356410]
18. Burleson MH, Todd M, Trevathan WR. Daily vasomotor symptoms, sleep problems, and mood: using daily data to evaluate the domino hypothesis in middle-aged women. Menopause. 2010; 17:87–95. [PubMed: 19675506]
19. Sowers, MF.; Crawford, SL.; Sternfeld, B., et al. Design, survey, sampling and recruitment methods of SWAN: a multi-center, multi-ethnic, community-based cohort study of women and the menopausal transition. In: Lobo, RA.; Kelsey, J.; Marcus, R., editors. Menopause: Biology and Pathobiology. Academic Press; San Diego: 2000. p. 175-188.
20. Skurnick JH, Weiss G, Goldsmith LT, Santoro N, Crawford S. Longitudinal changes in hypothalamic and ovarian function in perimenopausal women with anovulatory cycles: relationship with vasomotor symptoms. Fertility and Sterility. 2009; 91:1127–1134. [PubMed: 18499105]
21. SPSS for Windows, Rel. 17.0.0. SPSS Inc.; Chicago: 2008.
22. Centers for Disease Control and Prevention. National Center for Health Statistics. DHHS Publication No. (PHS) 94-1308. US Government Printing Office; Washington DC: 1994. Vital and Health Statistics, Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988–94.
23. Sternfeld B, Ainsworth BE, Quesenberry CP. Physical activity patterns in a diverse population of women. Preventive Medicine. 1999; 28:313–323. [PubMed: 10072751]
24. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. American Journal of Clinical Nutrition. 1982; 36:936–942. [PubMed: 7137077]
25. HLM for Windows, Rel. 6.08. Scientific Software International, Inc.; Lincolnwood, IL: 2009.

26. Dennerstein L, Dudley EC, Guthrie JR. Predictors of declining self-rated health during the transition to menopause. Journal of Psychosomatic Research. 2003; 54:147–153. [PubMed: 12573736]

27. Schwingl PJ, Hulka BS, Harlow SD. Risk factors for menopausal hot flashes. Obstetrics and Gynecology. 1994; 84:29–34. [PubMed: 8008318]

28. Thurston RC, Sowers MR, Sternfeld B, et al. Gains in body fat and vasomotor symptom reporting over the menopausal transition: the study of women's health across the nation. American Journal of Epidemiology. 2009; 170:766–774. [PubMed: 19675142]

29. Bromberger JT, Schott LL, Kravitz HM, et al. Longitudinal change in reproductive hormones and depressive symptoms across the menopausal transition: results from the Study of Women's Health Across the Nation (SWAN). Archives of General Psychiatry. 2010; 67:598–607. [PubMed: 20530009]

Table 1

Characteristics of Sample according to Ever Reporting Vasomotor Symptoms (VMS)

% (n) or mean (SD)	Total (n=625) *n, column %*	VMS (n=327, 52.3%) *n, column %*	No VMS (n=298, 47.7%) *n, column %*	p-value
Site				.01
Michigan	63 (10.1)	38 (11.6)	25 (8.4)	.04
Boston	68 (10.9)	43 (13.1)	25 (8.4)	.02
Chicago	68 (10.9)	46 (14.1)	22 (7.4)	<.01
UC-Davis	175 (28.0)	81 (24.8)	94 (31.5)	.55
UCLA	143 (22.9)	70 (21.4)	73 (24.5)	.36
New Jersey	46 (7.4)	23 (7.0)	23 (7.7)	.41
Pittsburgh	62 (9.9)	26 (8.0)	36 (12.1)	Referent
Race/ethnicity				.02
White	191 (30.6)	111 (33.9)	80 (26.8)	Referent
Black	123 (19.7)	73 (22.3)	50 (16.8)	.83
Chinese	122 (19.5)	50 (15.3)	72 (24.2)	<.01
Hispanic	46 (7.4)	23 (7.0)	23 (7.7)	.72
Japanese	143 (22.9)	70 (21.4)	73 (24.5)	.69
Education				.24
College/post-college	278 (44.8)	137 (41.9)	141 (47.3)	Referent
Some college	198 (31.9)	104 (31.8)	94 (31.5)	.09
High school/<hs	145 (23.3)	84 (25.7)	61 (20.5)	.49
Self-rated health				.03
Excellent	100 (16.2)	45 (13.8)	55 (18.5)	Referent
Very good	238 (38.4)	116 (35.5)	122 (40.9)	.53
Good	208 (33.6)	114 (34.9)	94 (31.5)	.11
Fair/poor	73 (11.8)	48 (14.7)	25 (8.4)	.01
Categorical BMI				.65
Normal/underweight (<=24.9)	269 (43.5)	134 (41.0)	135 (45.3)	Referent
Overweight (25–30)	162 (26.2)	87 (26.6)	75 (25.2)	.43
Obese (>30)	187 (30.3)	100 (30.6)	87 (29.2)	.44
Smoking status				.83
Current smoker	57 (9.2)	295 (90.2)	268 (89.9)	
Current non-smoker	563 (90.8)	29 (8.9)	28 (9.4)	
Menopausal status				<.01
Premenopausal	84 (13.4)	28 (8.6)	56 (18.8)	Referent
Perimenopausal	510 (81.6)	284 (86.9)	226 (75.9)	<.001
Postmenopausal	30 (4.8)	15 (4.6)	15 (5.0)	.11
Antidepressant use				.13
Yes	60 (9.6)	37 (11.3)	23 (7.7)	

% (n) or mean (SD)	Total (n=625) *n, column %*	VMS (n=327, 52.3%) *n, column %*	No VMS (n=298, 47.7%) *n, column %*	p-value
No	565 (90.4)	290 (88.7)	275 (92.3)	

	Mean, SD	Mean, SD	Mean, SD	
Age	48.80 (2.51)	48.99 (2.48)	48.58 (2.55)	.04
Physical activity	7.69 (1.73)	7.73 (1.73)	7.68 (1.70)	.74
Negative mood	1.66 (.57)	1.74 (.61)	1.56 (.49)	<.001
Positive mood	2.86 (.64)	2.79 (.63)	2.94 (.64)	<.01

Abbreviations: Vasomotor symptoms (VMS), body mass index (BMI), standard deviation (SD)

P-values drawn from logistic regression models or t-test with all variables entered independently.

Table 2

Multivariate association between negative mood and VMS within a 24 hour period

	Daily VMS	
	OR (95% CI)	**p-value**
Negative mood	1.72 (1.39–2.13)	<.001
Age	1.15 (1.04–1.28)	.01
Education		
College+	Referent	
Some college	1.57 (.84–2.92)	.16
High school or less	1.60 (.80–3.21)	.19
Health		
Excellent	Referent	
Very Good	.76 (.35–1.68)	.50
Good	1.27 (.56–2.90)	.57
Fair/poor	3.70 (1.21–11.35)	.02
Race/ethnicity		
White	Referent	
Black	.86 (.40–1.83)	.69
Chinese	.26 (.13–.54)	<.01
Hispanic	.48 (.14–1.68)	.25
Japanese	.52 (.25–1.05)	.07
Menopausal status		
Premenopausal	Referent	
Perimenopausal	3.09 (1.50–6.38)	<.01
Postmenopausal	5.17 (1.01–26.39)	.05

Abbreviations: Vasomotor symptoms (VMS)

All daily-level predictors and woman-level covariates simultaneously entered into hierarchical generalized linear models with VMS as a dichotomous outcome with a Bernoulli distribution.

Age has been grand-centered; all other variables entered uncentered.

Table 3

Multivariate associations between previous day negative mood and next day vasomotor symptoms (VMS)

	Next day VMS	
	OR (95% CI)	**p-value**
Previous day VMS	8.96 (7.55–10.64)	<.001
Previous day negative mood	1.07 (.85–1.35)	.55
Age	1.11 (1.02–1.20)	.02
Education		
College+	Referent	
Some college	1.48 (.90–2.42)	.12
High school or less	1.64 (.94–2.84)	.08
Self-rated health		
Excellent	Referent	
Very Good	.85 (.45–1.59)	.60
Good	1.27 (.65–2.45)	.49
Fair/poor	2.88 (1.20–6.91)	.02
Race/ethnicity		
White	Referent	
Black	.92 (.50–1.69)	.80
Chinese	.34 (.19–.60)	<.001
Hispanic	.49 (.18–1.33)	.16
Japanese	.57 (.32–.99)	.05
Menopausal status		
Premenopausal	Referent	
Perimenopausal	2.57 (1.42–4.64)	<.01
Postmenopausal	3.60 (.98–13.19)	.05

Abbreviations: Vasomotor symptoms (VMS), odds ratio (OR), confidence interval (CI)

All daily-level predictors and woman-level covariates simultaneously entered into hierarchical generalized linear models with VMS or negative mood as a dichotomous outcome with a Bernoulli distribution.

Age has been grand-centered; all other variables entered uncentered.

Table 4

Multivariate associations between prior day vasomotor symptoms (VMS) and next day negative mood

	Next day negative mood	
	OR (95% CI)	**p-value**
Previous day VMS	1.27 (1.03–1.58)	.01
Previous day negative mood	4.86 (4.20–5.62)	<.001
Age	0.90 (0.83–0.98)	.01
Antidepressant use	2.57 (1.37–4.82)	<.01
Self-rated health		
Excellent	Referent	
Very Good	2.42 (1.24–4.05)	<.01
Good	3.54 (1.90–6.60)	<.001
Fair/poor	8.74 (4.03–18.96)	<.001
Race/ethnicity		
White	Referent	
Black	.41 (.23–.73)	<.01
Chinese	.82 (.45–1.50)	.52
Hispanic	1.38 (.53–3.53)	.51
Japanese	.81 (.48–1.40)	.46
Menopausal status		
Premenopausal	Referent	
Perimenopausal	2.80 (1.58–4.95)	<.01
Postmenopausal	.70 (.22–2.18)	.53