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How self-reported hot flashes may relate to affect, cognitive performance and sleep

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ABSTRACT

Purpose: To explain the controversy about whether midlife women who self-report hot flashes have relatively increased affective symptoms, poor cognitive performance or worse sleep.
Methods: Retrospective data from 88 women seeking relief from bothersome day and night hot flashes were submitted to mixed linear regression modeling to find if estimated hot flashes, as measured by Women's Health Questionnaire (WHQ) items, or diary-documented hot flashes recorded daily, were associated with each other, or with affective, cognitive or sleep measures.
Results: Subjects averaged 6.3 daytime diary-documented hot flashes and 2.4 nighttime diary-documented hot flashes per 24 h. Confounder-controlled diary-documented hot flashes but not estimated hot flashes were associated with increased Leeds anxiety scores ($F = 4.9$; $t = 2.8$; $p = 0.01$) and Leeds depression scores (3.4; 2.5; 0.02), decreased Stroop Color–Word test performance (9.4; 3.5; 0.001), increased subjective sleep disturbance (effect size = 0.83) and increased objective sleep disturbance (effect size = 0.35). Hot flash effects were small to moderate in size. Univariate but not multivariate analyses revealed that all hot flash measures were associated with all affect measures. Different measures of hot flashes associated differently with affect, cognition and sleep. Only nighttime diary-document hot flash consistently correlated with any affect measures in multivariate analyses.
Conclusions: The use of differing measures for hot flashes, affect, cognition and sleep may account for the continually reported inconsistencies in menopause study outcomes. This problem impedes forging a consensus on whether hot flashes correlate with neuropsychological symptoms.

1. Introduction

Vasomotor symptoms, herein termed hot flashes, are the cardinal complaints of menopause [1–3]. They constitute an important health problem because they distress many women, sometimes for decades [4–10].

Experts cannot agree on whether a midlife woman's hot flashes entail increased neuropsychological symptoms, such as those related to mood, cognition or sleep [11–14,9,15–40]. Dennerstein thought the "diversity of opinion" about increased depression in midlife women was due to "methodologic problems" such as comparing different types of studies, "disciplinary bias" and "difficulties in classification, and how data are gathered, such as by rating scales vs. interviews." [41].

We studied the effect of different hot flash measures collected in women motivated to seek clinical relief from the were associated with differences in measures of affective, cognitive or sleep variables. We found that affective measures were mostly explained by a non-specific tendency to express negative affects through somatic symptoms. Worse performance on only one cognitive test was associated with hot flash measures. Only diary-documented hot flash measures were associated with objectively monitored sleep. We suggest that the continuing inconsistency of menopause study outcomes results from the use of different self-report measures to evaluate identically termed symptoms.

2. Materials and methods

2.1. Study design

The current study used previously collected data from a nutritional supplement trial for hot flashes to compare associations

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between five different measures of subjective hot flashes with cognitive, affective and sleep variables.

2.2. Study sample

Healthy, postmenopausal volunteers, ages 45 to 66 years, who were bothered by hot flashes and not using estrogen therapy (ET), were recruited by general newspaper and hospital bulletin board advertisements or from a primary care practice. Inclusion criteria: no menstrual periods for the past 12 months, not including exogenous estrogen-elated-related bleeding; at least five hot flashes during a 24-h period; no exogenous estrogen used for at least 60 days before study entry; agreement to take no new medications, hormones, or nutritional supplements except multivitamins during the study. Exclusion criteria: body mass index (BMI) greater than 34; systolic blood pressure greater than 160 mmHg; diastolic blood pressure greater than 95 mmHg; breast cancer within the last 5 years of, endometrial hyperplasia, known or suspected neoplasia, alcoholism, abnormal vaginal bleeding; active thrombophlebitis or thromboembolic disorders; cerebral or coronary vascular disease; liver disease; abnormal vaginal bleeding; active thrombophlebitis or thromboembolic disorders; cerebral or coronary vascular disease; liver disease; use of hypnotics, sedatives; antidepressants or addiction medication, concurrent participation in another clinical trial or use of an experimental medication or device in the 30 days before beginning the study; acute systemic infection within 7 days before study start; anticipated shift work during the study or history of shift work within the past 6 months.

3. Measures

We used 5 hot flash self-report measures to avoid relying on any single measure. Two baseline measures were adopted from the Women's Health Questionnaire (WHQ) developed for use in normal populations and validated by a study of 682 women, of whom 70% had been postmenopausal, none had had oöphorectomy and 8% had used estrogen treatment [40]. Daytime estimated hot flashes were measured by WHQ item score for "I have hot flashes." Nighttime estimated hot flashes were measured by the item score for "I suffer from night sweats." These items were chosen for their face validity and clinical relevance. They were scored as Present, for the responses "Yes, definitely" or "Yes, sometimes," or Absent for "No, not much" or "No, not at all." The third hot flash measure was the standardized WHQ hot flash factor score, which combines the previously described two items and weights them as in the original validation study [38]. The fourth and fifth measures were numbers of daytime hot flashes and nighttime hot flashes in subjects' daily diaries, presented here as weekly averages. Anxiety and Depression were measured at baseline and visit 4 by their appropriate WHQ factor scores and by factors extracted from the Leeds Anxiety and Depression scales [43].

The WHQ incorporated some items from each of these two scales verbatim, omitted some, and added others. The WHQ anxiety factor included Leeds anxiety items for fright or panic, agoraphobia, palpitations or "butterflies" in stomach or chest, omitted the Leeds items for restlessness, irritability and fearfulness and added an item for tense or "wound up" feelings. The WHQ depression factor included Leeds depression items for sad affect and losses of interest, enjoyment or appetite, omitted the Leeds items for insomnia and suicidal thoughts and added an item for feelings of well-being.

We entered the WHQ somatization factor into analyses as a confounder variable. This factor measures a general tendency to self-report symptoms, as indicated by items for sickness or nausea feelings, dizzy spells, pins and needles in hands and feet, pain in limbs or back, tiredness, headaches and urinary frequency.

We measured motor speed and cognitive status by computerized performance tests [44] that previously proved sensitive to subtle hormonal changes in menopausal women [45]. These tests included:

(1) The 30-s finger-tapping test of motor speed. Subjects are instructed to repeatedly press a button as fast as possible to produce the maximum number of button presses. Motor speed reportedly varies with age and cerebral dopamine activity [46].
(2) The 6-min continuous performance test of selective attention. Subjects are instructed to view individual alphabet letters displayed at 1 per second and to push a button as rapidly as possible only when the letter 'X' appears. Selective attention hypothetically reflects estrogen effects on a number of neurotransmitters and receptor types in a distributed brain network [47–50].
(3) The 7-min switching attention test. Two different 2-choice discrimination tasks are each presented one at a time in random order about every 3 s. Each trial starts with the display of the cue word, "side" or "direction," indicating which of the two tasks to perform. The next display instructs the subject to push a button located either on the same side of the screen that a box appears on or else a button located on the side of the screen towards which an arrow in the box points. This test engages executive functions, such as working memory, directional sense, suppression of primed responses, and the planned shifting of mental set, as described elsewhere [45].
(4) The 6-min Color–Word test. About every 3 s, a monitor screen displays a word denoting a color. Subjects are instructed to push a button only when the word displayed is shown in the color it denotes, e.g., when the word "red" is shown in red, rather than in yellow, green or blue. This test measures the inhibition of automatic decision-making, as putatively mediated in frontal brain networks [51].

Subjective sleep was measured by 7-day averaged data recorded on the St. Mary's Hospital Sleep Questionnaire [52]. This questionnaire was chosen for its brevity, good test-retest reliability, previous validation in older people, and previous use in a study of midlife women [53]. We analyzed 11 questionnaire items, of which 6 addressed subjective sleep quality: difficulty falling asleep; depth of sleep; early morning awakening; how well the subject slept; how clear-headed she felt on arising; and how satisfied she was with that night's sleep. The number of item response options ranged from 4, for difficulty falling asleep ("None or very little" to "Extreme difficulty") to 8 for depth of sleep ("Very light" to "Very deep"). Subjective sleep was measured by the first item factor previously extracted by factor analysis with varimax rotation in a population of comparable women. This factor had explained 99% of variance in subjective sleep among midlife women [54], and was weighted most heavily ($r < |0.6|$) by items for sleep depth, how well the subject slept, sleep satisfaction and clear-headedness, and was termed "goodness of sleep." The remaining 5 items were quantitative sleep measures, namely: bedtime; estimated time to sleep onset; number of times awoke; arising time and total amount of sleep.

Objective sleep was measured by motor activity recorded by an actigraph on the non-dominant wrist. Sleep/wake actigraphy scores agree with standard polysomnography scores 85% to 95% of the recording period [55]. Present data consist of 7-day averages of specific sleep measures. Factor analysis with varimax rotation had been previously used to reduce objective sleep measures into first and second factors, which explained 51% and 33% of the variance. The first factor, "solidarity of sleep", was weighted most heavily with sleep fragmentation (negatively weighted), percent immobility time, mean length of immobility interval, sleep efficiency and mean sleep bout time. The second factor, "sleep length", was