

# Is physical activity beneficial for hot flushes?

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**C**an physical activity help resolve menopausal vasomotor symptoms (VMS)? In this article, we summarize the reports regarding physical activity and VMS and discuss biological mechanisms by which physical activity might exert a beneficial effect. The potentially mediating role of mood, quality of sleep, and/or body weight on the relation between physical activity and VMS will be reviewed, as will the clinical and public health implications of our current state of knowledge.

## Review of the literature

Approximately 27 published articles have explored the relation between physical activity and VMS (a complete reference list is available from the author). Generally, these studies have evaluated Caucasian populations in the United States, Australia, and Sweden; a few have included African Americans and other racial/ethnic groups.<sup>1-3</sup>

Most studies feature observational, cross-sectional designs: one had a case-control design,<sup>4</sup> and one cross-sectional study assessed physical activity prior to onset of VMS.<sup>6</sup> Two observational studies followed cohorts prospectively,<sup>1,2</sup> and 6 were randomized controlled trials. Assessment of physical activity ranged from response to a single global question to detailed recalls of activity duration, frequency, and mode.

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Exercise interventions in the randomized clinical trials usually featured moderate-intensity walking programs, 30 minutes a day, 3 to 5 days a week for 12 to 16 weeks. One intervention specifically evaluated increased intensity of exercise over time.<sup>6</sup>

Symptom assessment also varied: some studies considered frequency, severity, and/or bother as separate domains; others used a single measure or symptom frequency. No study has objectively measured VMS.

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Many observational studies had null findings, but 2 reported significantly increased risk of hot flushes in active women.<sup>5,7</sup> One showed increased risk only in women who were highly active at a younger age.<sup>5</sup> Other studies have reported protective associations: In one study, the prevalence of moderate to severe hot flushes in women in an exercise program was reported to be 21.5% compared with 43.8% in nonparticipants.<sup>8</sup> A more recent study<sup>9</sup> noted that highly active postmenopausal women had a lower prevalence of hot flushes compared with those who had little or no exercise (5% vs 14%-16%;  $P < .05$ ); however, 35% of the sample used hormone therapy (HT). HT users were more likely to be active than nonusers.

Perhaps the strongest observational data indicating a protective association of exercise on VMS comes from the longitudinal Melbourne Women's Midlife Health Project, which followed 438 women for 8 years.<sup>2</sup> At baseline, physical activity was not associated with VMS in this cohort<sup>10</sup>; however, women who at study initiation reported exercising every day were 49% less likely to report bothersome hot flushes during follow-up (odds ratio [OR] = 0.51; 95% confidence interval [CI] = 0.27-0.96). Over follow-up, decreases in exercise level were associated with increased VMS.

The results from randomized trials are inconsistent. Two trials (only one was designed to test a specific hypothesis about VMS) reported no effect of exercise on VMS; one reported a significant increase in hot flush severity in exercisers vs controls. In contrast, 2 small, short-term trials reported statistically significant reductions in frequency and severity of VMS. A 4-month intervention enrolling 164 previously sedentary women randomized either to a walking group, yoga, or a control group<sup>6</sup> showed decreased VMS in both arms relative to the control group; however, the differences were not statistically significant. Change in VMS appeared to be mediated by increases in physical fitness: participants who had the most pronounced improvement in fitness also had the most significant decrease in symptoms.

In summary, although the evidence for a protective effect of exercise on VMS is minimal, the literature is limited. Most studies had insufficient power to detect any potential effect.

## Potential biological mechanisms of VMS

Although the etiology of the hot flush is not fully understood, experiments suggest a variety of potential mediators, many of which are associated with exercise.

Studies suggest that an increase in the body's core temperature precedes the onset of a hot flush.<sup>11</sup> Potentially, a narrowing of the thermoregulatory zone triggers the event. This may result from a decrease in the threshold for sweating and/or an increase in the threshold for shivering.<sup>12</sup>

Stress is a precipitating factor for hot flushes<sup>13</sup>; therefore, neuroendocrine substances—which play a role in the stress response and affect thermoregulation at the level of the hypothalamus—may be implicated in their etiology.

Prior to hot flush onset, increased levels of brain norepinephrine (NE) are observed and are further elevated during episodes,<sup>11</sup> suggesting that hot flushes may result from imbalances in the autonomic system. The “stress-buffering” role of the parasympathetic nervous system may be inadequate to counter the increased activation of the sympathetic nervous system.<sup>14,15</sup> Heart rate variability—an indicator of reduced vagal control—appears to be reduced during the hot flush itself,<sup>16</sup> providing some empirical support for this hypothesis.

Increased cortisol levels are observed during the later stages of the menopausal transition. Higher cortisol levels are associated with higher epinephrine and NE levels as well as with more severe VMS<sup>17,18</sup> and may also indicate an imbalance in the autonomic nervous system.

Animal studies suggest that b-endorphins may play a role in the pathogenesis of the hot flush. Administration of naloxone, an opiate

antagonist, in morphine-dependent rats causes symptoms similar to those of the hot flush, as well as luteinizing hormone (LH) surge.<sup>19</sup>

However, in postmenopausal women, the infusion of naloxone has not consistently reduced the frequency of hot flushes or LH pulses.<sup>20</sup> Studies of plasma b-endorphin levels prior to hot flushes have also been contradictory,<sup>21,22</sup> although plasma levels may not reflect the endorphin levels in the brain.

## Physical activity and neuroendocrine responses

Physical activity might reduce the incidence of VMS because of associated neuroendocrine responses. In response to acute exercise, increases in brain NE and its metabolites occur. However, 24-hour urinary NE appears to decrease with training,<sup>23</sup> perhaps because of an increase in vagal tone.

Exercise training also results in decreased resting heart rate, typically ascribed to a shift of autonomic balance in favor of the parasympathetic nervous system. Several studies have shown that heart rate variability is greater in active women compared with sedentary women<sup>24</sup> and that variability improves in response to training.<sup>25</sup>

Physical activity could favorably affect the frequency or bother of VMS because release of endogenous opioids, particularly b-endorphins, is increased, particularly in response to a single, sustained bout of vigorous exercise.<sup>26</sup> Although it is not known whether b-endorphins are responsible for the so-called runner's high,<sup>27</sup> the endogenous opioids are biochemically similar to exogenous opiates and have physiologic effects of temperature regulation, decreased sensitivity to pain, and decreased heart and respiratory rates.

Exercise does cause an acute rise in core temperature. If symptomatic

women have a narrowed thermoregulatory zone, exercise might actually induce hot flushes. However, it is unclear how bothersome an exercise-induced hot flush would be, given the sweating that occurs with exercise.

## Physical activity and well-being in midlife

Studies of midlife women show that physical activity is directly related to positive mood, vigor, and general well-being.<sup>28-30</sup> It is inversely related to negative symptoms, such as depression, anxiety, problems with memory and concentration, decreased sexual desire, difficulty sleeping, and perceived stress.<sup>29,31-33</sup> Sleep, mood, and quality of life are often negatively impacted by the occurrence of VMS. Possibly, the beneficial effects of physical activity may affect the frequency, severity, or bother of VMS. The Harvard Study of Moods and Cycles demonstrated that a significantly lower risk of VMS was associated with higher levels of physical activity in women with a history of major depression,<sup>34</sup> suggesting the mediating effect of mood.<sup>34</sup>

## Sleep, mood, and quality of life are often negatively impacted by the occurrence of VMS.

Body weight may mediate the effect of physical activity on VMS: Heavier women report more VMS. Weight loss resulting from increased activity may be a crucial step in the relationship between increased activity and decreased VMS. However, no empirical evidence supports this hypothesis.

## Future directions

Clearly, we face many unanswered questions about physical activity and VMS. Does participation in regular

physical activity affect frequency, severity, bother of hot flashes, or duration of VMS over time? If so, does exercise improve or worsen VMS?

Does the “dose” of physical activity matter: Is vigorous-intensity exercise more effective than moderate-intensity exercise? Is mode of exercise (eg, aerobic vs resistance exercise) a factor? If physical activity is effective, how does it work?

Well-designed and adequately powered randomized trials are required to answer these questions.

Within the next few years, the Menopause Strategies: Finding Lasting Answers for Symptoms and Health (MsFLASH) research network will be testing a series of innovative treatments for menopausal symptoms in randomized controlled trials, including one on the efficacy of aerobic exercise.

Meanwhile, the existing evidence of the health benefits of regular physical activity for midlife women suggests that all clinicians should prescribe regular physical activity to their patients, and that they be prepared to

discuss and problem-solve with their patients the barriers to becoming more physically active. One resource is “Exercise is Medicine” at [www.exerciseismedicine.org](http://www.exerciseismedicine.org). Public health professionals need to continue and enhance their ongoing efforts to promote physical activity among all midlife women. Even if regular physical activity does not prevent or treat VMS, the other health benefits that it confers will ensure both a healthy menopausal transition and healthy aging. ■

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