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Scientists Finally Understand Hot Flashes—and How to Stop Them

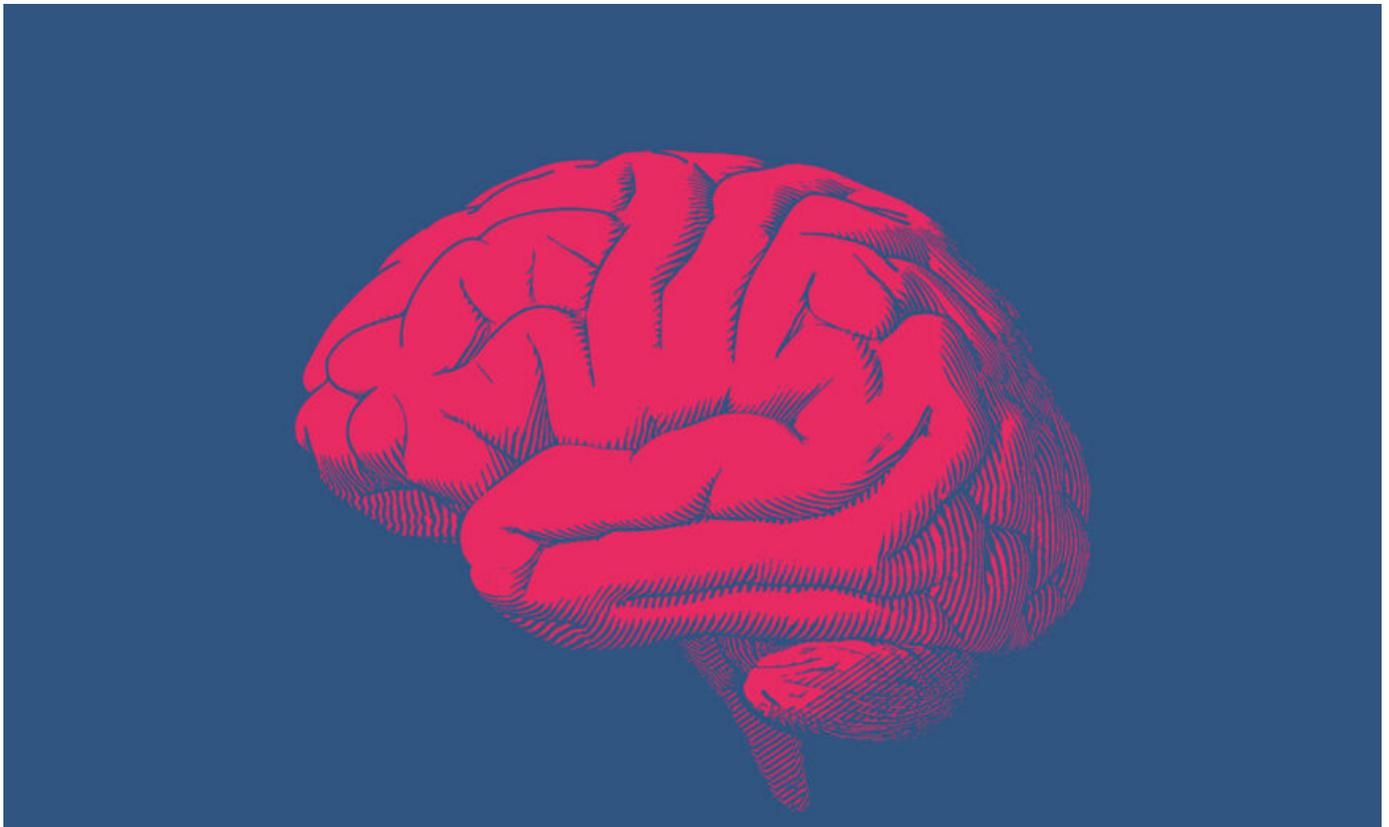
PREMIUM FEATURED HORMONES



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The dreaded hot flash—a sudden rush of incapacitating heat in the upper body, especially to the chest, neck, and face—sometimes accompanied by anxiety and rapid heartbeat. Hot flashes are an intense sensation that many women who are transitioning into [menopause](#) experience.

Any woman who has experienced a hot flash, or its “cousin,” night sweats, knows it is an unpleasant sensation. However, they may not have understood what is behind these bursts of intense heat, and neither did scientists.

Hot Flashes—It’s All in Your Head

Hot flashes and night sweats are associated with perimenopause and menopause. Although hot flashes and night sweats are linked with decreased estrogen in a woman’s body, the exact [cause](#) driving hot flashes is still unknown.

For years scientists had hypothesized that a part of the [brain](#), the hypothalamus (which controls hormone secretion), also played a role in hot flashes and night sweats since one function of the hypothalamus is [body temperature regulation](#)—but were unsure how.

Researchers got a clue about the mechanism of hot flashes and the hypothalamus over 30 years ago, explained Naomi E. Rance, M.D., Ph.D., professor of pathology, cellular and molecular medicine, and neurology at the University of Arizona, in an email to The Epoch Times. Rance, whose [research](#) on the topic was pivotal, noticed that there was a group of neurons in the hypothalamus of postmenopausal women that were increased in size due to a loss of estrogen.

Rance and her colleagues learned that the set of neurons, nicknamed KNDy neurons, release three different substances—kisspeptin, neurokinin B, and dynorphin—that each bind to a receptor. They also discovered that KNDy neurons contain estrogen receptors, meaning the neurons are estrogen sensitive. In response to decreased levels of estrogen, the KNDy neurons become more active and release neurokinin B. Once released, neurokinin B which binds with neurokinin 3 receptors (the primary receptor for neurokinin B) on the KNDy neurons and in the part of the hypothalamus that controls body temperature.

Studies in rats and mice showed that an increase in the activity of KNDy neurons (due to a loss of estrogen) could lead to “hot flushes” by releasing neurokinin B into an area of the hypothalamus that controls body temperature, explained Rance.

Further studies showed that blocking neurokinin 3 receptors could result in a decrease in hot flashes and night sweats related to menopause. In fact, a [2017 phase 2 clinical trial](#) demonstrated that women taking a daily neurokinin 3 receptor antagonist (blocker) had a significant reduction in the number of hot flashes they experienced. The study participants—women experiencing seven or more hot flashes a day—saw a 45 percent reduction in weekly hot flashes while on the neurokinin 3 receptor antagonist. Unfortunately, [clinical trials](#) also demonstrated that the risks associated with the medication exceeded the benefits it provided. Additionally, an elevation of liver enzymes was noted in study participants and further studies were discontinued.

A Cool New Treatment

Research on the role of the hypothalamus and KNDy neurons has led to the development of an experimental drug that could serve as a new, non-hormonal [treatment](#) for hot flashes. Fezolinetant, a medication created by Astellas Pharma Inc., is currently under review by the U.S. Food and Drug Administration (FDA) and works by blocking neurokinin 3 receptors. If approved, the drug may be available to patients in 2023.

[Phase 3 clinical trials](#) regarding fezolinetant's effectiveness appear promising. Studies have shown that fezolinetant is effective in reducing the frequency and severity of hot flashes at both the 30 mg and 45 mg daily dose of the drug. Research [data](#) on fezolinetant also showed that the drug reduced hot flashes by 2.5 to 4 episodes per day.

While efficacy is important, so is safety. SKYLIGHT 4, the most recent phase 3 clinical study studying the long-term safety of fezolinetant, confirmed the results of two previous phase three studies: SKYLIGHT 1 and SKYLIGHT 2.

In a [press release](#) from October 2022, Dr. Genevieve Neal-Perry, M.D., Ph.D., chair, UNC School of Medicine Department of Obstetrics and Gynecology, was quoted regarding the SKYLIGHT 4 study results. Neal-Perry is one of the researchers who participated in clinical trials of fezolinetant. She explained that the results “demonstrate the long-term safety and tolerability” of the drug and provide “further support for its potential use as a treatment” for hot flashes and night sweats.

On the day following the press release, Neal-Perry shared initial results from the [SKYLIGHT 4](#) phase 3 clinical trial at the North American Menopause Society's (NAMS) annual meeting, again showing that fezolinetant is a safe and effective treatment for hot flashes.

As with any medication, there is a cost-benefit ratio—fezolinetant is no exception. The study concluded that the side effects of fezolinetant were “generally mild to moderate in severity,” with headache named as one of the most common adverse events. Side effects were also reported with a similar frequency in participants receiving the placebo.

A small number of participants also experienced an increase in liver enzymes; however, according to the SKYLIGHT 4 trial, they were isolated and temporary, and usually resolved during or after treatment.

How to Manage Symptoms in the Meantime

[Kecia Gaither](#) is double board-certified in OB/GYN and maternal fetal medicine, as well as the director of perinatal services/maternal fetal medicine at NYC Health + Hospitals/Lincoln in the Bronx. She explained that access to a non-hormonal treatment for hot flashes and night sweats could be a boon to women navigating perimenopause and menopause.

The new drug potentially will be “a game changer for peri/postmenopausal women” who suffer from hot flashes and night sweats, said Gaither in an email to The Epoch Times. “As of this time, a paucity [few] of non-hormonal therapies exist.”

Prior therapy for hot flashes included hormone replacement therapy, “which carries certain health risks—like breast cancer, thrombotic phenomena, heart attacks and strokes,” explained Gaither.

Perimenopausal and post-menopausal women have been prescribed hormone therapy for many years to help alleviate a wide variety of symptoms—however, there are mixed opinions regarding its safety. A 2002 [study](#) conducted by the Women’s Health Initiative (WHI) showed an increased risk of breast cancer, stroke, cardiovascular disease, and blood clots in women who were taking estrogen and progesterone, which made many women refuse hormone treatment. Today, both types of hormone treatments are considered safer than the WHI suggests. The 2022 [North American Menopause Society’s \(NAMS\)](#) official position on hormone therapy states: “For women aged younger than 60 years or who are within 10 years of menopause onset and have no contraindications, the benefit-risk ratio is favorable.”

For women **who begin hormone therapy** 10 or more years from the start of menopause or age over 60 the risk associated with taking hormones is generally higher. Women in this group who are receiving hormone therapy have an increased chance of developing coronary heart disease, strokes, clots, and dementia.

Antidepressants have also been used to treat hot flashes. **Clinical studies** have shown that venlafaxine (Effexor), desvenlafaxine (Pristiq), paroxetine (Paxil), fluoxetine (Prozac), citalopram (Celexa), gabapentin (Neurontin), and pregabalin (Lyrica) may all help women get some relief from hot flashes.

Although no woman wants to have hot flashes or night sweats, not every woman wants to take medication to manage them.

A variety of **natural remedies** are also available to women suffering from hot flashes and night sweats including, but not limited to:

- Red clover.
- Dong Quai.
- Ginseng.
- Kava.
- Black Cohosh.
- Evening Primrose.
- **Magnesium.**

Supplements are not without risk and are not regulated by the FDA. Women should consult their physicians before taking any supplement product.

Dietary changes can also help women manage hot flashes. **Research** has shown that a plant-based diet that includes soybeans and limits foods high in fat may have a therapeutic effect on women. Avoidance of alcohol, caffeine, and spicy foods are easy diet changes that can also help reduce hot flashes.

Other alternative methods that may help lessen the frequency and severity of hot flashes and night sweats include **controlled breathing, relaxation techniques** and **acupuncture**.

Lifestyle changes can also help women stay cool. For women experiencing night sweats, keep the bedroom cool and layer bedding so it can be easily adjusted if things start feeling hot. To help manage hot flashes women can also:

- Dress in layers.
- Have a fan on at night and use a portable fan during the day.
- Quit smoking.

According to Gaither, maintaining a healthy body weight may also help lessen hot flashes.

“Heavier women tend to report having hot flashes more so than thinner women as body fat serves to act as an insulator and inhibits heat dissipation.”

The Takeaway for Women’s Health

Insight into the mechanisms behind hot flashes and the potential of a non-hormonal therapy to treat them is an important step forward in women’s health—one that couldn’t come soon enough for women suffering hot flashes and night sweats due to perimenopause and menopause.

Rance believes it is important to continue to fund research for issues that affect women’s health.

“In the case of hot flashes, for example, estrogen was the only effective treatment despite considerable controversy on the benefits versus the risks of this treatment,” she explained.

Now that scientists have a better understanding of the pathways in the brain that cause hot flashes, “we have the opportunity to develop new targeted treatments that do not rely on estrogen replacement,” said Rance.



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