

# THE ROLE OF THE HYPOTHALAMUS IN VMS

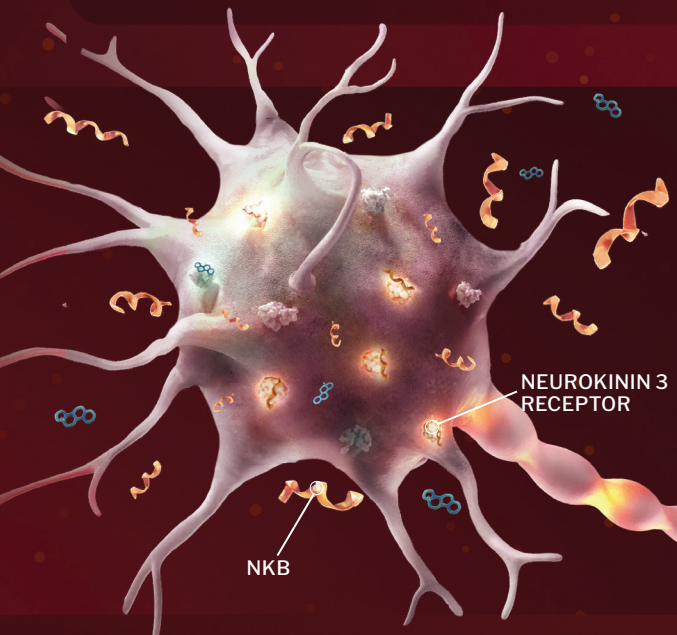
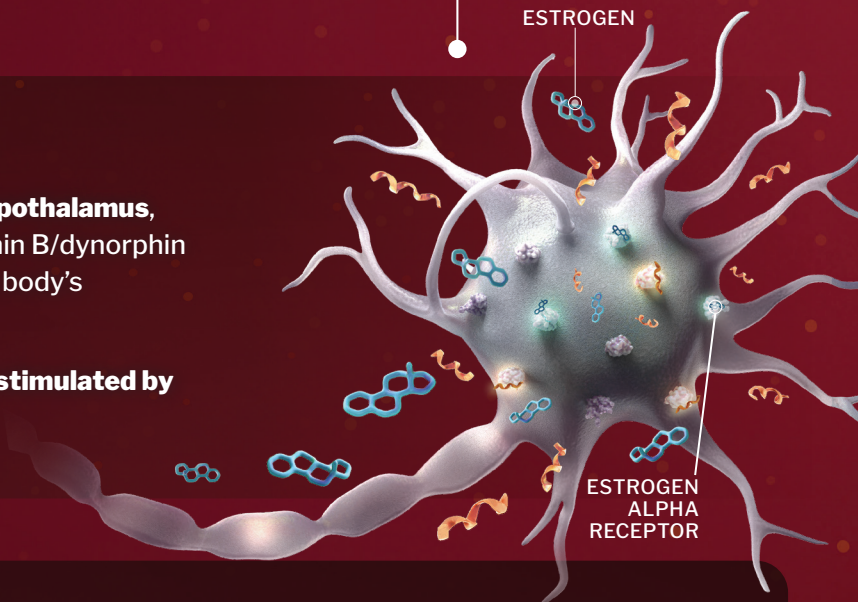
Recent scientific discoveries have shown that declining estrogen isn't the only cause of vasomotor symptoms (VMS) associated with menopause, commonly referred to as hot flashes and night sweats. **Take a closer look.**<sup>1-5</sup>



## Inside the source of VMS

### THERMOREGULATORY HOMEOSTASIS

- 1** Inside the thermoregulatory centre in the hypothalamus, specific neurons known as kisspeptin/neurokinin B/dynorphin (KNDy) neurons contribute to regulation of the body's temperature.<sup>1-3</sup>
- 2** KNDy neurons are inhibited by estrogen and stimulated by neurokinin B (NKB) in a delicate balance.<sup>1-3</sup>



### DURING THE MENOPAUSAL TRANSITION

- 3** Through the menopausal transition, estrogen declines, disrupting the balance with NKB. **Unopposed, NKB signalling causes increased KNDy neuronal activity**, which leads to hypertrophy of KNDy neurons and altered activity on the thermoregulatory centre.<sup>1,2,6</sup>
- 4** **As a result, the thermoregulatory centre triggers heat dissipation effectors** that are experienced as hot flashes and night sweats, or VMS.<sup>1,2,6</sup>

**References:** **1.** Padilla SL, Johnson CW, Barker FD, Patterson MA, Palmiter RD. A neural circuit underlying the generation of hot flashes. *Cell Rep.* 2018;24(2):271-7. **2.** Krajewski-Hall SJ, Blackmore EM, McMinn JR, Rance NE. Estradiol alters body temperature regulation in the female mouse. *Temperature.* 2018;5(1):56-69. **3.** Wakabayashi Y, Nakada T, Murata K, et al. Neurokinin B and dynorphin A in kisspeptin neurons of the arcuate nucleus participate in generation of periodic oscillation of neural activity driving pulsatile gonadotropin-releasing hormone secretion in the goat. *J Neurosci.* 2010;30(8):3124-32. **4.** Rapkin AJ. Vasomotor symptoms in menopause: physiologic condition and central nervous system approaches to treatment. *Am J Obstet Gynecol.* 2007;196(2):97-106. **5.** Modi M, Dhillon WS. Neurokinin 3 receptor antagonism: a novel treatment for menopausal hot flashes. *Neuroendocrinology.* 2019;109(3):242-8. **6.** Krajewski-Hall SJ, Miranda Dos Santos F, McMullen NT, Blackmore EM, Rance NE. Glutamatergic neurokinin 3 receptor neurons in the median preoptic nucleus modulate heat-defense pathways in female mice. *Endocrinology.* 2019;160(4):803-16.



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