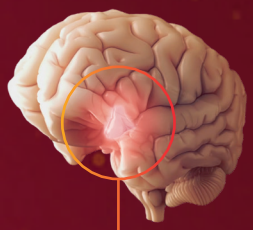
MENOPAUSAL VMS ARE MORE THAN JUST A HOT FLUSH



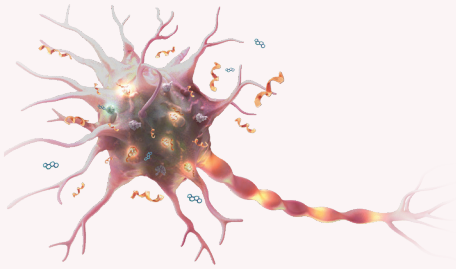
Over 10 years of research has clearly established that vasomotor symptoms (VMS), also known as hot flushes and night sweats, are caused by a decline in oestrogen. This decline triggers hyperactivity of KNDy neurons, a known source of VMS. [1-3]

Inside a known source of VMS

1 In the brain's thermoregulatory centre, hypothalamic KNDy neurons are stimulated by neurokinin B (NKB) via NK3 receptor and inhibited by oestrogen[3]

2 As oestrogen declines during menopause, unopposed NKB signaling causes heightened KNDy neuronal activity, triggering VMS[3-5]

3 Among the known neurokinin receptors—NK1R, NK2R, NK3R—NK3R has been implicated as playing a key role in the pathophysiology of menopausal VMS[3]



The frequency and severity of VMS can be used as a predictor of chronic disease in the future, such as cognitive impairment, cardiovascular disease, and osteoporosis. Knowing more about how VMS work allows for a clearer understanding of the menopausal transition and the associated symptoms.[6]

KNDy=kisspeptin/neurokinin B/dynorphin; **NK1R**=neurokinin 1 receptor; **NK2R**=neurokinin 2 receptor; **NK3R**=neurokinin 3 receptor; **NKB**=neurokinin B; **VMS**=vasomotor symptoms.

References: 1. Rapkin AJ. Vasomotor symptoms in menopause: physiologic condition and central nervous system approaches to treatment. Am Obstet Gynecol 2007;196(2):97-106. **2.** Modi M, Dhillo WS. Neurokinin 3 receptor antagonism: a novel treatment for menopausal hot flushes. Neuroendocrinology 2019;109 (3):242-8. **3.** Padilla SL, Johnson CW, Barker FD, Patterson MA, Palmiter RD. A neural circuit underlying the generation of hot flushes. Cell Rep 2018;24(2):271-7. **4.** 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. **5.** Krajewski-Hall SJ, Blackmore EM, McMinn JR, Rance NE. Estradiol alters body temperature regulation in the female mouse. Temperature 2018;5(1):56-69. **6.** Biglia N, Cagnacci A, Gambacciani M, Lello S, Maffei S, Nappi RE. Vasomotor symptoms in menopause: a biomarker of cardiovascular disease risk and other chronic diseases? Climacteric 2017;20(4):306-12.

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