The Role of Histamine in Sleep and Wakefulness

- The hypothalamus is a critical "control center" for sleep-wake state stability and contains several neuronal systems (e.g., hypocretin and histamine) that help maintain stable sleep and wakefulness.[1-6]
- Histamine neurons originate only in the tuberomammillary nucleus (TMN) in the hypothalamus.[4]
- These neurons play an important role in promoting and stabilizing wakefulness* by:
  - Activating wake-promoting neurons[3,4,7]
  - Inhibiting REM sleep-promoting neurons (i.e., preventing ***REM at the Wrong Time***™)[3-5]
  - Inhibiting non-REM sleep-promoting neurons[3,4,7,8]
- Histamine plays an important role in disorders associated with sleep-wake state instability, such as narcolepsy.[4,7]

**Based on in vitro and in vivo animal studies.*

1. Shan L et al. *Nat Rev Neurol*. 2015;11(7):401-413. **2.** Bonnavion P et al. *J Physiol*. 2016;594:6443-6462. **3.** Scammell TE et al. *Neuron*. 2017;93(4):747-7655. **4.** Haas HL et al. *Physiol Rev*. 2008; 88(3):1183-1241. **5.** Saper CB et al. *Nature*. 2005;437(7063):1257-1263. **6.** Broughton R et al. *Electroencephalogr Clin Neurophysiol*. 1988;70:473-481. **7.** España RA et al. *Sleep*. 2011;34(7):845-858. **8.** Williams RH et al. *J Neurosci*. 2014;34(17):6023-6029.

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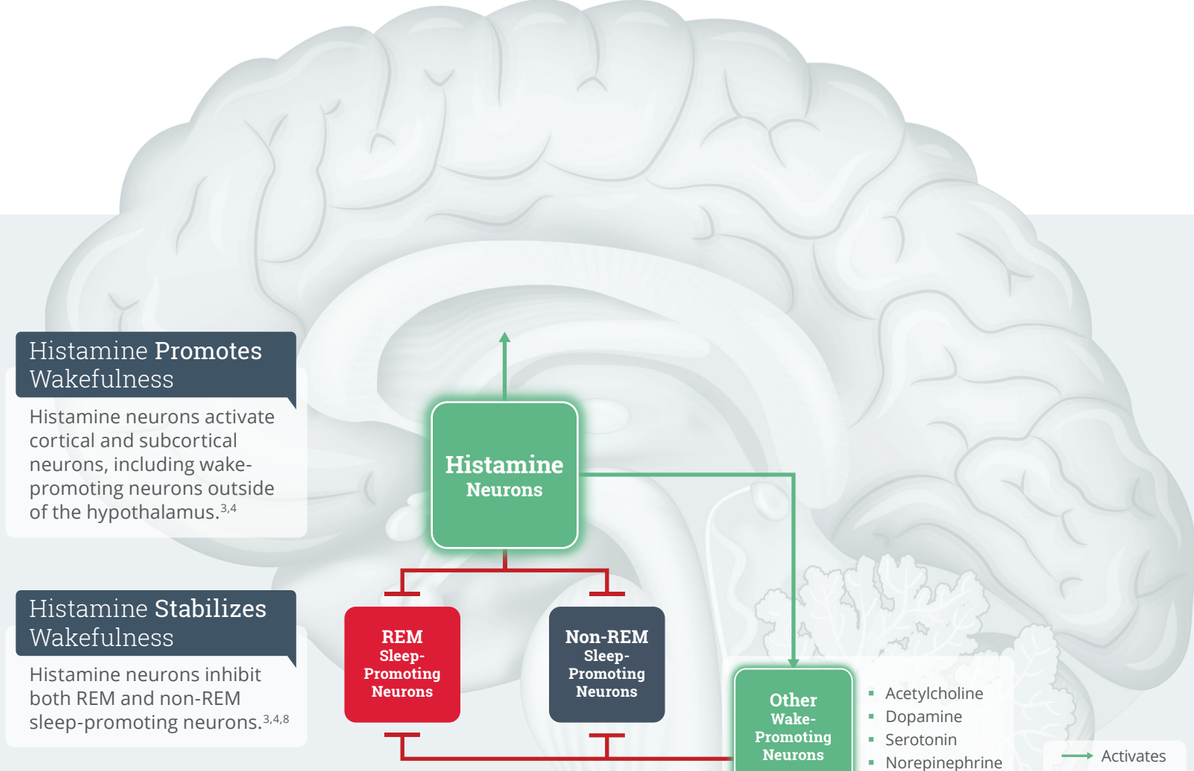
Histamine **Promotes** Wakefulness

Histamine neurons activate cortical and subcortical neurons, including wake-promoting neurons outside of the hypothalamus.[3,4]

Histamine **Stabilizes** Wakefulness

Histamine neurons inhibit both REM and non-REM sleep-promoting neurons.[3,4,8]



Graphic is for illustration purposes only and does not depict actual anatomical locations of neuronal systems.

Watch a video about the role of histamine at **KnowNarcolepsy.com/learn**