KNOW narcolepsy®

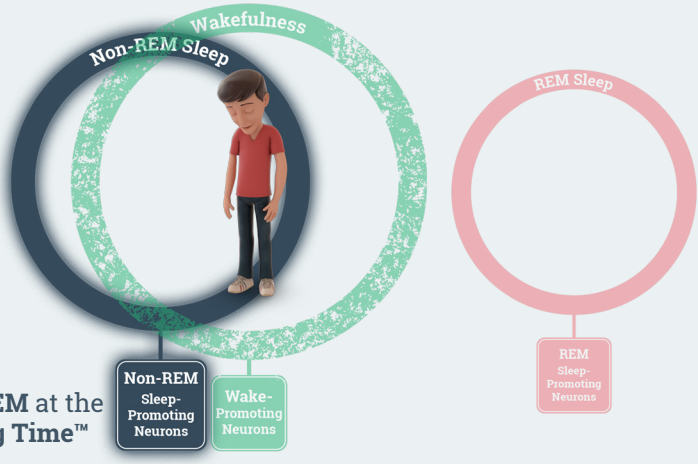
There's More to Know!

Rethinking Narcolepsy: A Disorder Characterized by Sleep-Wake State Instability

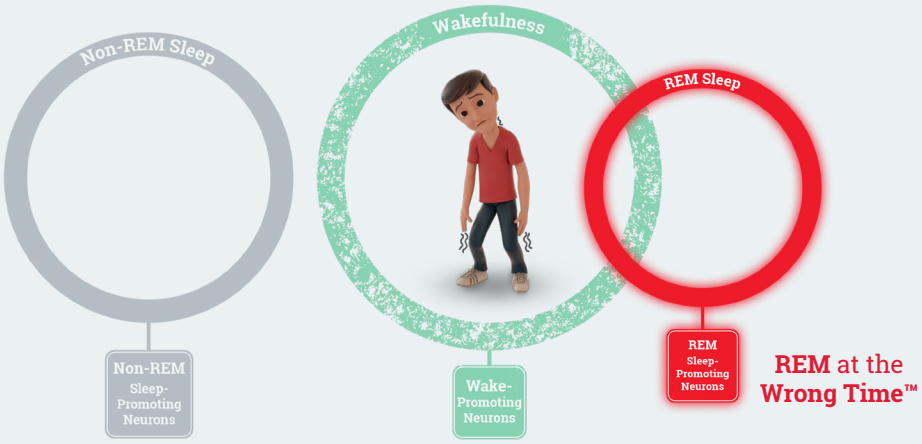
In most people with narcolepsy, loss of hypocretin neurons in the hypothalamus leads to sleep-wake state instability[1-3]

- Frequent, unpredictable transitions between sleep-wake states[3,4]
- Unstable boundaries allow elements of one state to intrude into another[4]

Excessive daytime sleepiness:
Non-REM sleep may intrude into wakefulness[2,5]



Cataplexy:
Elements of REM sleep (i.e., muscle atonia) may intrude into wakefulness[3,4]



The signs and symptoms of narcolepsy reflect the underlying sleep-wake state instability of the disorder, but the manifestations are not always obvious[2-4,6]

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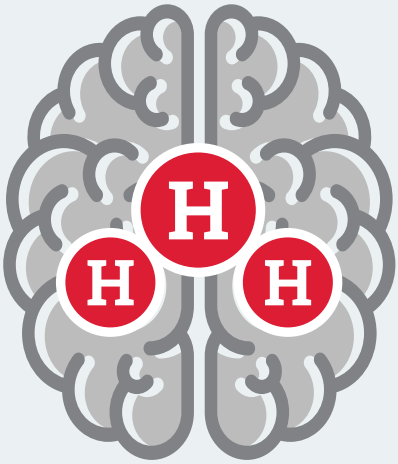
The Underlying Neuronal Processes Behind Stable Wakefulness



3Hs of Sleep-Wake State Stability™

Hypothalamus: A critical "control center" for sleep-wake state stability that contains neuronal systems that help stabilize wakefulness,[4,7-10] including:

- **Hypocretin** neurons
- **Histamine** neurons

Hypocretin and histamine neurons play complementary roles in wakefulness[11]

Like hypocretin neurons, histamine neurons help ***promote*** and ***stabilize*** wakefulness[8,10,12,13] by:

- Activating the cortex and select wake-promoting neurons outside the hypothalamus[12]
- Inhibiting REM sleep-promoting neurons[8,12]
- Inhibiting non-REM sleep-promoting neurons[10]

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