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## **Arousal**

Arousal is the physiological and psychological state of being awoken or of sense organs stimulated to a point of perception. It involves activation of the ascending reticular activating system (ARAS) in the brain, which mediates wakefulness, the autonomic nervous system, and the endocrine system, leading to increased heart rate and blood pressure and a condition of sensory alertness, mobility, and readiness to respond.

The principal neurons of the arousal and sleep circuits are comprised by glutamate and GABA neurons, which are distributed within the reticular core of the brain and, through local and distant projections orexin and interactions, regulate cortical activity, and behavior across wake-sleep states. These are in turn modulated by the neuromodulatory systems that are comprised by acetylcholine, noradrenaline, dopamine, serotonin, histamine, orexin (hypocretin), and melanin-concentrating hormone (MCH) neurons. Glutamate and GABA neurons are heterogeneous in their profiles of discharge, forming distinct functional cell types by selective or maximal discharge during (1) waking and paradoxical (REM) sleep, (2) during slow wave sleep, (3) during waking, or (4) during paradoxical (REM) sleep. The neuromodulatory systems are each homogeneous in their profile of discharge, the majority discharging maximally during waking and paradoxical sleep or during waking. Only MCH neurons discharge maximally during sleep. They each exert their modulatory influence upon other neurons through excitatory and inhibitory receptors thus effecting a concerted differential change in the functionally different cell groups. Both arousal and sleep circuit neurons are homeostatically regulated as a function of their activity in part through changes in receptors. The major pharmacological agents used for the treatment of wake and sleep disorders act upon GABA and neuromodulatory transmission 1).

Jones BE. Arousal and sleep circuits. Neuropsychopharmacology. 2019 Jun 19. doi: 10.1038/s41386-019-0444-2. [Epub ahead of print] Review. PubMed PMID: 31216564.

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