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### Research Interests

The brain responds to perturbation, irrespective of the nature of the stimulus. Brain responses to perturbation almost invariably include changes in behavior, which may be interpreted in a functional sense as designed to return systems to acceptable physiologic status. One behavior, sleep, is of particular interest because we do not know what sleep does for the brain. The critical nature of sleep is evidenced by how we feel when we do not get enough, and by the fact that prolonged sleep deprivation is fatal. Our research focuses on stressor-induced alterations in arousal state. Elucidating mechanisms by which stressors alter arousal state may shed some light on the fundamental question of what sleep does for the brain. We focus on two types of stressors, those that are psychological in nature (ie, no tissue injury, trauma, or physical insult), and infection. These classes of stressors overlap to a large extent in anatomical and chemical substrates activated, yet behavioral responses diverge; psychological stressors generally increase wakefulness and arousal, whereas infection increases sleep. To understand how different stressors that activate many of the same brain systems result in different behavioral outcomes, we focus on interactions in brain between neurotransmitters (corticotropin-releasing hormone [CRH], serotonin [5-HT]) and immune-active cytokines (interleukin [IL]-1). We have determined, for example that: blocking CRH actions in brain induces IL-1, which in turn increases in sleep; blockade of 5-HT<sub>2</sub> receptors interferes with changes in sleep normally induced by IL-1; that components of HIV are capable of altering sleep and upregulating IL-1 expression in brain; and that mice lacking a functional gene for an inhibitory cytokine, IL-10, not only sleep differently than intact animals in response to immune challenge, but also have altered sleep in the absence of any challenge. Collectively, results of these studies indicate that interactions in brain between neurotransmitters and immune-active substances are functionally relevant to the regulation of complex behavior. Whether the changes in sleep aid in recovery from challenge remains to be determined.



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