The glucocorticoid hormone cortisol is essential for many forms of regulatory physiology and for cognitive appraisal. Cortisol, while associated with fear and stress response, is also the hormone of energy metabolism and it coordinates behavioral adaptation to the environmental and internal conditions through the regulation of many neurotransmitters and neural circuits. Cortisol has diverse effects on many neuropeptide and neurotransmitter systems thus affecting functional brain systems. As a result, cortisol affects numerous cognitive domains including attention, perception, memory, and emotional processing. When certain pathological emotional states are present, cortisol may have a role in differential activation of brain regions, particularly suppression of hippocampal activation, enhancement of amygdala activity, and dendritic reshaping in these regions as well as in the ventral prefrontal cortex. The coordinated actions of glucocorticoid regulation on various brain systems such as those implicated in emotional processing can lead to perceptual and cognitive adaptations and distortions of events that may be relevant for understanding mood disorders.