

Abstract Submitted
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Dynamics of neuroendocrine stress response: bistability, timing, and control of hypocortisolism MARIA D'ORSOGNA, California State University at Northridge, TOM CHOU, LAE KIM, UCLA — The hypothalamic-pituitary-adrenal (HPA) axis is a neuroendocrine system that regulates numerous physiological processes. Disruptions in its activity are correlated with stress-related diseases such as post-traumatic stress disorder (PTSD) and major depressive disorder. We characterize “normal” and “diseased” states of the HPA axis as basins of attraction of a dynamical system describing the inhibition of peptide hormones, corticotropin-releasing hormone (CRH) and adrenocorticotrophic hormone (ACTH), by circulating glucocorticoids such as cortisol (CORT). Our model includes ultradian oscillations, CRH self-upregulation of CRH release, and distinguishes two components of negative feedback by cortisol on circulating CRH levels: a slow direct suppression of CRH synthesis and a fast indirect effect on CRH release. The slow regulation mechanism mediates external stress-driven transitions between the stable states in novel, intensity, duration, and timing-dependent ways. We find that the *timing* of traumatic events may be an important factor in determining if and how the hallmarks of depressive disorders will manifest. Our model also suggests a mechanism whereby exposure therapy of stress disorders may act to normalize downstream dysregulation of the HPA axis.

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