

Conserved Transcriptional Response to Adversity and Stress: Historical Roots, Neurobiological Mechanisms, and Yoga Interventions

Stress, defined as disruption of physiologic equilibrium by internal or external stimuli,¹ manifests through the conserved transcriptional response to adversity (CTRA), a genomic pattern of elevated proinflammatory and reduced antiviral gene expression.² Here, we examine the historical context of stress, CTRA's neurobiological mechanisms, and how yoga practices, rooted in ancient Indian traditions, counteract its effects, offering a synthesis of timeless insights and modern neuroscience.

Historical Perspectives on Stress and CTRA. The concept of stress has deep historical roots. Hans Selye developed the “general adaptation syndrome,” framing stress as a physiologic reaction to challenges.³ This milestone positions stress as a disruptor of equilibrium, with CTRA as its molecular correlate, driving inflammation and immune dysregulation.² Ancient Indian wisdom, particularly in the Bhagavad Gita, offers parallel insights. Arjuna symptoms—shaking body, burning skin, and overwhelming sorrow⁴—reflect sympathetic nervous system (SNS) and hypothalamic-pituitary-adrenal (HPA) axis activation, akin to CTRA's inflammatory effects.

Neurobiological Foundations of CTRA. CTRA is characterized by upregulated proinflammatory genes (eg, interleukin-6 and tumor necrosis factor-alpha [TNF- α]) and downregulated antiviral genes (eg, interferons), driven by the HPA axis and SNS.² This genomic shift fuels chronic inflammation, weakens immune defenses, and heightens risks for depression, anxiety, and infections.⁵ Neurobiologically, CTRA disrupts connectivity in the salience network (SN) and default mode network (DMN), reducing anterior cingulate cortex (ACC) volume and

impairing mesocortico-limbic pathways.⁶

Yoga Practices as CTRA Modulators. Yoga practices, including transcendental meditation, mindfulness (Vipassana), and Hatha yoga, draw from the Bhagavad Gita's call for mental balance.⁴ These interventions mitigate CTRA by reducing inflammation and enhancing immunity, as supported by neuroscientific evidence. Transcendental meditation, a mantra-based practice, lowers cortisol, heart rate, blood pressure, and proinflammatory cytokines (eg, TNF- α).⁷ Long-term practitioners (over 38 years) exhibit reduced CTRA gene expression, indicating enhanced stress resilience.² Transcendental meditation fosters parasympathetic dominance, countering SNS-driven inflammation and glucocorticoid resistance.^{5,7} Mindfulness-based meditation (Vipassana), practiced for over 2,500 years, promotes nonjudgmental awareness of mental and emotional states.⁸ It enhances vagal tone, reducing heart rate and CTRA-related inflammation. A 1-month mindfulness intervention increased ACC and medial prefrontal cortex (mPFC) activity, countering stress-induced neural changes and supporting emotional regulation.⁹ These effects restore DMN connectivity disrupted by CTRA.⁶ Hatha yoga, integrating postures and breath control, activates the dorsal ACC and SN, enhancing awareness of bodily states like pain or autonomic shifts.⁶ The right insula mitigates negative emotions, while the left amplifies positive ones, countering CTRA's emotional impact. Hatha yoga reduces cortisol, C-reactive protein, and blood pressure, directly addressing CTRA's inflammatory profile.⁷

Neurobiological Mechanisms of Yoga on CTRA. Yoga practices modulate CTRA through the psychoneuroimmunoendocrinology

(PNIE) axis. TM and mindfulness reduce HPA axis overactivity, lowering cortisol and inflammatory markers.⁷ Hatha yoga enhances SN connectivity, countering stress-induced hypervigilance, and restores DMN connectivity for improved self-reflection.⁶ These interventions mitigate glucocorticoid resistance and β -adrenergic signaling, which are key CTRA drivers.² Neuroimaging shows increased ACC/mPFC activity post yoga, correlating with reduced CTRA gene expression and improved mental health.⁹ CTRA links chronic stress to disease through inflammation and immune suppression, driven by SNS and HPA axis dysregulation. TM, mindfulness, and Hatha yoga counteract CTRA by reducing inflammatory gene expression and restoring neural connectivity. Individual variations in CTRA sensitivity, influenced by early adversity or genetics, emphasize the need for tailored interventions.⁵ As accessible practices, yoga and meditation address global mental health challenges, particularly post COVID-19.¹⁰

Yoga practices bridge ancient Indian wisdom and modern neuroscience, offering effective strategies to modulate CTRA and its neurobiological consequences. By targeting the PNIE axis and brain connectivity, transcendental meditation, mindfulness, and Hatha yoga reduce stress-induced inflammation and promote resilience. Integrating these practices into clinical care could address the rising burden of stress-related disorders, blending traditional insights with scientific advancements.

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