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The 5-HT7 receptor: A key mechanism of endocrine dysregulation in stress-related disorders?

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Chronic psychological stress is associated with behavioral and somatic disorders in modern society. Mediators of the stress response include the sympathetic nervous system and the hypothalamic-pituitary-adrenocortical (HPA) axis and their final mediators, adrenaline/noradrenaline, and glucocorticoids (i.e. cortisol in humans and corticosterone in rodents). These systems are modulated by brain neurotransmitters with serotonin (5-HT) playing an important role; indeed, drugs acting on this system (e.g. 5-HT uptake inhibitors) are prescribed clinically. HPA axis dysregulation involving hypercortisolemia is a common pathophysiological feature of stress-related disorders (SRD), such as major depression. Evidence suggests that chronic stress may lead to endocrine disruption and hypercortisolemia though the mechanisms involved remain unclear. It has been shown that relatively long periods of chronic stress may promote endocrine disruption, which translates into magnified corticosterone responses to acute stress in rodents. Interestingly, pharmacological blockade of 5-HT7 receptors normalized increased acute stress-induced corticosterone secretion in chronically stressed animals. Furthermore, disruption of the HPA axis by chronic stress was found to parallel increased expression of 5-HT7 receptors and increased 5-HT immunoreactivity in the adrenal cortex along with higher 5-HT levels and turnover in whole adrenals. Interestingly, ectopic expression of 5-HT7 receptors and increased potency of 5-HT to induce cortisol secretion via 5-HT7 receptors have been observed in human cortisol-producing adrenocortical adenomas. Remarkably, 5-HT7 receptor antagonists have been demonstrated to produce fast antidepressant-like effects and accelerate the antidepressant-like effects of several classes of antidepressant drugs. Then, blockade of 5-HT7 receptors, possibly at the adrenal level, might represent a novel therapeutic strategy in SRD.

Biography

Jose A Terron has completed his PhD at the age of 33 years from Centro de Investigación y de Estudios Avanzados del IPN (CINVESTAV-IPN) in Mexico City, and postdoctoral studies from McGill University, in Montreal, Canada, and the National Institute of Mental Health, in Maryland, USA. He is a full time Researcher at the Department of Pharmacology at CINVESTAV-IPN. He has published over 45 papers in reputed journals and serves as a reviewer of several international scientific journals, and reviewer of project proposals submitted to granting agencies such as the National Research Council of Mexico (CONACYT).

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