Abstract: Stress is the coordinated physiological processes to maintain a dynamic equilibrium under stressful conditions. The equilibrium is threatened by certain physiological and psychological stressors. Stressors trigger physiological, behavioural, and metabolic responses that are aimed at reinstating homeostasis. The hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic nervous system play an essential role in the stress response. Excessive, prolonged, or inadequate response that is termed as "allostasis" or "allostatic load" leads to pathological outcomes. Dysregulation of the HPA axis activity is involved in the pathogenesis of stress-related disorders including major depression. The complex brain-immune-endocrine network regulates the HPA axis, and hereditary predisposition as well as environmental factors such as traumatic experiences in early life also modifies the capacity of an individual to cope. Therefore, it is difficult to correctly assess the complex stress response. We have developed a microarray carrying 1,467 cDNAs that were selected to specifically measure stress response in peripheral blood leukocytes. Using this tool, we have succeeded to objectively assess individual response to acute psychological stress and to detect unique expression profiles in patients with depression. Gene expression profile in peripheral blood leukocytes may be a potentially useful for the detection of disease-associated, abnormal stress responses. J. Med. Invest. 52 : 137-144, August, 2005

Keywords: stress, allostasis, hypothalamus-pituitary-adrenal axis, stress assessment, microarray
Concept of “allostasis”

A. Normal

B. Lack of adaptation

C. Prolonged response

D. Inadequate response

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Regulation of the HPA axis

The hypothalamus regulates the release of hormones by the pituitary gland and the adrenal gland. The hypothalamus releases corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP) into the hypothalamo-pituitary portal system, which stimulates the anterior pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH then stimulates the adrenal cortex to produce glucocorticoids and mineralocorticoids. Glucocorticoids feedback to inhibit the release of CRH and ACTH, while mineralocorticoids have a similar effect on ACTH. Glucocorticoids also have a negative feedback effect on the hypothalamus and the pituitary gland.

Immune cells can also influence the HPA axis by producing cytokines such as interleukin-1 (IL-1) and interleukin-6 (IL-6), which can stimulate the hypothalamus to release CRH and AVP. This stimulation of the HPA axis by the immune system plays a role in the stress response and the regulation of immune function.

The HPA axis is regulated by various factors, including stress, sleep, and the circadian rhythm. The HPA axis is also involved in the regulation of body weight, metabolism, and blood pressure. Disorders of the HPA axis can lead to a variety of clinical conditions, such as Cushing's syndrome and adrenal insufficiency.
Neuro-immune-endocrine interactions

Development of a stress DNA chip

Gene expression profile in peripheral leukocytes from healthy students exposed to life event stress
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Future applications of stress DNA chip

The development of stress DNA chip holds great promise for the early detection and diagnosis of stress-related diseases. By analyzing the expression patterns of stress-induced genes, researchers can gain insights into the molecular mechanisms underlying stress responses and potentially identify novel targets for therapeutic interventions.

The diagram above illustrates the expression levels of various stress-related genes across different conditions. Each column represents a different sample or condition, while the rows correspond to individual genes. The color intensity reflects the magnitude of expression, with red indicating high expression and green indicating low expression.

This technology has significant implications for both research and clinical applications. In the context of mental health, stress DNA chips can help in the identification of early markers of stress-related disorders, which could lead to timely interventions and personalized treatments.

Moreover, stress DNA chip technology can also be applied to environmental monitoring, allowing for the assessment of stress levels in the environment and the potential impact on human health. This holistic approach can contribute to a better understanding of the complex interplay between stress, genetics, and environmental factors.
K. Rokutan, et al. Microarray for stress assessment