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ROLE OF STRESS IN ETIOPATHOGENESIS OF DISEASES AND ITS AYURVEDIC PERSPECTIVE – A REVIEW ARTICLE

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ABSTRACT

Stress plays a very Important role in manifestation of several Diseases. It Constitutes a State of threatened homeostasis triggered by intrinsic or extrinsic adverse factors (Stressors) and is counteracted by Physiological and Behavioural responses. The Adaptive Stress response depends upon highly interconnected neuroendocrine, cellular and molecular infrastructure i.e., Stress system includes Hypothalamic Pituitary Adrenal (HPA) and Autonomic Nervous System (ANS) which interact with other vital centers in the Central Nervous System. In Ayurveda the word *Sahasa* is used for Stress. *Chinta*, *Shoka*, *Bhaya*, *Pragnaparada* are main Causative factors for Stress where person's *Dhi*, *Dhruti*, *Smruti* gets impaired leading to *Dosa Prakopa*. It enhances the risk of Obesity, Anxiety, Depression, Diabetes mellitus, Thyrotoxicosis, Behavioural Disorders etc., and it responsible for *Ojakshaya* and manifest psychosomatic Diseases. Ayurveda provides the best Management for Stress like *Daivavyapasraya*, *Yukthivyapasraya*, *Satvavajaya* therapies along with lifestyle modifications like proper diet, Sleep, *Sadvrutta*, Yoga etc.

Keywords: Stressors, *Pragnaparada*, Anxiety, *Ojakshaya* .

INTRODUCTION: Stress commonly understood by society is completely different than that of Stress considered in Medical Science. General Anxiety Disorder[1] (GAD) as mentioned by Hans Selye as medical Stress vividly. Eustress contributes for positive achievements, Whereas Distress leads to many medical concerns.

Medical Stress is better understood by the mechanism of Limbic system, processed mainly through Amygdala and Hypothalamus. This maintains the equilibrium between an emotion perceived and expressed. Any deviation in this can lead to altered mental health. While Enumerating the Etiological factors, *Dharaneeya* (controllable), *Adharaneeya* (Non controllable) urges are contributing to both somatic and psychosomatic manifestation of Diseases[2]. *Bhaya* (Fear), *Lobha* (Greed), *Shoka* (Grief), *Krodha*[3] (Anger) etc. are considered as controllable urges. They are directly contributing for etiopathogenesis of General Anxiety Disorders w.s.r. to Stress and Anxiety.

Many Lifestyle Disorders are believed that they have direct relation with Stress either as etiological factor (or) plays a significant role in etiopathogenesis at one or other mechanism. For example: Hypertension, Coronary artery diseases,

peptic ulcer, Irritable bowel syndrome, Diabetes mellitus, Thyrotoxicosis, Behavioural disorders like Anxiety, Depression, Asthma, Migraine etc.

Satwa, Rajo, Tamo Gunas can be accessed through *shareeraka Doshas*. *Raja*[4] and *Tama guna* become dominant over *Sattva* that can increases Stress levels in individual. *Raja* is aggravated due to *Krodha*(Anger), *Chinta*(Anxiety), while *tamas* become aggravated due to *Bhaya*(Fear), *Shoka*(Grief) etc. When *Raja* and *Tamas* overcome the mind, it will result in manifestation of Stress. Hence Panchakarma procedure helps us to handle the gross pathogenesis to Disintegrate. Other modalities like *Medhya Rasayanas* and *Satwavajaya*, *Daivavyapasraya*[5] *Chikitsa* also contribute a Significant role in Medical Management of Stress.

AIMS & OBJECTIVES:

Stress system - Physiology and Interactions:

Neuroendocrine effectors of the Stress response -''The stress system ''

The Central components of the Stress system are located in Hypothalamus and Brain stem includes Corticotropin Releasing Hormone (CRH) and Arginine Vasopressin Neurons (AVN) of Paraventricular Nuclei of Hypothalamus and CRH neurons of Para Giganto Cellular & Parabrachial Nuclei of Medulla, Locus coeruleus (LC) and other Catecholaminergic [6], Nor Epinephrine (NE) synthesizing cell groups of medulla and pons (Central sympathetic nervous system). The Peripheral limbs of the Hypothalamic Pituitary Adrenal axis [7] (HPA) together with Efferent Sympathetic or Adreno Medullary System constitute the peripheral components of this Inter connected system.

Psychological theories of Stress:

The Physiological Arousal that thrusts the organism into action in response to a threat caused by activation of Autonomic Nervous System. Furthermore, activation of key structures of the Limbic system is fundamental in regulating the Stress response. The Amygdala is considered to be the threat detection centre of the brain, whereas the Hippocampus and Hypothalamus are of Vital Importance in perceiving the Danger and Generating the fear that drives the Stress response[8].

When faced with a Stressor[9], Corticotropin Releasing Hormone (CRH) is produced by Hypothalamic Paraventricular Nucleus (PVN), following excitation of Brain stem Catecholamine producing pathways that project to CRH containing nerves of Hypothalamic PVN. In turn Sympathetic and Para sympathetic activity is mediated by projections to Sympathetic and Para sympathetic Pre ganglionic neurons[10] in the Brain stem. Activation of Sympathetic Preganglionic and α1 Adreno receptors leads to an increase in Sympathetic arousal, whereas activation of Para Sympathetic pre ganglionic α2 adreno receptors is found to decrease para sympathetic activity. The Sympathetic division is crucial in activating the stress response whereas para sympathetic division hits the brakes on the stress response once the danger has paused.

LIMBIC SYSTEM:

It is a Complex network of Brain structures that are located Lateral to the Thalamus, beneath the Cerebral cortex, and above the Brainstem. The Components of Limbic system that plays a role in Stress includes Amygdala, Hypothalamus, Hippocampus, Cingulate cortex. The

limbic system[11] supports various functions including Emotion, Behaviour, Motivation, Long- term memory, Olfaction and Stress response.

ROLE OF AMYGDALA IN STRESS:

The Amygdala is therefore considered to be the threat detection[12] centre of the brain, receiving information from the environment about the nature of the stressor as well as drawing from memory to decide what risk the stimulus possess. Furthermore, the Amygdala regulates Hypothalamic PVN activity[13], where a stimulus is considered to possess a threat, activation of PVN leads to the production of CRH and the physiological experience of Stress[14]. The cognitive appraisal of the environmental stimulus or event is therefore further supported by our neurobiology understanding of threat detection and fear conditioning.

PHYSIOLOGICAL AND BIOLOGICAL ACCOUNTS OF STRESS:

The Hypothalamus mediates a number of basic functions of life ranging from appetite control, sleep, to regulate body temperature, reproductive behaviour and the stress response. When a threat happens, automatic arousal leads to the activation of two interrelated stress systems the Sympathetic Adrenal Medullary (SAM) and the Hypothalamic Pituitary Adrenal axis (HPA). so, activation of SAM and HPA axis leads to changes in Respiratory, Gastrointestinal, Cardiovascular, Immune and Central nervous system.

Activation of the Hypothalamic PVN produces an immediate, short acting stress response, as well as long acting Neurohormonal response through SAM and HPA axis. The Hypothalamic PVN produces CRH, which binds to receptors on the Anterior pituitary gland and stimulates the release of Adreno Corticotropic Hormone (ACTH). The release of ACTH act on adrenal cortex, which in turn releases androgens and glucocorticoids. Specifically, cortisol[15] the stress hormone. This chain of endocrine events describes the neurohormonal mechanisms of the HPA axis which drives the long-lasting stress response. Negative feedback is then exerted by cortisol on the hypothalamus and the anterior pituitary, inhibiting further release of CRH and ACTH restoring homeostasis. Basal ganglia located near the hypothalamus which is a part of responsible for voluntary movements.

The Hippocampus is part of Limbic system which regulates emotion and autonomic Behaviour. It shows negative feedback mechanism on HPA axis which releases glucocorticoids and Stress response. There are two Hippocampi on either hemisphere of the brain and they are the main memory areas in the brain. The main sub-structures of the hippocampus are the Dentate Gyrus (DG) and the Cornu Ammonis (CA). The DG is primarily related to spatial memory which corresponds to how the brain understands where the body is in time and space. It also allows a person to distinguish between different locations and objects, allowing for navigation and discrimination. Episodic memories are also associated with the hippocampus.

Stress can have opposing effects on the Hippocampus, including impairing Long-Term Potentiation (LTP) and enhancing Long-Term Depression (LTD). Stress can also alter Hippocampal Dendritic morphology and inhibit neurogenesis.

However, stress can disrupt Hippocampal functions such as memory and learning.

Fig:1 Behavioural and Physiological changes in response to Stress are influenced by Neurohormonal mediators that act on specific receptors in maintaining homeostasis and adaptation of Stressful events

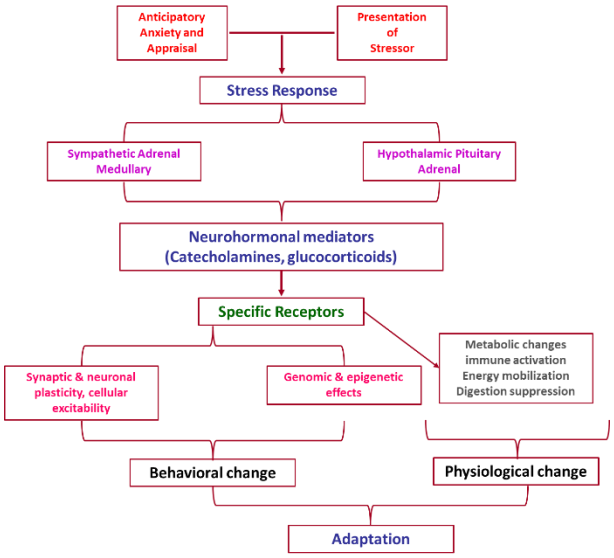

Table no.1: Clinical conditions associated with altered Hypothalamic Pituitary Adrenal Axis Activity and Dysregulation of the Adaptive Stress Response

Diseases associated with Chronic Stress	
➢ Stroke ➢ Panic Disorder ➢ Anorexia Nervosa ➢ Cardiovascular Diseases ➢ Obsessive Compulsive Disorder ➢ Psychiatric Disorders including Mood and Anxiety Disorders, Psychosis, Neurodegenerative Disease	➢ Obesity ➢ Hyperthyroidism ➢ Diabetes mellitus ➢ Cushing syndrome ➢ Peptic Ulcer Disease ➢ Irritable Bowel Syndrome ➢ Increased risk of Infections due to effects on the Immune System

MANIFESTATION OF STRESS

STRESSORS: Stressors in Ayurveda can be classified as those causing physical Stress like excessive physical exercise, fasting, injury, exhaustion, uneven body postures, etc. Physiological factors like *Kroda*(anger), *Bhaya*(fear), *Shoka*(Grief), *Loba*(Greed), *Moha*(attachment), etc. *Manasa Doshas* like *Rajas*[16] and *Tamas* and *Pragnaparada*[17] has key role in etiopathogenesis of Stress and related Disorders.

Pragnaparada is the most important factor for Stress in today's era. Impairment of *Dhi*(intellect), *Dhruti*(patience), *Smruti*(memory) are responsible for harm to the mental faculties and causes Stress. These factors responsible for degenerative change in *Dhatus* (body tissues) and *Ojakshaya*. Mental Stress directly proportional to *sattva* of mind. If it is overcome by *Rajas* and *Tamas* then it leads to decrease in mental strength or one that is not able to cope with Stress.

Fig 2: Flow Chart shows *Samprapti* of Stress Disorder :

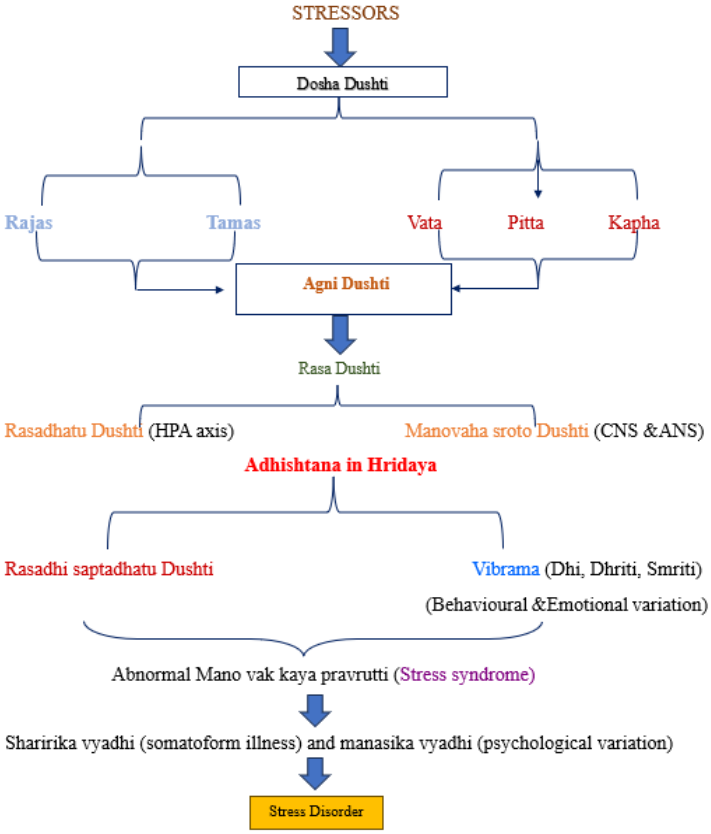

Table no.2: Clinical features of Stress in *Vata Dosha* dominance

Physical symptoms	Behavioural symptoms	Psychological symptoms
Palpitation	Restlessness	Doubt everything
Anxiety attacks	Emotional out burns	Erratic thoughts
Headaches	Anger	*Divaswapna*(daytime sleep and dreaming)
Insomnia	Disturbance in relationship	Sad/depression
	Abnormal quietness	Not feeling well
		Emotional detachment

Table no.3: Clinical features of Stress in *Pitta Dosha* dominance

Physical symptoms	Behavioural symptoms	Psychological symptoms
Profuse sweating	Hyper hostile nature	Firm decision-making power
Tremors	Possessive relationship	Violent thoughts
Perspiration	Aggressive behaviour	Moderately stressed
		Happy mindset
		Emotionally attached

Table no.4: Clinical features of stress in *kapha Dosha* dominance

Physical symptoms	Behavioural symptoms	Psychological symptoms
Weigh gain	Cool minded	Stable mindset
Fluid retention	Stable relationship	Positive thoughts
Fatigue	Positive behaviour	Mild stress

MANAGEMENT OF STRESS: -

Management of Stress can be in two ways by avoiding the factors which induces Stress and increases the coping capacity of body by following *Rasayana* therapy [18], *Achara rasayana, Dinacharya, Rutucharya, Sadvrutta.*

Achara Rasayana suggests a regular code of conduct to remain Stress free like one should speak the truth, avoid anger, be calm and peaceful, one should have Self-control, Nonviolence etc. one who follows *Achara rasayana* in daily life can remain free from mental factors that causes Stress.

Ajastrika Rasayana is about observing a nutritious and balanced dietary routine. A balanced diet has six *Rasas* and modified according to *Prakriti, Desha, kala, Bala* of an individual. In health, the balanced diet is considered the best *Rasayana*.

Aushada Rasayana is the drug treatment becomes effective only when first two are appropriately followed. Several *Rasayana* herbs used as anti-Stress agents have shown Antioxidant, Immunomodulatory, Hepatoprotective, Anti-depressant, Anxiolytic effects etc. Several *Rasayana* drugs [19] like *Satavari (Asparagus racemosus), Brahmi (Bacopa monnieri), Punarnava (Boerhavia diffusa), Mandukaparni (Centella asiatica), Sankapushpi (Convolvulus prostratus), Guduchi (Tinospora cordifolia), katuki (Picrorhiza kurrooa), Pippali (Piper longum), Aswagandha (Withania somnifera), Yastimadhu (Glycyrrhiza glabra)* have been reported to have significant Antioxidant action. Therefore, these *Rasayanas* have wide spread clinical use to counter act the Stress. In this way the Rasayana drugs has shown to influence both Cellular and Humoral immunity by acting on Immune function mediators.

CONCLUSION: Stress is a psychological and physiological response to threat that plays a Crucial and Adaptive role in our Everyday lives. The Diseases occurred due to chronic and Oxidative Stress can be managed. Hence *Rasayana* therapy in Stress helps improving Physical and Mental wellbeing. *Achara rasayana*, *Rutucharya* and *Aushada rasayana* plays a pivotal role in the Management of Stress.

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