REVIEW ARTICLE

IMPACT OF STRESS ON VARIOUS ORGAN SYSTEMS AND ITS THERAPEUTIC MANAGEMENT

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ABSTRACT

The marked disruption of homeostasis of a physiological system (a cell, tissue, organ, or whole organism), is more commonly known as stress. However, physiological systems are constantly exposed to more acute stresses. Psychological stress is an important component with the potential to affect physiology adversely as has become evident from various studies in this area. Advances in our understanding of molecular response of several physiological systems to stress are discussed in this review article. It is hoped that such understanding will facilitate the development of approaches to ameliorate some of the limitations these stresses place on individuals. Although studies have established numerous effects of psychological stress on human physiology, yet there is no such review article in which effects of stress on different organ systems is compiled.

KEYWORDS: Stress, Organ system, Management

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INTRODUCTION

Stress is described as a social, environmental or internal demand, which ensues in a physiological, psychological or behavioral reaction which disturbs physical and psychological well-being[1] affecting-most of the people. According to a definition of H. Selye, stress is called an acute risk to organism's homeostasis, which may be physical or psychological caused by events from within or in the outside world. Notably, stress arouses adaptive reactions that assist to shield internal environment constancy and organism's survival[2]. Autonomic nervous system, hypothalamic-pituitary-adrenal (HPA) axis and fight-or-flight response are conventional ways of envisaging biological and behavioral response to danger from a perilous situation, such as, a predator, a mugger, an accident or natural disaster[3].Stressors appear in 3 different forms i.e., numerous life happenings,enduringworries andeverydaydisturbancesfrequently considered as trivial but can provoke biological, psychosomatic, or social responses. Persistent stress affects nearly all parts of body,nervous system, cardiovascular system, gastrointestinal system, renal system and musculoskeletal system and they become chronically over-activated or under-activated[1]. Hence, this review summarizes the impact of stress on various organ systems of body and informs therapeutic options to prevent stress-related disorders.

STRESS AND ORGAN SYSTEMS

1. Stress and Cardiovascular system

There is a colossal data on psychological stress and cardiovascular disease. The acute stressors i.e., disasters (earthquakes) and intense emotional stress while, chronic stressors such as job stress and marital unhappiness contribute to varied pathophysiological changes comprising myocardial ischemia, myocardial infarction, wall motion abnormalities and owing to fluctuations in hemostasis and sympathetic nervous system activity sudden death and changes in cardiac regulation can result[4].

Earthquakes are allied with an increased cardiovascular risk. The marked escalation in heart rate (160 beats/min) follow in the wake of earthquake, which ensues because of increase in sympathetic nervous system activity with resultant increased blood viscosity, blood pressure and thrombotic propensity

of blood. Moreover, there is a greater threat of pulmonary embolism at the time of earthquakes and numbers of deaths per day owing to cardiovascular disease increases histrionically on the day of earthquake4. Likewise, left ventricular dysfunction has been reported owing to immensely raised interstitial infiltrates, plasma catecholamines and contraction band abnormalitiesin patients with no former cardiovascular disease historyin case of intense emotional stress. Previously, analogous outcomes have been perceived in terms of critical and reversible cardiomyopathy provoked by catastrophic stress in patients with no past history of cardiovascular disease[5].

Work stressors like job insecurity and job strain like high job demands and long working hours increase possibility of coronary heart disease and stroke (10-40%). Moreover, increasedpsychosomatichassles and low individual control over these demands leads to physiological strain and ultimatelyincreased risk of cardiovascular disease. In line with this imbalance between extreme effort and little reward is stressful. Earlier studies had inspected correlation amid job insecurity and coronary heart disease [6]. High work load and low control are more likely to cause initial myocardial infarction while, people suffering from permanent stress at work place or at home have more than 2.1 fold chance for experiencing heart attack[4]. Similarly, marital stress also influence on prevalence of coronary artery diseases. Marital stress is allied with 2.9 times increased risk of cardiovascular events and in accordance with astudy chronic work stress and marital termination escalatethreat of cardiovascular mortality in men[7].

Chronic stress presents with atherosclerosis[8]. Atherosclerosis, comprising plaques development and arterial walls thickening is a common pathology in cardiovascular disease[6]. Moreover, elevated ambulatory blood pressure (ABP) and greater intima-medial thickening (IMT) had been stated in carotid arteries of people[9] in the course of highly challenging and less manageable days[10]. IMT is an ultrasonographic marker of atherosclerosis that is linked with greater risk for future heart attack and stroke[11]. According to a study among young adults, job stress has been associated with increased intimal medial thickening in carotid arteries[12]. An arduous psychosocial environment may provoke persistent instigation of sympathetic nervous system pathways that may augment ABP along with some pathophysiological alterations that contribute to early signs of atherosclerosis[9,13].

2. Stress and Gastrointestinal system

Major systems of body (cardiovascular, muscular, urinary, gastrointestinal, etc.) are altered by stress, often with adverse consequences. Stress influences gastrointestinal function, expressing different symptoms within gastrointestinal tract for instance, diarrhea, dyspepsia, abdominal pain. Stress affects gut physiology by escalating intestinal permeability, gastrointestinal motility, alteration in abdominal secretions, increase in visceral sensitivity and undesirable effects on enterobacteriaceae, regenerative capacity of gastrointestinal mucosa and mucosal blood flow. Gastrointestine receive signals from central nervous system via multiple parallel pathways including autonomic nervous system, hypothalamic pituitary-adrenal axis (HPA), brain-gut-axis (BGA) and stress dysregulate brain-gut-axis resulting in various gut diseases[2].

In response to stress various stressors are released and central stressors prompt the release of corticotrophin releasing factor (CRF), adrenocorticotropic hormone (ACTH) and glucocorticoids which have anti-inflammatory roles. Corticotrophin releasing factor and urocortins (Ucns) (centrally released stressors)stimulate parasympathetic nerves, which then innervate enteric neurons within gut wall to stimulate or inhibit motility and increase secretion. (Figure 1). Throughout stress, corticotropin releasing factor from brain hypothalamus excites adrenocorticotrophic hormone secretion from pituitary gland that incites the discharge of glucocorticoids from adrenal gland thus mediate neuroendocrine stress responses[14] (Figure 1).

Stress may intensely disturb BGA through modulation of several imperative neuropeptides (like CGRP) that are concerned with alterations in digestive fluids, protection and restoration of gastric mucosal lining and mucosal blood flow[15].Hence, dysregulation of BGA ensues in generation of a wide range of gastrointestinal maladies. Stress induced exacerbation of GERD symptoms is ascribed to increased acid sensitivity and lower esophageal sphincter inhibition[2]. Moreover, development of PUD upon exposure to stressful life events is attributable to numerous factors involving modifications in gastric acid secretion and gastric motility, reduction in mucosal blood flow and bicarbonate secretion, acid back diffusion, diminished propagation and compensation of bruised mucosa[16]. There is a strong evidence that stress exposure triggers brain-gut axis and worsens IBD, thus leading to release of gastrointestinal hormones and neurotransmitters, changes in gastrointestinal motility, gut microbiota, endocrine functions and visceral sensitivity, increased manifestation and discharge of pro-inflammatory cytokines, discharge of key neuropeptides and up-regulation of immune system (low level inflammation)[2]. The pathogenesis of IBS is multifactorial and involves profound dysregulation of brain gut axis. Among the aforementioned gut disorders, most important is visceral hypersensitivity[17].

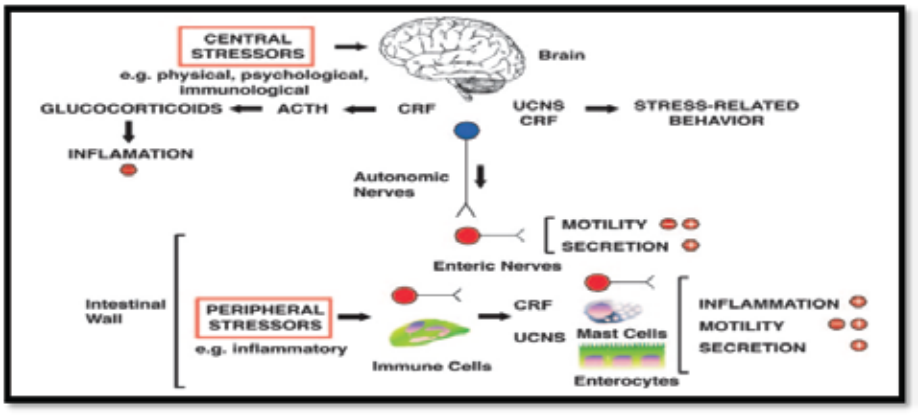

Figure 1: Stress-induced alterations in gastrointestinal functions

3. Stress and Immune system

Influence of stress on immune system are multifaceted, incorporating many endocrine and neuronal interactions[18] in regulating metabolism and energy distribution. Furthermore, psychological stress initiate that inflammatory innate immune responses in the body[19].

During psychological stress, as an effect of hypothalamic pituitary adrenal systemmobilizes glucose out of the cells that induces IL-6 production (pro-inflammatory cytokine) from monocytes. Resultant increased plasma glucose concentration beyond a certain limit, create a chronic stress situation. This inflammatory condition then again cause compensatory phase response activation which would expand beyond its normal range owing to repeated induction consequently cause obesity and other concomitant metabolic syndromes[19].

The psychosocial condition of a person can have direct impression on immune system. For instance, stress has diverse effects on immune system. First, sympathetic nerves innervating both primary and secondary lymphoid tissues liberate variety of substances, affecting immune response by interacting the receptors on lymphocytes bearing adrenergic receptors. In line with this activation of sympathetic adrenal medullary axis, hypothalamic-pituitary-adrenal axis and hypothalamic-pituitary-ovarian system secrete adrenal as well as pituitary hormones and brain peptides which attach to particular receptors on WBCs and execute several regulatory actions. In addition, at times efforts of people to cope with hassles of stressful experience prompt them to indulge in behaviors for example alcohol use or changes in sleeping patterns that could also alter immune system processes. Hence, these represent potentially important pathways associating stress with immune system[20].

Acute stress (examination stress or experimentally induced stress) stimulates immune system[18], whereas, chronic stress (work-related stress, bereavement, marital problems) provokes simultaneous intensification and suppression of immune response by modifying patterns of cytokine secretion. Th1 cytokines that trigger cellular immunity to provide defense against many infectious and many types of cancers are repressed. This suppression assembles Th2 cytokines, which initiate humoral immunity. This swing occurs via effects of stress hormones such as cortisol. Shift from Type 1 helper T cells to Type 2 helper T cells varies immune response. Declined Th1 facilitated cellular immune response might increase predisposition to infectious and cancerous diseases. Likewise, elevated Th2 mediated humoral immune response increase sensitivity to allergic and autoimmune diseases because of loss of self-regulation[20]. Henceforth, decreased effectiveness of immune system could result in enhanced functional impairment and death[18].

4. Stress and Renal system

Stress is a condition in which environmental factors surpass adaptive capability of a person to a level where physiological as well as psychosomatic reactions increase the susceptibility of disease[21]. Furthermore, stress is not a single reaction but a process because the moment a person experiences tension; a biochemical process is instituted, leading to acute and chronic hormonal changes that may comprise imbalances which excite development of lithiasis[22]. Stress can also cause development and progress of chronic kidney diseases[21].

Many studies have established that chronic stress situations are allied with allostatic overload i.e., body's effort to gain stability through stressful change, hence ensuing in modifications of cortisol and insulin levels in hypothalamo-hypophyseal axis (HPA), kinins and other pro-inflammatory substances amid other homeostatic alterations. These variations have physiological implications, involving changes in physiology of kidney. These conditions may result in renal repercussions, like high pressure level maintenance and association with incidence of renal calculi among other manifestations[23]. Previ-

ously, it has been evidenced that stress increased risk factors of chronic kidney diseases like high blood pressure. It is acclaimed that stress allied with socio-economic impairments causing chronic kidney diseases accompanied by psychological facets and fatal actionfor example alcohol, cigarette smoking and drug misuse[21].

Stressful conditions are a menace for stone formation. Under stressful events, the neurologically elicited fight or flight reaction excites neurosecretory cells in supraoptic and paraventricular nuclei of hypothalamus. The mechanism comprises discharge of vasopressin from HPA that acts to produce hypertonic urine and then of adrenocorticotropin, which acts through a secondary hyperparathyroid mechanism to elevate serum calcium levels. In addition, as a result of stress, ACTH increase and excite the production of parathormone, which ensues in hypercalcemia, trailed by hypercalciuria. Contemporary evidence suggests that local vitamin D signaling protects from stress tempted worsening effects on heart and brain. Vitamin D deficiency is faced by more than 1/3 of stone formers, which may contribute to hyperparathyroidism. On the other hand, stressful life events are considerably more amongst persistent colic of renal lithiasis. Serum white blood cell count at acute phase of renal colic predicts stressful event and spontaneous passage of stone[24].

Stress has also been presented to be linked with hypertension, diabetes or obesity[1]. Numerous investigations exploring correlation amongst stress and CKD pathophysiology have concentrated on consequences for instance heart rate, vascular reactivity and blood pressure and specified that both heart rate and blood pressure escalate and endothelial sensitivity falls in many studies of acute stress. These connections among stress and pathophysiology are assumed to be linked with variations HPA, pro-inflammatory mediators, endothelin A and sympathetic autonomic nervous system activity. These alterations propose that pathologic connection between stress, high blood pressure and chronic kidney disorder is conceivable as kidney sympathetic innervations and neuronal mechanisms regulate water and salt retention. It also has been submitted that stress may be allied with CKD through insulin resistance and diabetes. Environmental stressors have been instituted to be connected with decreased insulin sensitivity, obesity and metabolic disorder, eventually type 2 diabetes through modifications in neuroendocrine systems. In CKD patients, level of release, a hormone that processes sympathetic nervous system products are reduced[1]. Hence, it is probable that long term mental stressors bring about unimpeded increase in SNS tone that ensues a vicious reaction[21]. New researches revealed that exposure of discrimination and racism might be linked to chronic kidney disease risk factors such as elevated blood pressure and exposure to these stressful experiences unfavorably disturbs progressive renal damage and allied complications[1].

5. Stress and Musculoskeletal System

Numerous psychobiological studies depict that influence of mental disorders can be assessed in terms of prominent psychophysiological provocation including cardiovascular response and level of stress hormone[25].

Stress is expressed as mental and somatic symptoms in an individual[26]. Psychosocial factors at work (monotonous work, work demands, time pressure, and decision latitude, lack of social support from colleagues, low control on job, stress symptoms and psychological distress) have been presented to show imperative role in musculoskeletal pain development. Though, perceived stresses from physical environment of workplace (vibration, noise and heat) and ergonomics (move or lift heavy objects, fast pace and work in uncomfortable position for long period) are described as psychosocial risk factors that might ultimately reflect physical risks at work[27].

It has been stated that not only ergonomic conditions, psychosocial factors and biomechanical load at work but also mental stress (general worry/psychological tension, general coping style, response to pain and depression/anxiety) at work may persuade muscle tension and raised stress levels (catecholamines, cortisol, blood pressure, heart rate) thus, generating increased risk for musculoskeletal disorders. The extent of stress hormones secretion reflect work related stress intensity and concurrently, catecholamines (epinephrine, and norepinephrine) and cortisol form a connection between psychosocial stress and health damage via their impact on various body functions and organs[28].

However, long-lasting instigation of motor units cause degenerative processes in company with pain. Continuing psychological stress may also avert damaged muscle fibers repair[28]. Besides, it has also been anticipated that stress incited hyperventilation declines blood CO_2 and upsurges blood pH levels, which adds to intensified neuronal excitability, upraised muscular tension, and suppression of parasympathetic activity. The sympathetic ascendency may augment responses to catecholamine differentially, centered on qualitative interpretation of exposure to stress[25].

The muscle spindles possess a central role in muscles by generating a viscous circle with sequentially increasing muscle stiffness and accretion of inflammatory elements (arachidonic acid, bradykinin etc.) that excite nociceptors and hence contribute to enlarged sensitivity of pain. Psychological stress and higher sympathetic provocation have been instituted to decrease or even abolish regulatory

functions (optimal allocation of activity in muscle and co-ordination of movements) of muscle spindles and thus, increase danger of burden in certain parts of muscle. This degenerative process may spread to other muscles, far from the primary one through nerve signals[29]. Neurotransmitter release may also exhibit a vital role in muscle pain exacerbation. It has been perceived that serotonin, which is released during stress, enhance the effects of endogenous pain mediators e.g., bradykinin, thus, exerting a nociceptive effect on muscle. Moreover, stress exposure employs an inhibitory effect on inflammatory or immune reactions. Glucocorticoids (cortisol) decrease cytokines and other inflammatory mediator production and impede actions of these agents on target tissues. It is conceivable that subsequent to mechanical insult, repeated evocation of stress response does not permit pain-sensitive tissues to recuperate[30].

6. Stress and Neurogenesis

The hippocampus is predominantly accompanied with developing and recollecting memories and spatial navigation and associated with stress regulation and mood possibly by modulating adult neurogenesis[31]. Stress has been presented to impact memory and learning along with precipitation and exacerbation of mood disorders[32]. A chief factor of ''fight or flight'' response implicates activating energy stores for effectively evading immediate peril that comes at the expense of less energetic functions. The growth-inhibiting and catabolic effects of stress hormones have long been documented. Glucocorticoids repress cell propagation and boost the cell death in many cell types, comprising myocytes, thymocytes and osteoblasts[33].Latest studies in neurogenic cells direct that molecular pathways triggered by glucocorticoids (main stress hormones) are controlled by crosstalk with other stress pertinent mechanisms, containing neurotrophic factors, inflammatory mediators and morphogen signaling pathways[31]. Numerous studies have stated that both acute and chronic stress diminutes propagation of progenitor cells in dentate gyrus (DG) of hippocampus[33]. Stress influence on adult neurogenesis is very short lived, with lessened cell proliferation resulting in decreased immature neuron production followed by a period of enhanced cell survival, as the ultimate number of new mature neurons appears unchanged[34].

Molecular mechanisms involved in inhibiting neurogenesis involve glucocorticoid signaling pathway[33,35,31].Dickkopf 1 (DKK1)alongwithinterleukin-1β and NF-KB signaling routes. Moreover, Brain-derived neurotrophic factor (BDNF) normally increase neurogenesis. Studies direct that crosstalk between GR and BDNF signaling follows and this might add to intricacy of interaction among stress and BDNF[31] as shown in Figure 2.

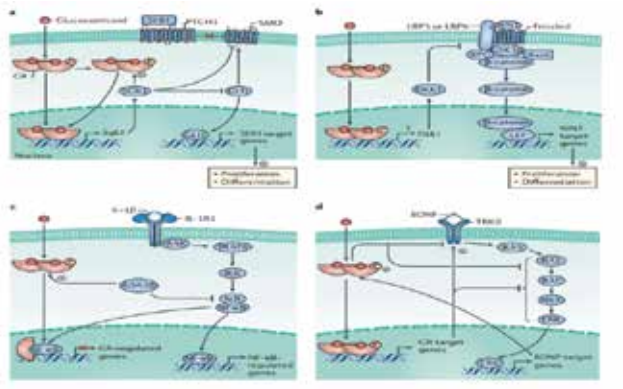

Figure 2: Possible mechanisms of stress and neurogenesis (Adapted from Egeland et al., 2015).Serum/glucocorticoid-regulated kinase 1: SGK1, Smoothened: SMO, Glucocorticoid receptors: GRs, Dickkopf 1: DKK1, Canonical wingless: WNT, Low-density lipoprotein receptor-related protein 5: LRP5, interleukin-1β: IL-1β, Nuclear factor-κB: NF-κB, Glycogen synthase kinase 3β: GSK3β,Brain-derived neurotrophic factor: BDNF, Mitogen-activated protein kinase: MAPK, Tropomyosin-related kinase B receptors: TRKB

7. Stress and Obesity

Obesity and its associated health risks have ascended vividly. Deskbound social activities and stress-free accessibility of highly palatable nutrient rich foods encourages overweight and obesity. Chronic societal stress frequently arising from job/unemployment stress, low socioeconomic status, poor interpersonal relationships and poor self-esteem have been allied with obesity and its related complaints[36]. Instantly after a stressful incident happens, there is a corticotrophin-releasing-hormone (CRH) interceded food intake subdual. Subsequent to this, glucocorticoid induced offshoot of hunger and eating activities. During constant mental stress, chronically raised glucocorticoids ensue in chronically roused eating manners and undue weight increase. Expressly, stress can augment proclivity to eat high calorie food through its interface with central reward pathways[37].Chronic instigation of SNS and HPA axis contribute to anabolic state that upholds fat storage within visceral depots that upturns the risk of type 2 diabetes, cardiovascular disease, dyslipidemia and other aspects of metabolic syndrome. Stress could cause overweight and fat build up through fluctuations in eating manners. Long-term stress modifies food consumption behavior, dietetic tastes and less desire for craving [36].

Initial life anxiety transforms genetically NR3C1 (receptor for cortisol and corticosteroid) expression in hypothalamus as well as hippocampus, arginine vasopressin and corticotrophin-releasing hormone in hypothalamus, resultant in inhibited glucocorticoid receptor and amplified AVP and CRH activity in reaction to stress later in life. Early life stress can

also potentially persuade augmented release of satiety hormones like insulin, leptin and ghrelin, again prompting feeding behavior, appetite and metabolism all through life. CRH released after acute stress inhibits appetite. Similarly urocortins especially urocortin 1 is also involved in appetite suppression[37].Enduring stressful event increase levels of glucocorticoids. Consequently, chronically raised glucocorticoids lead to visceral fat buildup owing to raised lipoprotein lipase enzyme activity.

8. Stress and Nervous system

Memory and cognitive function

Stress system constitutes brain regions situated in hypothalamus and the brain stem including parvocellular corticotropin-releasing hormone and arginine vasopressin neurons of the paraventricular nuclei of the hypothalamus, the CRH neurons of the paragigantocellular and parabranchial nuclei of the medulla, the locus ceruleus and noradrenergic cell groups of the medulla and the pons. Peripherally, stress system involves the hypothalamic-pituitary-adrenal axis along with the efferent sympathetic adreno-medullary system in company with components of the parasympathetic system[38] as shown in Figure 3.During periods of acute stress various physiological functions including ingestion, development and reproduction may be a detriment to physical integrity and even survival. Subsequent to the perception of stress, stress hormones are produced by the sympathetic nervous system and hypothalamic-pituitary adrenocortical axis. Sympathetic nervous system along with the activation of paraventricular nucleus of the hypothalamus producing corticotropin releasing factor, which in turn stimulates the pituitary to produce adrenocorticotropin. Recurring stress can cause cognitive impairments and structural changes in the hippocampus, mainly through the actions of glucocorticoids[39].

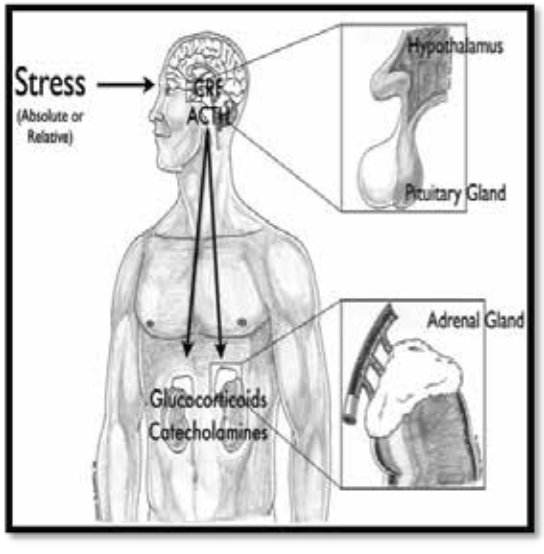

Figure 3: Diagrammatic illustration of stress influence on nervous system

Effect on sleep

Since, many studies have revealed that stress bringsabout sleep difficulties including trouble in falling asleep, distorted sleepas well asrecurringhallucinations, increased arousal and delay sleep onset[40]. In healthy individuals, sleep deprivation induces extensive neuro-physiological as well as hormonal fluctuations causing compromised perceptive operations notwithstanding higher local brain functioning[41]. Sleep disorder severely disturbs quality of life and reduce working efficiency. Acute stress cause suppression of parasympathetic nervous system along with heart rate anomalies caused by acute stress might impair sleep quality[42].

Stress and Cutaneous system

Skin is complicated organ composed of sensory and motor nerves, endocrine glands, blood supply, smooth muscles, connective tissues and immune cells innervated by catecholamines and glucocorticoid hormones released by sympathetic nervous system innervation and locally by keratinocytes. It is revealed that both physical and psychologic stressors cause well defined neuroendocrine responses influencing several aspects of skin physiology. As, systemic stress response is regulated by two principal biologic effectors i.e., hypothalamic pituitary adrenal axis and sympathoadrenal medullary system producing numerous changes including reasoning stimulation, mobilization of fuel stores to meet metabolic requirements. Acute psychosocial stress associated with sleep deprivation cause disruption in skin barrier function and homeostasis in women owing to cytokine secretion. Previous studies have demonstrated that stress augment some immune parameters including discharge of pro-inflammatory cytokines and delayed-type hypersensitivity reactions. Moreover, human study has revealed that wound healing is decreased by persistent stress[43].

9. Stress and Endocrine system

Stress alters the level of various hormones by eliciting HPA axis hormones, sympathetic endocrine activity, inflammation and metabolism[44]. Stress leads to the liberation of glucocorticoids, monoamine neurotransmitters, growth hormone and prolactin to adapt the individual to its new circumstance. Stimulation of corticotrophin releasing factor is mediated mostly by norepinephrine, serotonin and acetylcholine. Incitement of pituitary-adrenal axis results in increased cardiac output, sodium retention, skeletal muscle blood flow, cutaneous vasoconstriction, reduced intestinal motility, increased glucose, bronchiolar dilatation and behavioral activation. Moreover, there is suppression of circulating gonadotropins and gonadal steroid hormones leading to disturbance of the normal menstrual cycle while prolonged exposure to stress condition can lead to complete mutilation of reproductive function.

10. Stress and reproductive system

Effect on female reproductive system

Females in are more prone to attain emotional disorders than men which might be because of structural changes, endocrine vicissitudes and ecological impacts such as stress. During stress, estrogen could modulate the neurobiological and behavioral responses. Female reproductive system is synchronized by hypothalamic-pituitary-adrenal and hypothalamic-pituitary-ovarian axes. Primary regulators of these axes are corticotrophin releasing factor and gonadotrophin releasing hormone that stimulates follicle cell stimulating hormone and leuteinizing hormone secretion and consequently, estradoil and progestrone discharge by the ovary. In hypothalamus estrogen activate neurosecretory neurons including gonadotropin-releasing hormone (GnRH) and dopamine neurons and local circuitry neurons such as proopiomelanocortin (POMC) implicated in controlling the physiological functions of reproduction, stress responses, thermoregulation, eating and striving patterns. Glucocorticoids released during stress condition suppresses gonadal axis function at the hypothalamic, pituitary and uterine level. It has been revealed that ovarian CRH has anti-reproductive actions that might lead to earlier ovarian failure as observed in women exposed to high psychosocial stress38. Psychological stress increases the production of cortisol that directly or indirectly affects the physiology of ovary by inducing granulosa cell apoptosis and affecting the estradiol 17ß biosynthesis in the ovary. Reduced estradiol level in the ovary impairs growth and development of follicles and deteriorates oocyte quality by inducing apoptosis45(Figure 4)(Prasad et al., 2016).

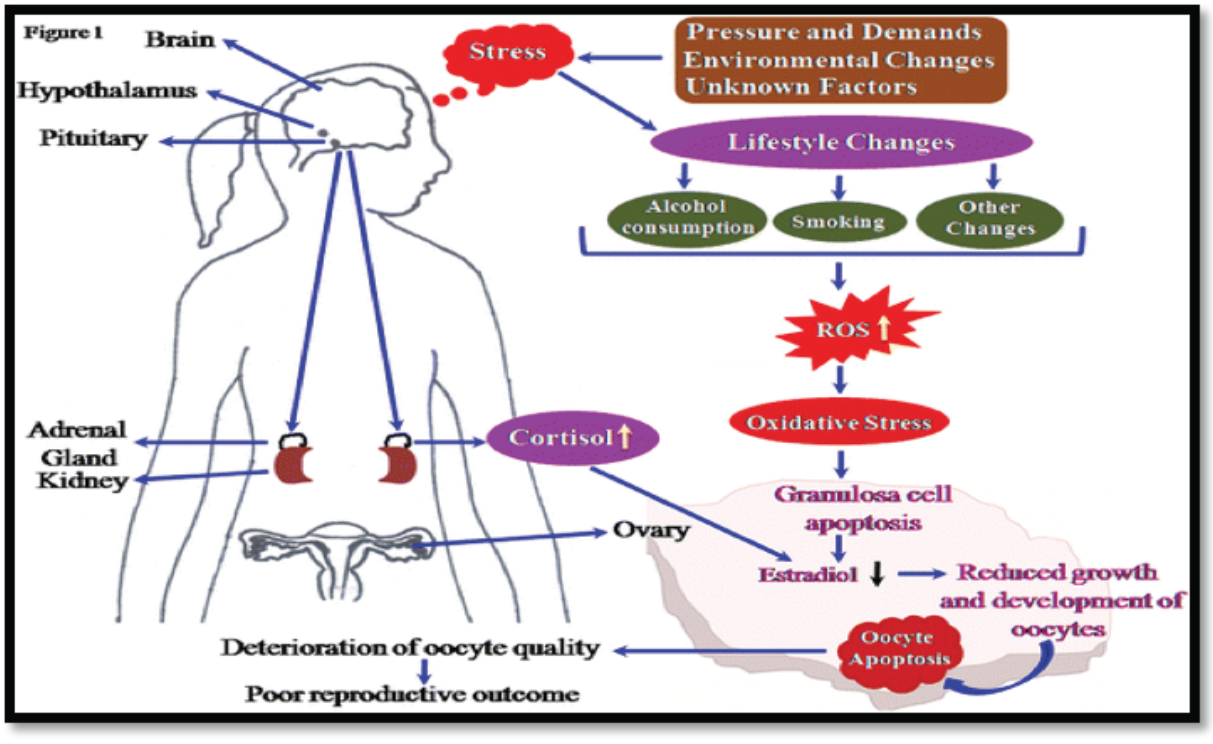

Figure 4: Schematic diagram showing the impact of stress on female reproductive system

Effect on male reproductive system

Studies on male fertility have stated that psychological pressure reduces paternity allied with anomalous semen parameters. Psychological stress might acutely impinge on spermatogenesis by affecting testosterone secretion in particular, hypothalamic-pituitary-adrenal axis directly inhibits hypothalamic-pituitary-gonadal axis and Leydig cells in the testes. Both acute and chronic psychological stress can lead to erectile dysfunction as well[46].

THERAPEUTIC MANAGEMENT OF STRESS

For understanding the worth of life and its progress, stress is a censorious viewpoint now a day. All living beings have to face intimidations to their stability in everyday life and our future as individuals and as a species relies upon our capability to become accustomed to potent stressors affecting our potentials. Therefore, it is indispensable to treat/manage stress through various interventions like brain oriented/neurological approaches, pharmacological interventions along with social support to live a pleased and satisfied life full of achievements.

Brain oriented approaches

Stress response is typically mediated by brain and remedial interventions must be projected to lessen

the burden of stress. As brain oriented strategies are very well-known and involve behavioral and changes in living patterns by alleviating sleep deprivation improving societal support, and developing a positive outlook on life, along with taking a healthy diet, smoking cessation and engaging in regular, moderate physical activities. Both public and private authorities can design policies to promote these interventions by smoking cessation programs, creating incentives and launching communal amenities and prospects promoting the quality standard of living[3].

Behavioral interventions

Cognitive-behavioral stress management has an encouraging influence on the quality of life of patients dealing with chronic and life-threatening stress. Such interventions cut down perceived stress and depression, improve problem-focused coping, and modify cognitive assessment together with decreased SNS stimulation and cortisol discharge from the adrenal cortex. Psychosocial therapy appears to be helpful by decreasing their agony and professed pain as well as improve their physical activity. These behavioral interventions also decrease patients' overuse of medications39. Moreover, a slothful way of living is a peril to many ailments such as diabetes, obesity, cardiovascular problems, depression and dementia. It has been found that adequate physical activity would be beneficial for the neural, vascular as well asmetabolic disorders. Moreover, deliberate physical engagement has been shown to increase neurotrophin expression in cortex and hippocampal regions of the brain as well as to increase neurogenesis in the dentate gyrus of young and aging animals. Social support, another behavioral intervention, is composed of emotional and influential support. It is an interpersonal process characterized by mutual exchange of information that improved mental health. Societal support involves regular social contacts with compassionate friends or relatives or health professionals, who offer emotive care and delivered valuable information that reduce stress and improve mental health and results in healthy life-style[3].

Pharmacological interventions

Many drugs, such as sedative/hypnotics, beta blockers, tranquilizers and antidepressants that offset some of the problems allied to stress. Moreover, antioxidants, anti-inflammatory drugs, hypolipidemics and drugs that treat insulin insensitivity or lasting ache also useful in managing metabolic and neurological effects of stress. Although these medications are valued to some degree, but have some side effects and limitations, thus affecting quality of life.

CONCLUSION

In this article deleterious effect of stress on various body systems has been summarized. There are brain oriented, pharmacological and behavioral interventions to improve life style resolving the damaging influences of stress.

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