Neurophysiological response to stress in younger individuals of the modern generation

Arun M. Kumar, Vasanthi Ananthakrishnan, Jaisri Goturu

Department of Physiology, MS Ramaiah Medical College, Bengaluru, Karnataka, India

Abstract

Introduction: Stress and its response among young adults in the modern generation are not evaluated fully. There is a need to understand the normal physiological changes in the individual in response to a stressor. Serum cortisol and state-trait anxiety inventory (STAI) are most commonly used to assess the quality and quantity of stress in an individual. STAI measures the quantum of stress the person perceives. Serum cortisol measures the neurophysiological response to the stressor. Relationship between STAI and serum cortisol is studied in order assess the stress pattern and its response in the individuals.

Materials and Methods: A total of 80 subjects in the age group of 18-24 were included in this study. STAI Questionnaire was administered. Serum cortisol assay was done. Subjects were divided into three groups based on the STAI score. The pattern of serum cortisol was studied in all the groups.

Results: The mean age of the participants was 21.5 ± 2.07 years with a range of 18-24 years. The mean values of body mass index were 21.85 ± 4.05 kg/m², serum cortisol was 130.07 ± 64.38 ng/dl, and STAI scores were 46.81 ± 6.15, respectively. The mean difference in serum cortisol level between the groups was found to be statistically significant (P = 0.016). Negative correlation was seen between STAI scores and serum cortisol in the entire group (r = −0.235, P < 0.05) as well as all their groups.

Conclusion: Group 3 (STAI score >50) had increased stress, but mean serum cortisol level was least when compared with other two groups. This indicates that group individuals had experienced more stress, but physiological adaptations in response to stress was insufficient. This is also true in Group 2 who showed similar findings. There is a need for understanding the type of stressor and their intensity in stimulating the appropriate defense mechanism. Accordingly the stress coping techniques has to be inculcated in the young adults of present generation.

Introduction

Stress is an integral part of life. The term stress was first introduced into the health sciences in 1926 by Hans Selye. According to the Selyean concept stress, is “the nonspecific response of the body to any demand. It’s not what happens to you that matters, but how you take it.” Epictetus is credited with saying, “Men are disturbed, not by things, but the views which they take of them.” The term stress is used to refer to a physiological reaction or response, regardless of the source of the reaction.

Stressor is defined as the stimulus, which evokes a stress response. There are two primary forms of stressors: Psychosocial stressors and biogenic stressors. Psychosocial or psychogenic stressors involve the cognitive assumption of the stressor event as the magnified threat, which is greater than what actually is defined in general. It is a stressor in only that group of people who takes it as stress, and it also depends on physical and mental makeup of the stressed individual. Biogenic stressors are true stressors, which in reality has stressor quality. They are in general eliciting almost common response in all individuals. This stimulant characteristic, commonly referred to as a sympathomimetic characteristic, is found in substances such as tea, coffee and cocaine. Extremes of heat and cold and even physical exercise exert sympathomimetic effects. Biogenic stressors cause overall physiological changes in the individual irrespective of how the person thinks or interprets it internally.
Living organisms survive by maintaining an immensely complex dynamic and harmonious equilibrium, or homeostasis. They have to face the challenge of threat in the entire lifetime, and withstand with opposite mechanisms to fight against the disturbing forces. The disturbing forces can be external or internal. External stress is mainly due to the anticipation, struggle and survivability against the foreign invasion. There is always a constant need to meet the basic physiological requirements and also reestablish the deranged physiological parameters. This process involves development of several novel changes, which could make the organism more endure and sustainable. This process is called homeostasis. This requires constant adaptation against the deranging forces, which are called as stressors. Response elicited by stressor in an organism is called general adaptation response. Stressors are mainly meant to increase strength of the organism to survive against environmental forces. But if the strength of the stressor increases beyond adaptation capability of the organism then the overall homeostasis in disturbed to a larger extent. This causes a lot of adverse effects in the organism, and the quality of life reduces significantly till the responses are back to its normal state.

All types of stressors psychosocial stressors (emotional) and biogenic stressors (physical) causes both central and peripheral responses, which are meant to stabilize homeostasis and prevent derangement. This is described as fight and flight response. The central responses are facilitation of neural pathways which mediates several functions such as arousal, alertness, cognition, focused attention, and appropriate aggression. There is simultaneous inhibition of pathways involved in vegetative functions like feeding and reproduction. These adaptations are very important to face the everyday challenge and thrive successfully, which can be specific to the stressor or nonspecific. This nonspecific response can be significantly similar and can occur only if the severity of the threat to homeostasis exceeds a certain limit.\[2\]

Peripheral changes occur mainly occur to increase the redirection of energy. Which the basic requirements like oxygen and nutrients are directed to the central nervous system (CNS) and the stressed body sites. There is change in the physiological parameters like increase in the cardiovascular tone (increases blood pressure, heart rate), increase respiratory rate and enhancement of metabolism (gluconeogenesis, and lipolysis). All these promote enhanced availability of vital substrates. There is restraint of growth and reproduction, which is actually a compensatory loss, wherein energy is redistributed to the adaptive changes making it more efficient.

The general adaptation response depends on several factors like need for responding quickly and the strength and endurance to match the counter-regulatory elements which also works in preventing the over-response. Therefore, every element of the stress response must briskly respond to restraining/replenishing forces. Otherwise, these responses lose their adaptive quality and contribute to the process of pathological change.\[3-6\]

All psychosocial stressors have been shown to elicit autonomic arousal and increases in plasma catecholamine and cortisol levels. The subjects exposed to psychosocial and physical stressors also demonstrated an increase in plasma adrenocorticotropic hormone (ACTH).\[8,9\]

The stress of events during exercise training produced marked changes in a number of neuroendocrine responses compared with baseline measures. Increases in serum cortisol were robust and comparable to levels documented in individuals exposed to real-world, life-threatening events. Stress-induced neuropeptide Y release was also marked and was significantly greater in soldiers who successfully completed extensive training.\[3\]

The stress responses in young adults of the present generation have not been explored fully. Modern life has led to immense changes in day today activities. This has resulted in increased physical and mental workload which in turn needs the development of coping mechanisms to combat and manage these situations effectively. This has led to a need for understanding the changes in their basal levels of response to any stressors.

In this study, we are trying to measure neurophysiological response to stress in younger individuals of modern generation. The response of individuals to stressors has been studied using both psychological and physical parameters. Impact of stress on the physical and emotional aspects of the individual can be studied by measuring hormones like cortisol, adrenocorticotrophic hormone, cortisol releasing hormone, catecholamines like adrenaline and noradrenaline. The circulating level of cortisol has been used as the index as a response to stress.\[2,3\] State trait anxiety inventory (STAI) is a standardized and one of the most commonly used questionnaires for quantifying stress in individuals.\[6,9\] The score in the questionnaire measures the capability of the individual to subjectively perceive stressful events and also the impact of these stressful events on the individual’s cognitive appraisal. This study is intended to understand the influence of daily stressors and its impact on neurophysiological response.\[8\]

**Materials and Methods**

A total of 80 subjects in the age group of 18-25 years have been included in this study. All participants were students selected from the MS Ramaiah College and Hospitals. Subjects apparently healthy and willing to participate were included in the study. Subjects with any illness, fever or on medications, history and signs suggestive of nutritional deficiency, psychiatric illness, and chronic diseases were excluded from the study. The others excluded from the study were those with history of intake of drugs such as steroids, nicorandil, anti-inflammatory drugs, and oral nicotine replacement therapy or any other drug that is known to disturb the autonomic function, cortisol and amylase levels. The study protocol was explained and written informed consent was obtained from all the participants.

A detailed history was taken, and physical examination was done. Anthropometric measurements like height and weight...
were measured. All participants were administered the STAI questionnaire. The participants were then asked to report to the lab between 8 am and 10 am next day. Blood samples were collected and stored at −10°C for the estimation of serum cortisol.

STAI questionnaire consists of 20 questions with four responses for each. Each response is scored from 1 to 4. Hence, the score of an individual can range from 20 to 80 based on the participant’s perception. The participants are given sufficient time to mark the response in the questionnaire. Normal STAI score for young adults is <40. So, based on the STAI score the participants were classified into three groups: Group 1 with a score <40, Group 2 with STAI score 41-50 and Group 3 with STAI score >50. Serum cortisol assay was done using the Human Cortisol RIA Kit from DRG instruments GmBH, Germany.

**Results**

The mean age of the participants was 21.5 ± 2.07 years with a range of 18-24 years. Of the 80 participants in the study, 38 were males, and 42 were females. The mean values of body mass index were 21.85 ± 4.05 kg/m², serum cortisol was 130.07 ± 64.38 ng/dl, and STAI scores were 46.81 ± 6.15 respectively. The STAI score in the majority of the subjects in Group 2 ranged from 45 to 50 (36 subjects). This is represented in the Graph 1.

Based on the STAI score, all the participants were categorized into three groups. Group 1 consisted of participants whose STAI score was <40. There were a total of 14 subjects in Group 1 with a mean STAI score of 37.5 ± 2.411 and mean serum cortisol of 146 ± 39.85 ng/dl.

Group 2 consisted of participants whose STAI score ranged from 41 to 50. There were 48 subjects in Group 2 with mean STAI score of 46.51 ± 2.67 and mean cortisol level was 135 ± 70.1 ng/dl.

Group 3 consisted of participants whose STAI score was more than 50. There were 18 subjects in Group 3 with mean STAI score of 55.06 ± 2.73 and mean cortisol level was 130.07 ± 64.38 ng/dl.

Mean serum cortisol and STAI score for the individual groups have been depicted in Table 1. The comparison of mean serum cortisol in all the three groups is represented in Graph 2. ANOVA test was applied to compare the mean differences between the three groups. The mean difference in serum cortisol level between the groups was found to be statistically significant ($P = 0.016$).

Negative correlation was seen between STAI scores and serum cortisol in the entire group ($r = −0.235$, $P < 0.05$). Moreover, negative correlation was also seen between STAI scores and serum cortisol in Group 1 ($r = −0.088$, $P < 0.05$), Group 2 ($r = −0.050$, $P < 0.05$) and Group 3 ($r = −0.362$, $P < 0.05$). This is represented in Graph 3.
Discussion

The 80 participants in this study were divided into three groups based on their STAI scores. STAI scores were used to assess the stress levels in the individuals; higher the score, higher the stress.\(^5\) Accordingly Group 3 subjects had the highest stress levels. Subjects in Group 2 had moderate stress levels and those in Group 1 had the least stress levels.

Mean serum cortisol level in Group 3 was lower when compared to Groups 1 and 2. The group with higher stress according to the STAI scores had lesser cortisol level compared with the group with lower stress. Wider fluctuation was observed in the cortisol levels in Groups 3 and 2 [Table 2] as compared to Group 1 individuals who had a lower STAI score. The differences in the cortisol levels between these groups were found to be statistically significant (\(P = 0.016\)).

Basal cortisol levels are crucial in changing the levels of other hormones which are required in the maintenance of homeostasis during exposure to stress. The higher cortisol secretion seen in Group 1 could be explained as a mechanism whereby it is likely to accord protection. It equips the person to be physically and mentally prepared against the physiological manifestations of stressor. Similar findings were seen in a study done by Charles et al. 2001 where the interrelationship between plasma cortisol, catecholamines, neuropeptide Y, and human performance was analyzed during exposure to uncontrollable stress. Cortisol levels are deranged with wider fluctuations only when stress level is very high or persistent. The sequence of action of hormones is also found to be impaired.\(^5,10\) It is also known that cortisol has a permissive action in fellow hormones like catecholamines and glucagon to bring about several actions.\(^11\)

Table 1: Demographic parameters in all the subjects

<table>
<thead>
<tr>
<th>Parameters (n=80)</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>21.5±2.67</td>
</tr>
<tr>
<td>Height in cm</td>
<td>148.26±11.34</td>
</tr>
<tr>
<td>Weight in kg</td>
<td>59.52±10.36</td>
</tr>
<tr>
<td>BMI kg/m(^2)</td>
<td>21.34±4.05</td>
</tr>
<tr>
<td>STAI score</td>
<td>46.81±6.15</td>
</tr>
<tr>
<td>Serum cortisol ng/dl</td>
<td>130.07±64.38</td>
</tr>
</tbody>
</table>

SD: Standard deviation, BMI: Body mass index, STAI: State trait anxiety inventory

Table 2: Mean serum cortisol and STAI score in all the three groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Criteria</th>
<th>Range: Serum cortisol (ng/dl)</th>
<th>Mean serum cortisol (ng/dl)</th>
<th>STAI score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>14</td>
<td>&lt;40</td>
<td>112-261</td>
<td>146±39.85</td>
<td>37.5±2.41</td>
</tr>
<tr>
<td>Group 2</td>
<td>48</td>
<td>41-50</td>
<td>28-329</td>
<td>135±70.1</td>
<td>46.51±2.67</td>
</tr>
<tr>
<td>Group 3</td>
<td>18</td>
<td>&gt;50</td>
<td>13-223</td>
<td>105.83±61.91</td>
<td>55.06±2.73</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>-</td>
<td></td>
<td>130.07±64.38</td>
<td>46.81±6.15</td>
</tr>
</tbody>
</table>

STAI: State trait anxiety inventory

The perception of the stress forms the major factor of the stress response, which depends on the psychological imprint and influence of environment on the stressor. Other factors include the biological properties of the individual to respond and cope with and adapt to the stressor till it vanishes. It can also be described as the capability or physical and mental adaptations, which govern the strength and endurance of the individual to cope with stress. All the participants in this study were exposed to the same stressors and were within a narrow age group. They also had the same kind of work routine. Hence, the amount of daily stress, to which they were exposed to, was almost same. In spite of this the response to the stressor varies widely between individuals. There are several factors, which could be responsible for this.

 Exposure to anything that is new or not previously experienced could be a potential stressor. Defining the standards of a stressor is very difficult as it varies from person to person. Collectively the definition of what could be stronger stressors, which elicit sustained stress response is still a debate. The euphoric activities of normal life when adapted to the mechanical distressing life of the 21st century have changed to dysphoric activities leading to stress. Normal activities are perceived as stress. An attempt has been made to briefly describe a few of these aspects.

 Stress emerges in the area of cognitive preoccupation with subjectively significant problems. This preoccupation may manifest as worrying which a common human experience is leading to dysfunction, i.e., enhancing stress and anxiety instead of reducing it. Or it may constitute constructive problem-solving activity, enabling the individual to cope with life problems. Worrying may appear in anticipation of everyday demands after awakening and thus may be more pronounced on weekdays than on weekend days.\(^12\)

 Sleep disturbances like microarousals,\(^13\) working night shift, and working late night are common modern stressors.\(^14\) These activities usually originate as “cortical” but they can also be generated as a response to disturbances in sense organs, such as respiratory interruption, apnea, snoring, and noise, changes in heart rate, blood pressure and movement disorders. An imbalance in work and appropriate reward or over commitment may also be considered as a potent stressor because it leads to an imbalance between demands and own coping resources and this leads to poor subjective well-being.\(^15\) Watching television, listening to loud sounds, drowsy attitude in the lecture classes are considered as relaxation or breaks only for limited short duration of time. But when continued for longer duration this itself might become a potent stressor. Added to this unhealthy food habits, inappropriate habits like drinking, smoking tobacco, exposure to polluted air from vehicles and industries have all contributed to non-culpable stress among the younger generation leading to various adverse health effects.\(^14,16\) The fluctuations in the serum cortisol level due to the addition of these modern stressors is more frequent than
expected or intended as a part of the normal physiological response.

The two principal components of the stress response are the corticotropin-releasing hormone (CRH) and the locus ceruleus-norepinephrine/autonomic (sympathetic) nervous systems.[11] The CRH system is widespread throughout the brain, but is best characterized in the paraventricular nucleus of the hypothalamus.

A key element in the adaptive response to physical or psychological stress is the activation of the hypothalamic-pituitary-adrenal (HPA) axis. Following exposure to aversive or threatening stimuli, a series of hormones are released, beginning with corticotrophin-releasing factor (CRF) from the paraventricular nucleus of the hypothalamus, adrenocorticotropic hormone from the anterior pituitary, and glucocorticoids (GCs) from the adrenal cortex. These hormones affect entire physiology of the organism, including the CNS. Stress has profound effects on brain areas associated with conscious, memory and executive functions. In the hippocampus, stress can disrupt long-term potentiation and hippocampus-dependent learning and memory via glucocorticoid receptor activation.[6,7] There are also profound effects of stress and GCs on the mesococumbens dopamine system, which contributes to motivation and goal-directed behaviors.

The body’s response to stressors and various factors involved in it encompasses neurophysiological circuits involved in cortisol production in stress. Stress causes increases in plasma GCs to high “pharmacologic” levels that in the short run are life-saving.[11]

The serotonin system is one of the major pathways, which mediate main activity of cortisol and its reactivity to stressors. These pathways influence the neural activity at suprachiasmatic levels and also modulate the each level of the HPA axis. In particular, serotonin fibers activate the hypothalamic CRF containing neurons that initiate the hormonal cascade leading to cortisol release.[18,19] Fibers from the amygdaloid nuclei mediate responses to emotional stresses. Fear, anxiety, and apprehension cause marked increases in ACTH secretion. Input from the suprachiasmatic nuclei provides the drive for the diurnal rhythm. Impulses ascending to the hypothalamus via the nociceptive pathways and the reticular formation trigger increased ACTH secretion in response to injury. The baroreceptors exert an inhibitory input via the nucleus of the tractus solitaries.[17,19,20]

In our study, Group 3 participants might be vulnerable to greater stress related diseases and disorders. Hence, it is concluded that it is important to identify the stressor, quality of the stressor and appropriate training has to be instituted for better performance in the instituted. This can prevent the consequences of prolonged stress or distress in an individual. It is also suggested that there is a need for better stress estimation techniques, followed by teaching better stress management principles for all younger adults for the present generation.

References

17. Viau V, Chu A, Soriano L, Dallman MF. Independent and overlapping effects of corticosterone and testosterone on...


