

# Lifestyle, Stress and Cortisol Response: Review I

## — Mental Stress —

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### Abstract

The incidences of diseases related to mental stress are increasing in Japan. Mental stress, unacknowledged for long periods, has been shown to lead to the development of a number of diseases. Thus, an index for mental stress is important to induce awareness of its presence. We focused on the relationship between cortisol and mental stress in this review. We will discuss both the usefulness and problems of cortisol as a mental stress index by summarizing the relationship between cortisol and mental stress. The present findings suggested that cortisol appears to be an adequate index for mental stress. However, there are several problems; the present group clarifies these problems and builds the comprehensive mental stress assessment systems by using saliva samples.

**Key words:** experimental stress, psychological stress, chronic stress, daily life event

### Introduction

In Japan, the incidences of diseases related to mental stress have been increasing. Therefore, it is necessary to understand the physical responses to mental stress and determine ways in which cope with it. As chronic mental stress, it may induce some diseases, an appropriate index for mental stress is important to evaluate its severity.

Endocrinological reactions to stress are well known. The main stress reaction pathways are “stress-hypothalamus-pituitary-adrenal cortex” and “stress-autonomic nervous system-adrenal medulla”<sup>1</sup>. Cortisol is a major steroid hormone secreted by the adrenal cortex and is a possible candidate as an index for stress. This is an essential hormone to human survival, and plays a key role in adaptation to stress<sup>2</sup>. Following the pioneering study of Selye<sup>3</sup>, the pituitary-adrenal system has been viewed as central to human adaptation to changes in the internal and external environment. About 80% of the circulating cortisol in plasma is normally bound to an  $\alpha$ -globulin (cortisol-binding globulin)<sup>2,4,5</sup>. This bound cortisol is not readily available for physiological activity, but about 10% of plasma cortisol is loosely bound to albumin and another 10% is unbound. This unbound fraction is available for physiological activity and metabolic degradation. The proportion of free and loosely bound cortisol increases as the concentration of

cortisol increases<sup>2</sup>. Some unbound cortisol is secreted in saliva or passed through the kidneys, whereas cortisol metabolites are excreted in urine as 17-hydroxycorticosteroids (17-OHCS) and 17-ketogenic steroids (17-OHCS plus cortisol and corticosterone)<sup>6</sup>.

We focused on the relationship between cortisol and mental stress in this review. Indeed, endocrine responses to mental stress have been frequently reported, and in general, distressing psychological stimuli are associated with increases in cortisol level. We examined both the usefulness and problems of cortisol as a mental stress index by summarizing the relationship between cortisol and various mental stresses. From the viewpoint of preventive medicine, cortisol appears to be an adequate index for mental stress.

## 1. Experimental stress

### 1.1. Mental stress in laboratories

Mental stress in the laboratory (e.g. public speaking, mental arithmetic, audience and anticipatory period, memory comparison task, geometrical recognition task, attention test, concentration task, arithmetic test with noise, speech task, reaction time task) increased cortisol levels<sup>7–11</sup>. A positive correlation was reported between visual display-task performance and task-related increases in cortisol levels<sup>12</sup>. Subjects who experienced flight simulator tasks did not show increases of cortisol levels as compared with their pre-task levels<sup>13</sup>. However, subjects with high levels of cortisol showed a poor performance<sup>13</sup>.

A significant cortisol elevation was reported during negative emotions triggered by film presentations of 30–90 min<sup>14</sup>. There were no significant differences in cortisol levels before film presentation between the low and high anxiety groups<sup>15</sup>. The cortisol responses of the high anxiety group was not changed during and

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following the unpleasant film, but that of the low anxiety group was increased<sup>16</sup>.

Bungee jumping has been shown to increase in salivary and blood cortisol levels<sup>17,18</sup>. Cortisol was also reported to be markedly increased after parachute jumping<sup>19,20</sup>, but cortisol levels did not increase after repeatedly faced with parachute training<sup>21</sup>. Parachute jumpers with high levels of cortisol were reported to show poorer performance and were more defensive<sup>22</sup>.

Astronauts are exposed to conditions of micro gravity and social isolation. In the ESA-ISEMSI '90 (European Space Agency-Isolation Study for the European Manned Space Infrastructure), the average pre-experiment cortisol levels were always higher than the typical control levels seen in the laboratory<sup>23</sup>. On day 2, the values declined slightly but increased on day 16<sup>23</sup>. However, the values again decreased on days 22 and 27<sup>23</sup>.

### 1.2. Relaxation

Relaxation and meditation were found to be correlated with decreases in cortisol levels compared with control conditions<sup>24-26</sup>.

A decrease in cortisol levels was reported during transcendental meditation and after biofeedback-assisted relaxation, Tai Chi and REST (Restricting Environmental Stimulation Technique; consisting of an insulated container filled with salt water maintained at a temperature of 35.5°C)<sup>27-31</sup>.

However, a decrease in the same magnitude occurred in control subjects and, thus, appeared to reflect a non-specific gradual decrease throughout the course of the experiment<sup>32-34</sup>.

The rise in plasma cortisol levels during gastroscopy was shown to be significantly reduced under the influence of music<sup>35</sup>; subjects listening to a 60-min music program showed a marked decrease, and at the end of the music session, their cortisol levels were significantly lower than the initial values<sup>36</sup>.

## 2. Chronic mental stress (Table 1)

There is evidence that acute mental stressors increase cortisol excretion<sup>7-23</sup>. However, the effects of chronic mental stress, are less clear.

Some of these studies indicated that prolonged mental stress such as that seen in combat veterans, in combat training, hostages, bereavement and subjects living in proximity to a damaged power plant was associated with elevated cortisol levels in a typical laboratory situation<sup>1,37-40</sup>. However, prolonged combat exposure, com-

bat-related PTSD and the fatal illness, earthquake victims and death of a close relative have been shown to be associated with chronically lowered cortisol excretion rates<sup>41-45</sup>.

Several studies have indicated that there are no significant differences between subjects with chronic mental stress, exposure to chemical disaster<sup>46</sup>.

## 3. Mental stress in daily life event (Table 1)

There have been many studies concerning the relationship between cortisol and mental stress. However, there have been fewer studies limited to mental stress in daily life event.

Marital conflict itself does not affect the cortisol level<sup>47</sup>.

Members of a cardiac surgery team were monitored<sup>48</sup>. Days when self-perceived mental stress was reported were associated with higher levels of urinary cortisol<sup>48</sup>. VanEck and Nicolson did not find any differences in the diurnal rhythm of salivary cortisol between subjects with high scores on the Perceived Stress Scale compared to those with low perceived mental stress<sup>49</sup>.

New students showed significantly higher subjective anxiety scores and cortisol concentrations than second year students at first visit to school and themselves at the second visit<sup>50</sup>. After academic examination, saliva cortisol levels were increased compared to those before levels<sup>51</sup>.

Mental work demands were associated with increases in plasma cortisol<sup>52</sup>. Those men who responded to increased workload with increases in cortisol, possibly reflecting increased job involvement, also had higher average cortisol levels<sup>53-55</sup>.

Unemployed men and women were shown to have higher cortisol levels compared with employed subjects<sup>56-58</sup>.

## 4. Laboratory-field associations

The problem was to compare cortisol responses measured in the laboratory with those measured in real life<sup>59</sup>. The usefulness of laboratory assessment tests, in part, on the assumption that laboratory responses reflect those occurring under natural conditions<sup>60</sup>.

Only one study has investigated laboratory-field associations of cortisol excretion patterns<sup>61</sup>. In a sample of nine student teachers, saliva cortisol responses were compared in a real and a standardized lecturing situation<sup>62,63</sup>. Reactivity was operationalized as an increase in cortisol excretion at start of the lecture<sup>62,63</sup>.

**Table 1** The relationship between daily stress and cortisol modification

Type of daily stress	Duration	Subjects	Cortisol reaction
Loss of a parent	Long	Adults who lost their parents	↓
Children ill	Acute stress	Parents whose children were terminally ill	↓
Bereavement	Long	Women whose spouse was terminally ill	↑
Work load	Acute stress	Workers	↑
Job	Unemployment		↑
Perceived stress			No change
Perceived stress	High stress day	Members of a cardiac surgery team	↑
War, hostage	Long	Combatants	↑
Power plant accident	Long	Residents	↑
War	Long	Post-traumatic stress disorder patients	↓
Chemical Disaster	Long	Residents	No change

↓: Reduce, ↑: Increase

### 5. Mental stress during medical treatment

Subjects with high anxiety demonstrated lower cortisol responses to surgery compared with those with a level of low anxiety<sup>64,65</sup>. However, these findings were not confirmed by other studies<sup>66</sup>. Individuals repeatedly faced with medical procedures showed habituation of the cortisol level<sup>66</sup>. No significant elevation of cortisol occurred during dental examination or root canal therapy or in subjects receiving restorative dental work<sup>67</sup>. However, the extraction group showed slight increases in cortisol compared with the above groups<sup>67</sup>.

#### Future applications

##### 1. Index for mental stress

Recent research has provided considerable insight into the psychological mechanisms involved in the impairment of human performance caused by stressors, such as sleep loss, noise and mental fatigue<sup>68</sup>.

In summary, it is suggested that cortisol appears to be an adequate index for mental stress. However, the above studies indicated that actual mental stress did not have the same effects on

cortisol responses, although many studies experimentally demonstrated increases in cortisol levels under conditions of mental stress<sup>7-23</sup>. There are two main reasons for this uncertainty, the first is that cortisol levels were measured under a variety of conditions, time courses, and in different kinds of samples and using different methods. Cortisol shows circadian rhythms, and its level is highest in early morning and lowest at night<sup>69</sup>. The question arose whether a true demonstration of the relationship between cortisol and stress could be shown by taking samples at one point in a single day. There was no fixed sampling time and it was difficult for subjects to give blood many times a day.

Another cause of the uncertainty is that most of studies did not consider individual factors (personality, lifestyle etc.). Individuals perceive and respond to mental stress in different ways. It was reported that cortisol levels in males were greater than those in females after the power plant disaster at Three Mile Island in the U.S.A.<sup>1</sup>). Mental stress is considered to be related to many factors, e.g. lifestyle, personality, environment and human relationships. However, few studies have adjusted for such individual factors<sup>70-72</sup>.

To solve these problems, we used saliva samples and these were taken mostly at the same time, same method in school, in the

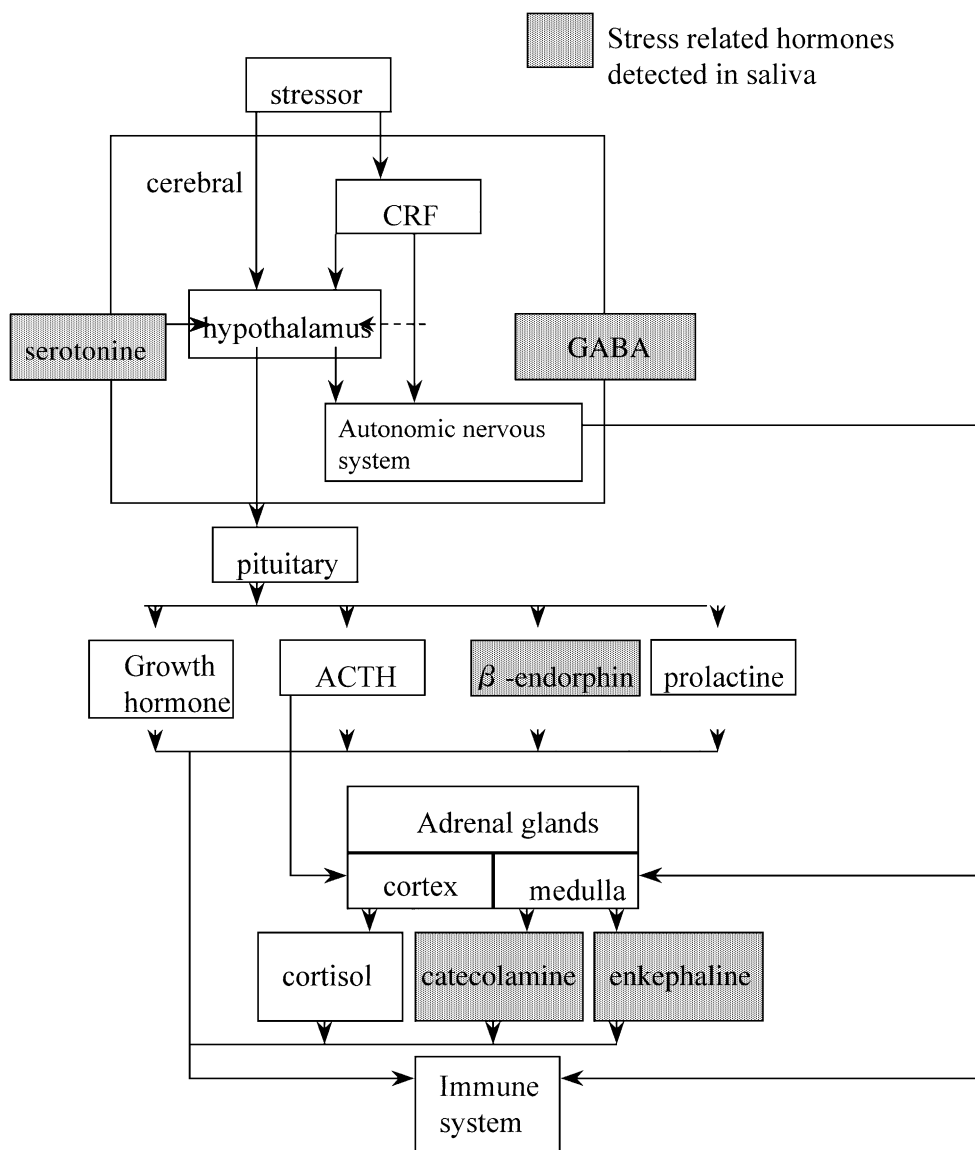


Fig. 1 Stress related hormones detected in saliva.

workplace etc. We also questioned subjects their lifestyle and mental status using similar contents. It is possible to examine the usefulness of cortisol as an index for mental stress at similar statuses and adjusting for confounding factors. It is suggested that a comprehensive mental stress assessment system can be built by using these findings.

## 2. The usefulness of saliva samples for the mental stress index

The assessment of cortisol in saliva has recently become a valuable alternative to blood analysis<sup>2)</sup>. Due to the noninvasiveness and laboratory independence of sampling, salivary cortisol

can be measured at almost unlimited frequency under a wide variety of clinical and field settings.

Serotonin, melatonin and beta-endorphin and, other stress-related hormones, were detected in saliva<sup>73-75)</sup> (Fig. 1). However, there are two main problems in measuring those hormones simultaneously; a large amount of saliva is needed to detect several kinds of hormones, and each hormone is measured in a different way. Thus, it is necessary to develop better methods by which to measure those hormones simultaneously using a very small sample of saliva.

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