

Stress: Medical aspects

By Takanobu Yamamoto,

Health Science Laboratory,
Tezukayama University

Introduction

Stress causes various diseases. This is called "stress-related-disease". The *stress* in the field of medical science has been introduced by Dr. Hans Selye (1907-1981). Figure 1 shows the typical response of the stressor. Stressors can be classified into four groups; 1) Mental stress (anxiety, sadness, fear) 2) Biological stress (bacteria, virus, parasite) 3) Physiological stress (Fasting, sleeplessness, fatigue, thirst) 4) Physic & chemical stress (temperature, chemical substance, radiation, atmospheric pressure). In this chapter, effect on human health of mental and temperature stress from the whole body to the cell level, will be focussed upon.

In mental stress, for example; PTSD (post-traumatic stress disorder) and techno-stress, causes failure such as coronary heart disease, particularly in nervous people who have a high score "Type A behavior" which behavioral characteristics shows excessive hard-driving, time urgency and aggression. Scientific mechanisms of mental stress consist of brain neurotransmitter release from the hypothalamus by stressor. This phenomenon of stress responses induce various physiological changes; for emotion, endocrine & autonomic system, awakens, memory, decision-making, motor performance and immune system.

Ischemic heart disease(IHD) and mental stress

The typical pathways to the formation of the IHD are as follows;

- (1) Stress--cerebral cortex--hypothalamus--spinal cord-- sympathetic nerve-- adrenal medulla--adrenaline secretion--adipose tissue--lipolysis--VLDL- and LDL-cholesterol--atherosclerosis in the coronary artery--IHD
- (2) Stressor--cerebral cortex--hypothalamus--spinal cord-- sympathetic nerve activation--noradrenaline release--increase of blood pressure & cardiac output--overload of heart constriction--IHD

Stress

Stomach & duodenal ulcer and mental stress

The main pathways to ulcer formation are as follows;

- (1) Stress--cerebral cortex--anterior hypothalamus--
medullaoblongata--parasympathetic nerve--
acetylcholine release--histamine release--HCl secretion
-- gastrin release--histamine
--movement of smooth muscle--ischemic
--ulcer

- (2) Stress--cerebral cortex--posterior hypothalamus--
spinal cord--sympathetic nerve--vascular constriction--
ischemic--ulcer

Monoamine hypothesis for depression and stress

Sustained stress induces an increase of noradrenalin and serotonin in the forebrain, and a decrease of noradrenalin and dopamine in the hypothalamus and striatum. These findings show that stress has an effect on brain function, which may be related to depression, because the effect is shown on active agents such as tricyclic antidepressant and selective serotonin reuptake inhibitor (SSRI).

Effect of stress on the immune system by stress

Stress is known to cause thymus shrinkage, in contrast with hypertrophy of adrenal tissue. These mechanisms are known to be caused by the following pathways ; Stress--cerebral cortex--hypothalamus--pituitary--ACTH release--adrenal tissue--thymus. Thymus has the role of differentiation and growth for the T-cell. Therefore, the damage of thymus shrinkage causes decrease of T-cell (lymphocyte)(Figure 2).

Cell response to stress

In the case of heat shock stress, living cells synthesize heat shock protein (HSP); HSP 104, 90, 70, 60, 40, 28, and ubiquitin. These synthesis start from above 35°C, especially, HSP 70 which marked increase over 43°C. The role of HSP for stress helps recovery such as functional and structural assembly for abnormal proteins in the cell, and also the catabolism and inhibition of toxic and abnormal proteins. In the normal condition, HSP has a role of

Stress

building, modeling, assembly, transport, functional expression, structural maintenance and catabolism. Figure 3 shows the change of HSP 70 protein after psychological stress.

For pain stimulation, c-fos mRNA expression is induced in the hippocampus, cerebellum and spinal cord. For thirsty stress, c-fos protein synthesizes in the hypothalamus relates to ADH production.

Prevention of stress

There is data of prove that prediction and preparation before stress is effective in its prevention (Figure 4).

Post-traumatic stress disorder (PTSD) is caused by strong unexpected stressful damage such as the case of soldier who experienced the Vietnam war. In the group who showed a high score of PTSD, significant decrease of natural killer (NK) was observed (Figure 5). Thus, PTSD has an affect on the immune system. PTSD score may be an important indicator of the relationship between the mental and physical health conditions. A society of hyperchange may cause "future shock trauma" in our daily working life, as well as PTSD.

Summary

Hans selye (1907-1981) introduced the concept of "stress" into medical science (1936) and since then it has been used in the physical sciences. There are many types stress; biological, physiological, physic-chemical aspects. Recently, there has been warning in an increase of mental stress. In case of a high score of *type A*, there is a high ratio of coronary heart disease. In addition, gastric ulcer and immunue dysfunction may be caused by mental stress. In the body, stress protein such as HSP 70 play an important role in repairing and assembling protein structures and in the catalyze and inhibition for degeneration of proteins.

Prediction and preparation for stress may contribute to prevention of PTSD.

References

Earle, R.C.B.(1997). *Scientific Live/SAPIENS (What is Stress?)*, Nisseisangyo Co.: Tokyo. (Chapter 6).

Isosaki, M. and Nakasima, T. (1998). *Jpn. J. Pharmacol.* 76(3) 305-308. (Chapter 6).

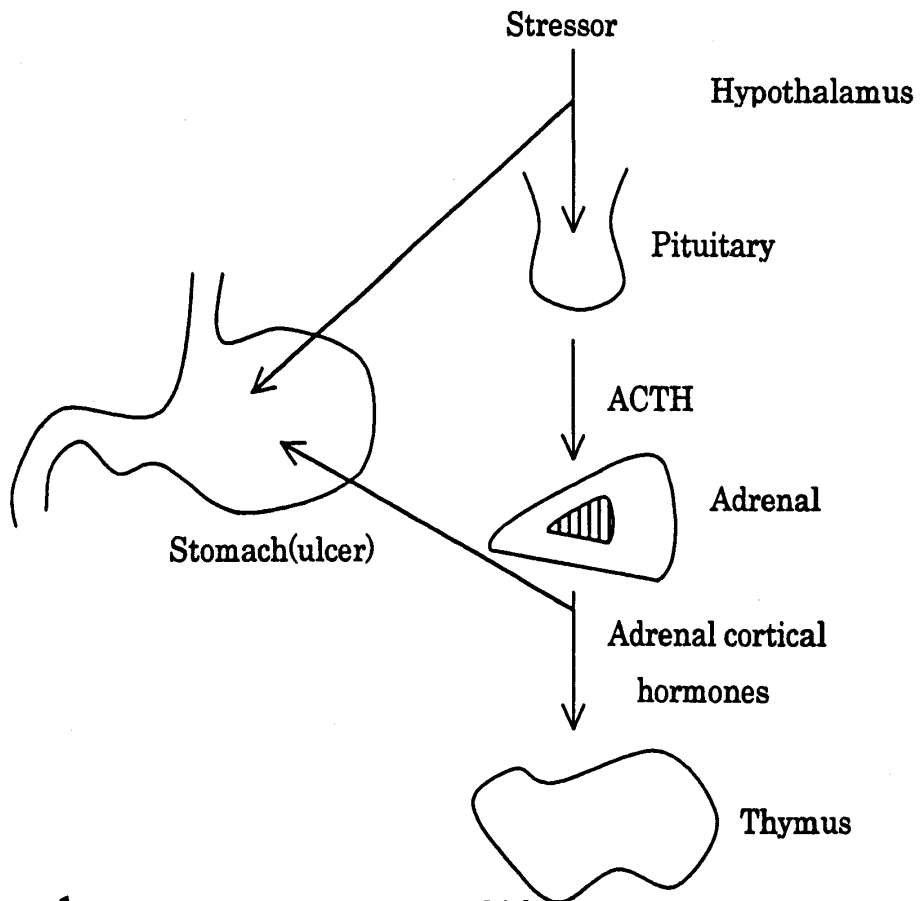


Figure 1 : The fundamental process which has response to stressor.

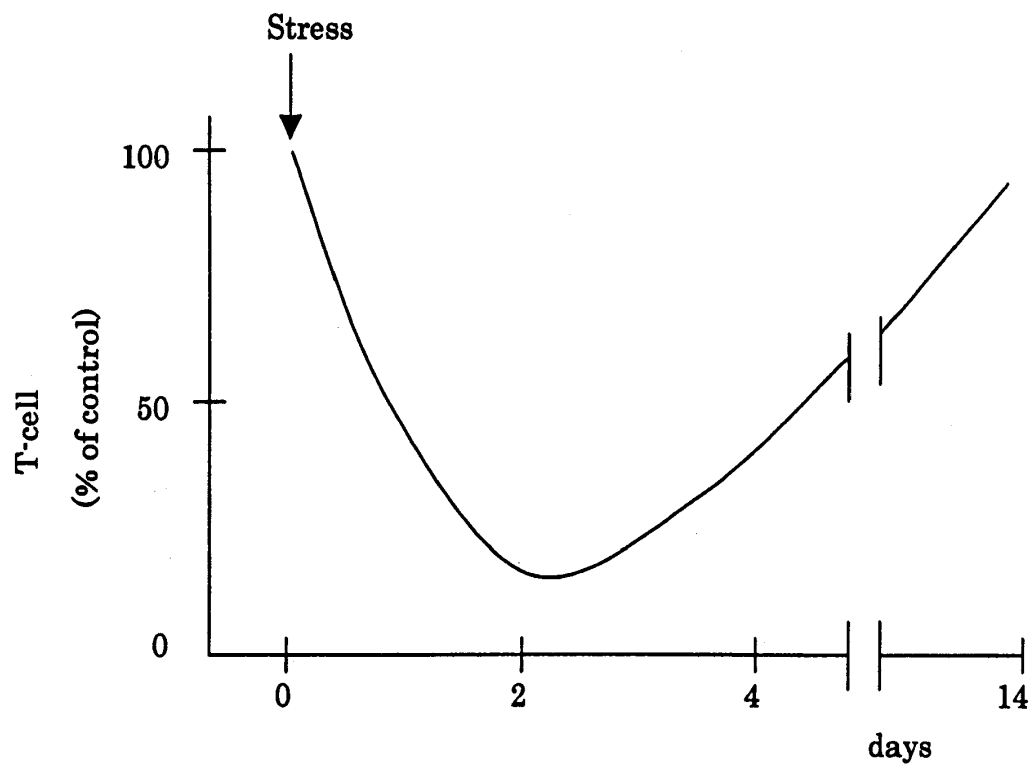


Figure 2 : Change of the number of T-cell in thymus by immobilization (17hr) stress.

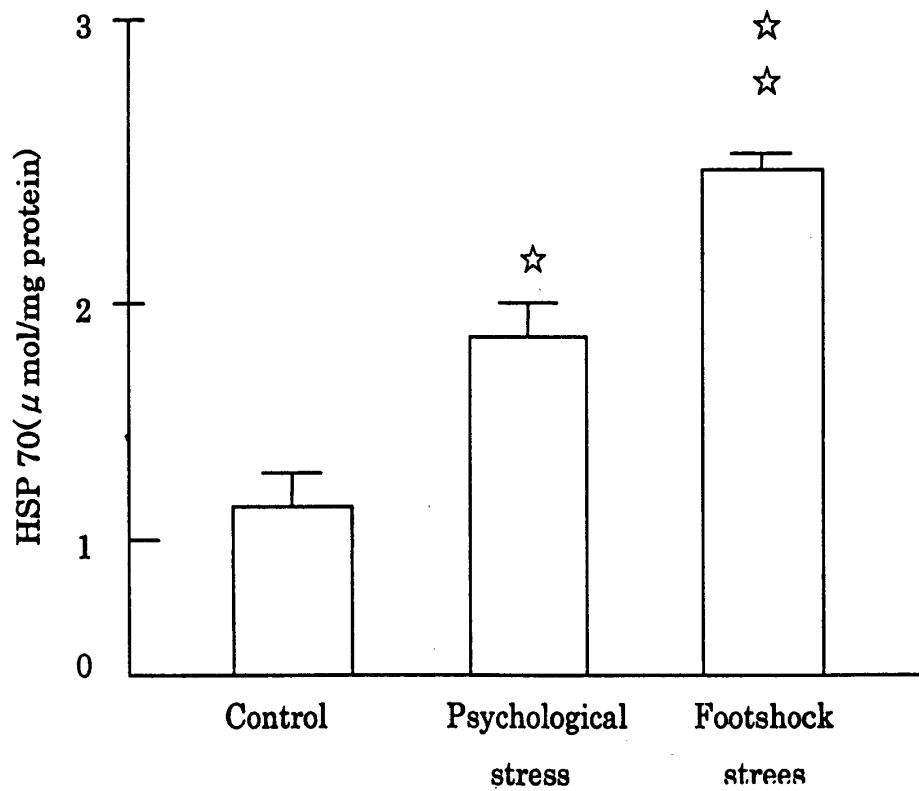


Figure 3: Quantification of HSP 70 protein in the aorta.

☆ $p < 0.05$, ☆☆ $p < 0.01$ vs Control

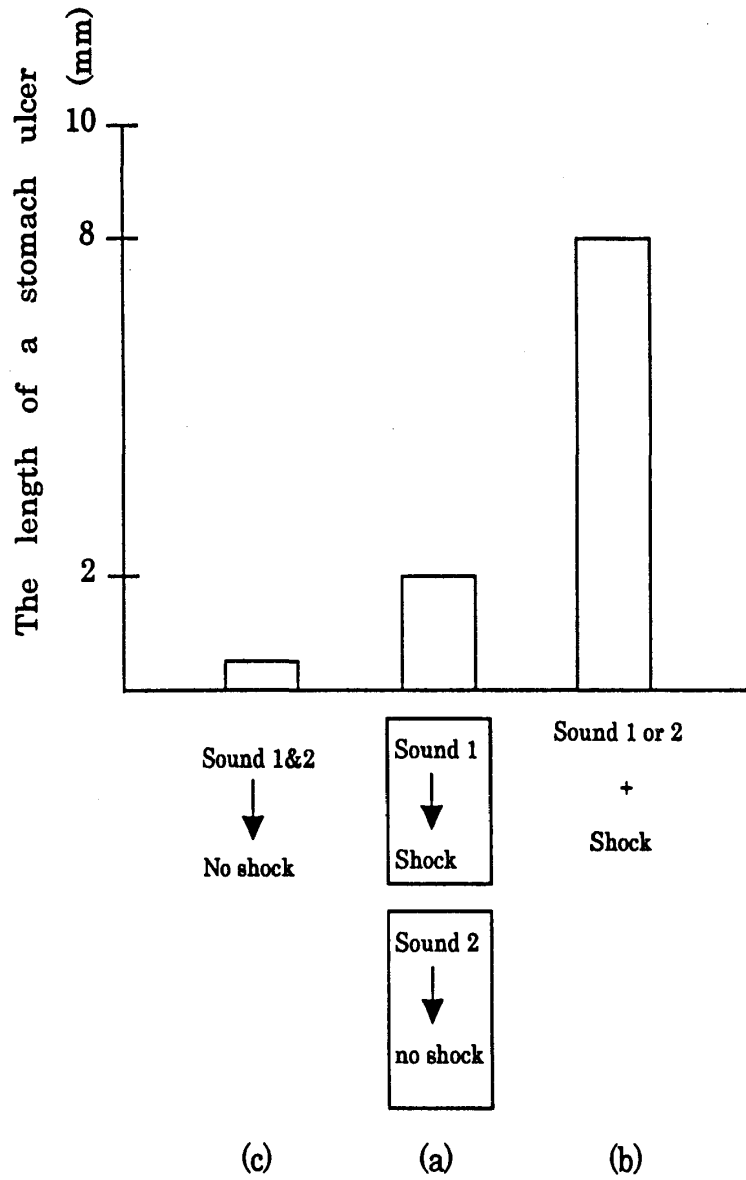


Figure 4: A predictable stress (a) is short length of ulcer in compared with (b) which can't predict a stress.

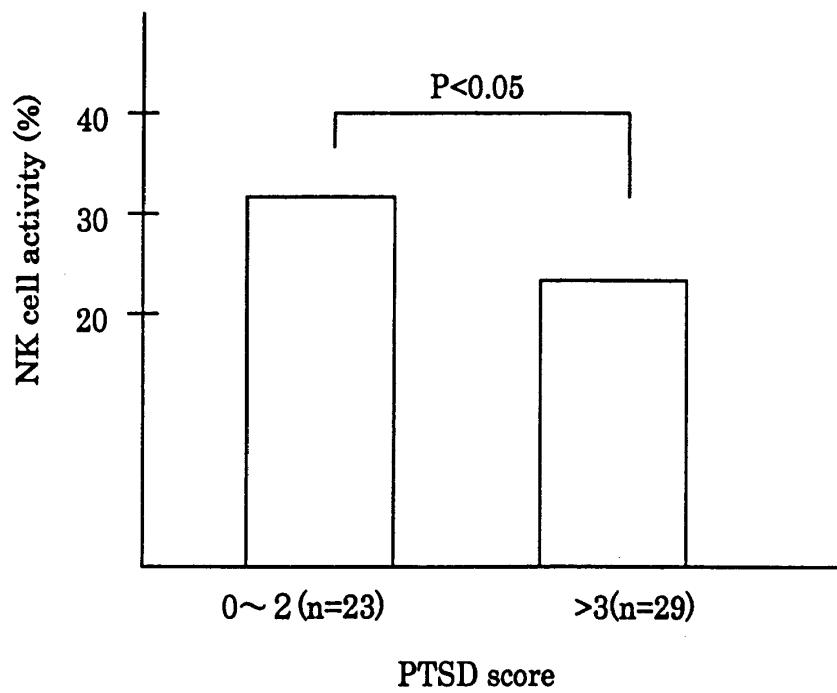


Figure 5 : PTSD score and NK cell activity. The high - score group (>3) was lower level of NK cell activity than low - score group (0~2).