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## Effect of psychological stress on pituitary hormone secretion

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下垂体ホルモン分泌における心理的ストレスの影響

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正常人において心理的ストレス状況下での下垂体ホルモンの分泌について検討した。対象は19～22才の健康な学生15人である。心理的ストレスとしては鏡映描写テスト (MDT) を行なった。MDTは5分施行後1分の休みをおいて再度5分施行した。中間の休みの時に、Thyrotropin Releasing Hormone (TRH) 500 $\mu$ gを単回静注し、静注前及び静注後15分、30分、60分、90分、120分に採血を行ない、HGHとPRLを測定した。対照として同一対象にTRH静注のみ及びMDTのみの場合の検討も行なった。

MDTを施行しそれに加えてTRHを静注した時には、前値に比べ15分、30分後に有意 ( $p < 0.001$ ) のHGH増加反応を示した。MDTのみを行なった場合には、HGHの有意の変化はみられなかった。TRH静注だけでも強い増加反応はみられなかった。さらにTRH静注だけと、MDT施行中にTRH静注を行なう場合を比較すると、MDTとTRHの同時の負荷の時に、有意に ( $p < 0.01$ ) 強いHGHの増加反応がみられた。PRLの反応は、TRH静注のみと、MDTとTRH静注と、両者共に同じ様な反応を示した。即ち、心理的ストレス (MDT) と身体的刺激 (TRH静注) の両方の負荷が同時にある時に、有意のHGH増加反応がみられた。

### ABSTRACT

The human growth hormone (HGH) response to thyrotropin releasing hormone (TRH) was investigated under the state of psychological stress in normal subjects. Fifteen subjects were 4 males and 11 females. Their age ranged from 19 to 22 years. The mirror drawing test (MDT) was performed to induce psychological stress. Plasma growth hormone and prolactin were determined serially before, during and after the test. Three kinds of tests, namely, TRH test only which was performed by injecting iv 500 $\mu$ g synthetic TRH, mirror drawing test only and TRH test with MDT were done. The changes of HGH to MDT only were not significant. HGH response to TRH only showed no remarkable change. The HGH responses to TRH with MDT were significantly higher than the responses to TRH only. The changes of prolactin to TRH with MDT and TRH only showed almost the same response pattern. Only under the state of combination of these two stimuli, somatic and psychological, the changes of HGH secretion were significant.

### INTRODUCTION

The secretion of the human growth hormone, one of the pituitary hormones, is regulated

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by the work of the hypothalamus. HGH has no definite target organs, and that is different from other pituitary hormones, for example TSH, LH, FSH and ACTH. So, the secretion of HGH is not within the negative feedback mechanism from peripheral systems. Hypothalamus itself regulates the secretion of HGH by HGH secretion inhibition factor and HGH secretion releasing factor. It has been reported that the secretion of HGH is influenced by several factors and psychological stress is one of these increasing factors<sup>1) 2)</sup>.

In this paper, I would like to show not only the HGH response to psychological stress, but also the effect of psychological stress on HGH response to TRH, one of hypothalamus hormones. Namely, this study is on the responses to somatic stimulation which is TRH injection, and psychological stimulation which is the mirror drawing test, and the interaction of two stimulations. The present investigation is more concerned with dynamic and more usual and daily stress situation than previous reports<sup>5) 9)</sup>.

### MATERIALS AND METHODS

#### Subjects:

Fifteen subjects were healthy and paid volunteers, 4 males and 11 females. All subjects were not obese, not under medication, nor had they history of psychiatric disturbances. Their ages ranged from 19 to 22 years (mean age of 20).

#### Methods:

As the psychological stress, various methods of stress loading were performed, but generally, any of these methods was not recognized and not established as the definite method. Recently, Mirror Drawing Test is widely utilized as a method of nonspecific stress loading. We too used MDT as psychological stress.

The mirror drawing apparatus (PSYMO-CF-502, Seiwa ME-Research Institute, Osaka, Japan) was used to induce psychological stress. The test figure, a five-pointed star, 3.3 cm from tip to tip, drawn in such a way that a 7 mm wide star-shaped path, enclosed reflected by a vertical mirror. Direct vision of the figure is obscured by a shield protruding horizontally. The task is to trace the figure as quickly and accurately as possible with an electrical stylus while looking at the mirror reflection. The position and movement of the stylus are sensed electrically and deviation from the path causes an alarm by a buzzer installed beneath the floor. The speed (number of star-arms traced per min) and accuracy (frequency of the stylus leaving the double star lines) are automatically recorded on digital records.

All subjects were placed at rest with catheterization of the antecubital vein by use of a short indwelling catheter and under the fasting condition. The first blood sample was obtained before MDT was done. Before MDT, subjects were given instruments such as faster and more accurately. MDT was done 5 min as the first trial and the interval was 1 min, and more 5 min as the last trial. TRH injection iv 500 $\mu$ g was performed at the interval of MDT. At the cessation of the MDT, the subject returned at rest and blood samples were obtained at 15, 30, 60, 90, 120 min after MDT.

Blood samples were centrifuged immediately after collection, and the serum was frozen and stored at  $-20^{\circ}\text{C}$  until assayed. Serum HGH and Prolactin were measured by the double antibody radioimmunoassay technique.

Control study was done. To the same subjects, TRH test only was performed and at another time MDT only was too done. Three kinds of tests, namely TRH test only, MDT only and MDT with TRH, were performed in no special order to exclude the effect of habit to MDT.

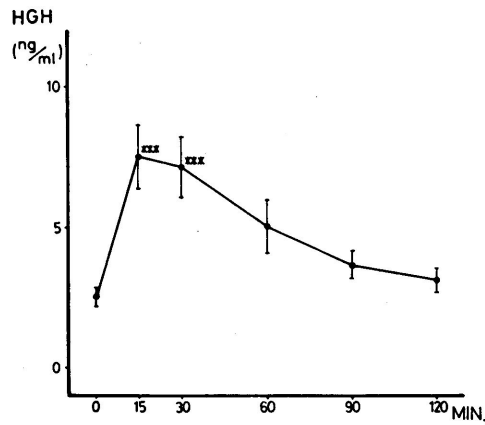


Fig. 1. GHG responses to TRH with MDT. The value of GHG showed a significant raise. Mean  $\pm$  SE, N=15, \*\*\*  $p < 0.001$

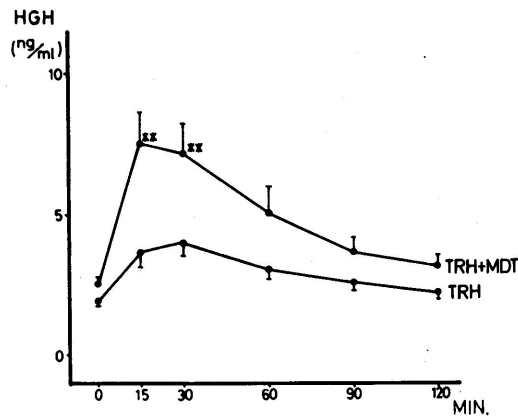


Fig. 2. GHG responses to TRH with MDT and TRH only. GHG responses to TRH with MDT were significantly higher at 15 and 30 min than responses to TRH only. Mean  $\pm$  SE, N=15, \*\*  $p < 0.01$

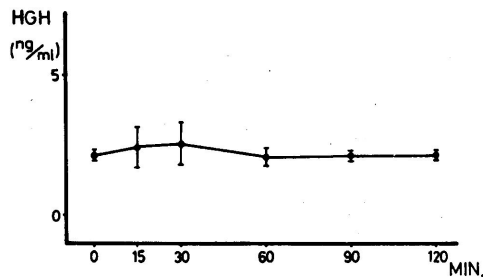


Fig. 3. GHG responses to MDT. The changes of GHG were not significant. Mean  $\pm$  SE, N=15

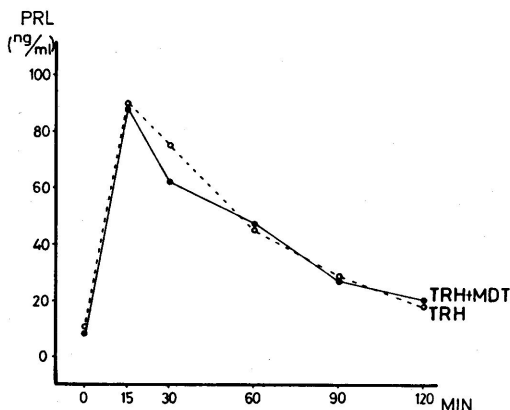


Fig. 4. PRL responses to TRH with MDT and TRH only. Two groups showed almost the same response pattern. N=15

### RESULTS

The changes in the mean values of GHG response to TRH test during MDT are shown in Fig 1. The value of GHG showed a significant raise,  $7.5 \pm 1.2$  ng/ml (mean + SE) at 15 min ( $p < 0.001$ ),  $7.1 \pm 1.1$  ng/ml at 30 min ( $p < 0.001$ ), while GHG value at rest was  $2.5 \pm 0.3$  ng/ml. GHG response to TRH only showed no remarkable change and all values of GHG were under 5 ng/ml. The GHG responses to TRH with MDT were significantly higher at 15 and 30 min ( $p < 0.01$ ) than the responses to TRH only, while at rest, the difference of GHG values of two groups were not significant. They are shown in Fig 2. The changes in the mean values of GHG response to MDT only are shown in Fig 3 as not significant.

The changes of prolactin to TRH with MDT and TRH only are shown in Fig 4. Two groups showed almost the same response pattern.

### DISCUSSION

It is well known that the secretion of GHG is influenced by several kinds of stress. Greenwood et al<sup>3)</sup>, reported that emotional stress increased the level of GH. In his experiment, saline and not insulin, had been injected in a subject who was told that he had received a large dose of insulin and would experience severe hypoglycemic symptoms. As a result, his plasma sugar remained unaltered, but there was a demonstrable increase in his plasma cortisol and growth hormone.

Schalch<sup>4)</sup> reported that in an effort to determine whether psychic stress per se, unattended by physical stress or exercise, might be associated with a rise in plasma growth hormone, ten male medical students were studied during a traditionally difficult final oral examination in medicine. There was no significant difference between either the mean plasma glucose or growth hormone concentrations on the control and experimental days. In one admittedly tense individual in the group, however, the plasma growth hormone levels on the day of the examination were considerably higher than those on the control day.

The authors also reported on the effect of emotional stress, which included a stress interview and a stress movie, on human growth hormone secretion<sup>5)</sup>.

The secretion of HGH is influenced by mainly two factors, that is, somatic and psychological factors. In the present study, these two factors in combination were investigated. As a somatic factor, TRH which is a hypothalamus hormone was used and as a psychological factor, MDT which induces acute psychological stress was performed<sup>6) 7)</sup>. It is known that, in normal subjects, the secretion of TSH and Prolactin to TRH increases and the secretion of HGH to TRH shows no remarkable change. But, in some patients with acromegaly, depression and anorexia nervosa the increased responses of HGH to TRH are shown<sup>8)</sup>. At stress in the state of fasting, also HGH secretion to TRH has shown a tendency of increased response<sup>9)</sup>. In this study, normal subjects showed no remarkable change in the response of HGH to TRH, while HGH value to TRH slightly increased in comparison with the value of HGH at rest, but its change was within normal range. Thus, it is supposed that in some states or in the abnormal state, TRH facilitates the secretion of HGH.

The mirror drawing apparatus was originally devised to test psycho-motor learning in man, but it can also be used to produce psychological stress regularly associated with physiological responses, such as elevation of blood pressure<sup>10)</sup> and increase of catecholamine and cortisol secretion<sup>6) 11)</sup>. In this study, MDT as an inducer of psychological stress was performed to investigate the effect on HGH secretion. During MDT only, the change of HGH secretion was not significant. It is supposed that the stimulus of MDT influenced blood pressure and the secretion of cortisol, but it can not be such stress as to influence the secretion of HGH. Namely, the stimulus of TRH only does not induce a marked increase on HGH secretion and stimulus of MDT only does not induce a change in HGH secretion. But, the simultaneous stimulation of TRH and MDT induced a significant increase of HGH secretion. While somatic changes to some somatic stimulus are not shown under the state of no psychological loading, somatic changes to the same somatic stimulus are shown with psychological loading. That is to say, the changes of HGH secretion to psychological stimulus only are not shown and the changes of HGH secretion to somatic stimulus only are not significant. Only under the state of the combination of these two stimuli, the changes of HGH secretion are significant.

It is supposed that some changes in the hypothalamo-pituitary hormonal system are brought about under the state of psychological stress in normal subjects. Conversely, in some patients with anorexia nervosa or depression, the changes of HGH secretion to TRH only are significant. These patients are exposed continuously to psychological stress, or are very fragile to psychological stress.

On the onset mechanism of psychosomatic disease, the same changes mentioned as above may be raised up and the changes of somatic level may be brought about by the participation of psychological factors.

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