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A CONTROL SYSTEM FORMULATION OF THE MECHANISM THAT CONTROLS THE SECRETIONS OF SERUM GROWTH HORMONE IN HUMANS DURING SLEEP

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16. Abstract

Plasma growth hormone concentrations during sleep have been determined experimentally by Takahashi et al. (ref. 1). In these experiments an elevated level of plasma growth hormone was observed during the initial phase of sleep. For the cases considered in this paper, the growth hormone level remained elevated for approximately 3 hr before returning to the steady-state level. Moreover, subsequent to a prolonged interruption of sleep, of the order of 2–3 hr, an elevated level of plasma growth hormone was again observed during the initial phase of resumed sleep. Researchers have speculated on the possible causes of increased growth hormone secretions during sleep without arriving at a satisfactory explanation. The present paper uses a control system formulation of the mechanism that controls the secretions of serum growth hormone in humans, to account for the growth hormone responses observed.

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SUMMARY

Growth hormone secretions during sleep have been determined experimentally by Takahashi et al. (ref. 1). Results of these experiments strongly suggest that during the initial phase of sleep, the transmission of control information along the feedback path is interrupted. The term feedback, when used in connection with physiological or other control systems, implies the transmission of information regarding the behaviour of one part of a system to another part, in order to alter the performance of the entire system. The experimental evidence further indicates that the system response to this condition is a hormonal oscillation, which is undamped and ceases after one cycle. In addition, the experimental results show that during the initial phase of sleep, the steady-state level of growth hormone is increased to a value equal to the amplitude of the hormonal oscillation. At the termination of the one-cycle oscillation normal operation is restored. Moreover, subsequent to a prolonged interruption of sleep, of the order of 3 hr, the transmission of control information along the feedback path is again interrupted during the initial phase of resumed sleep. It is shown in reference 2 that this behaviour is consistent with predictions based on a control system formulation.

INTRODUCTION

One of the objectives of physiological research is to acquire a greater understanding of the mechanisms that control bodily functions. Since many of these mechanisms are amenable to analysis by the methods of classical or modern control theory as applied to engineering systems, an understanding of the physiological control systems embodied in the mechanisms can be obtained, if enough is known to describe the controlled function in mathematical terms. By formulating mathematical models of physiological mechanisms and deriving the transfer functions that describe the mechanisms in terms of control theory, results are obtained that often shed new light on the nature of the controlling device and facilitate the diagnosis of unusual responses. For example, when the stimulus applied to a glandular mechanism, such as the pituitary gland, is appropriate to the physiological environment, and the response is unusual, as in the case of sleeping subjects, a defect or a readjustment of the controlling mechanism is suggested. This procedure can be applied to any physiological subsystem that is amenable to control system formulations (ref. 2).

The proposal to consider physiological mechanisms as control systems is not new. Indeed, the study of the functioning systems of the body dates back about 100 years to the systematic investigations of Claude Bernard, who emphasized that the function of the human body is under the dictates of a myriad of control systems. However, neither Dr. Bernard nor his contemporaries had access to the large body control theory that is available today.

Basically, each cell of the human body is a living structure with numerous control systems for regulating the chemical composition and physical structure of the cellular elements. At the organ level, another hierarchy of control systems regulates intraorgan function, and at the total body level, a higher hierarchy of control systems maintains the proper interrelationships among the different organs. It has been known for many years that homeostatic mechanisms maintain a constant internal environment, and that many other physiological variables are regulated at fairly constant levels. If the body temperature, for example, should tend to rise due to an increase in the temperature of the external environment, the temperature regulating mechanism of the body would oppose the rise and readjust the body temperature back towards its normal level. Control theory helps to explain how such a system works and how the body can always return its temperature to approximately the same level, regardless of the direction of the initial change. Many anomalous physiological conditions are simply abnormalities of a particular physiological control system, or represent control system adjustments to altered physiological states. A formulation of the control system for predicting the hypophyseal, growth hormone response of human subjects to various physical activities is described in reference 2.

RESULTS AND DISCUSSION

The simple equations describing that aspect of the pituitary control system being considered in this report are given in reference 2. The solution of the equations gives a description of the physiological phenomena in the time domain, that is, a graphical picture of changes in the physiological variables being studied as time varies. The equations were used to compute the hormonal response of human subjects to interrupted and uninterrupted sleep. For the convenience of readers, Takahashi's experimental results are reproduced in figures 1 through 3, which show the experimental results with the theoretical values superimposed. In all cases, it is seen that the condition of sleep is accompanied by a hormonal oscillation, which ceases after one cycle, and that the period of the oscillation is approximately 3.5 hr.

CONCLUSIONS

Within the limits of experimental error, it is seen that there is good agreement between experimental and theoretical results. On the basis of these findings, it is reasonable to expect that the control system formulated on the basis of the relationships established in reference 2 will find other applications. For example, altered physiologic states, frank pathology, or defective homeostatic mechanisms may disassociate the gland from regulatory influences, and thus impair its ability to control the secretions of growth hormone. Conditions that give rise to hormonal oscillations, either damped or undamped, would suggest a defective control mechanism.

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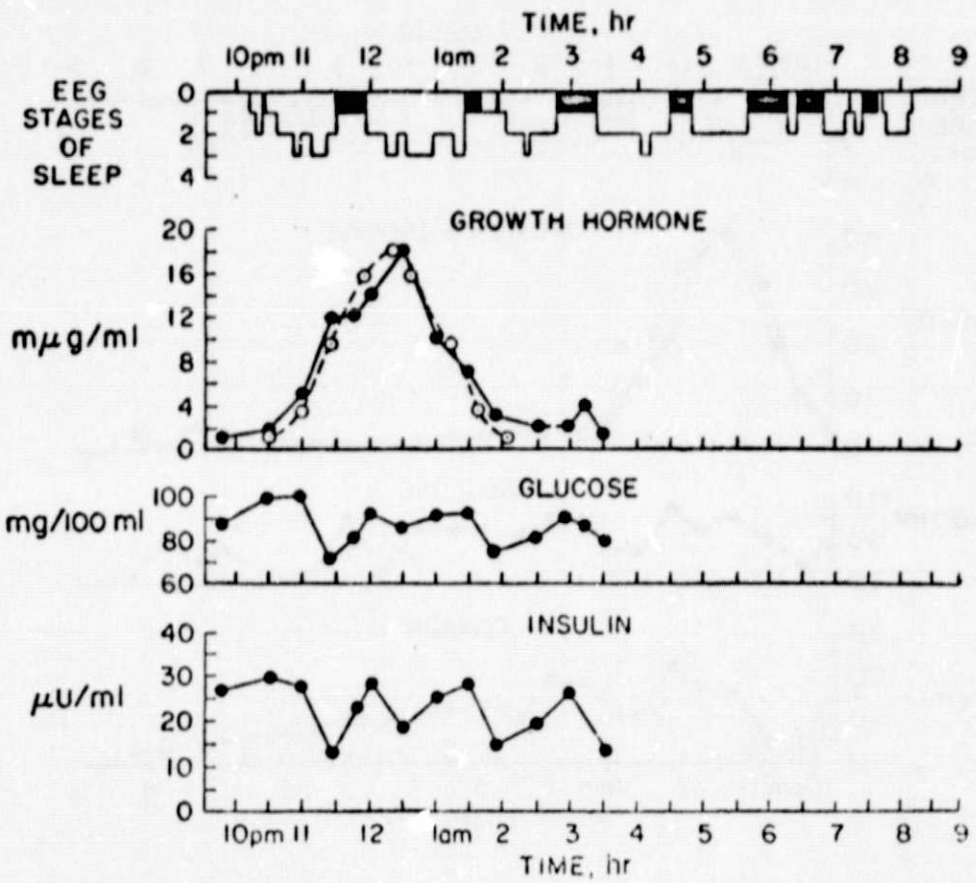
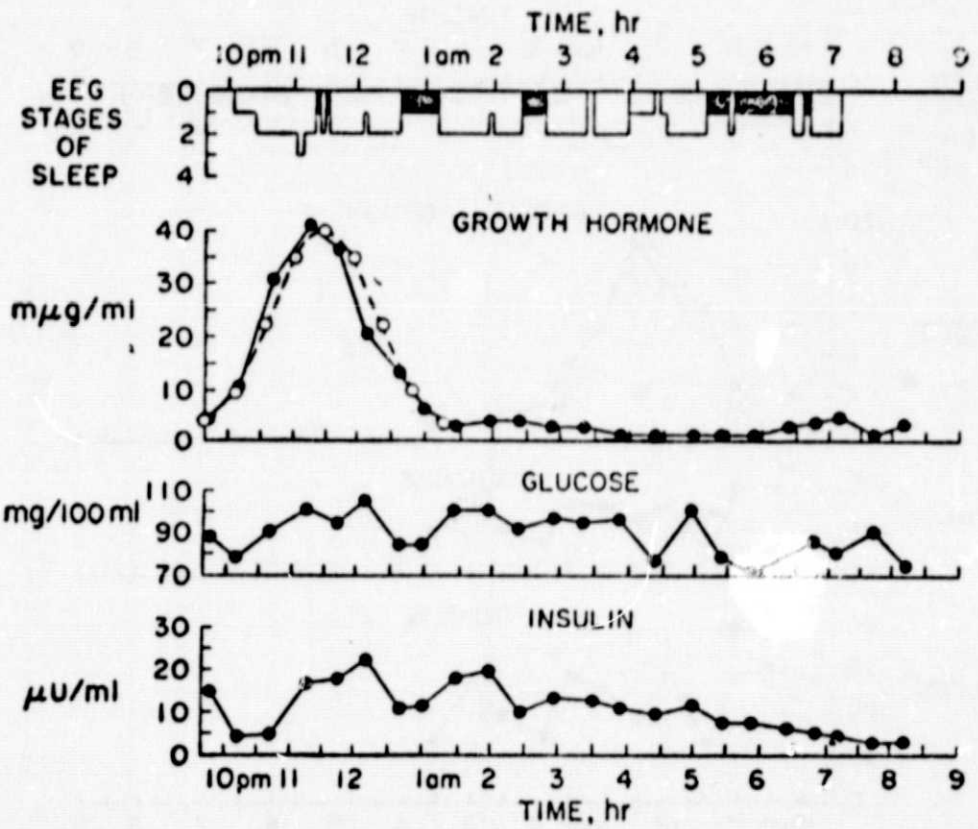


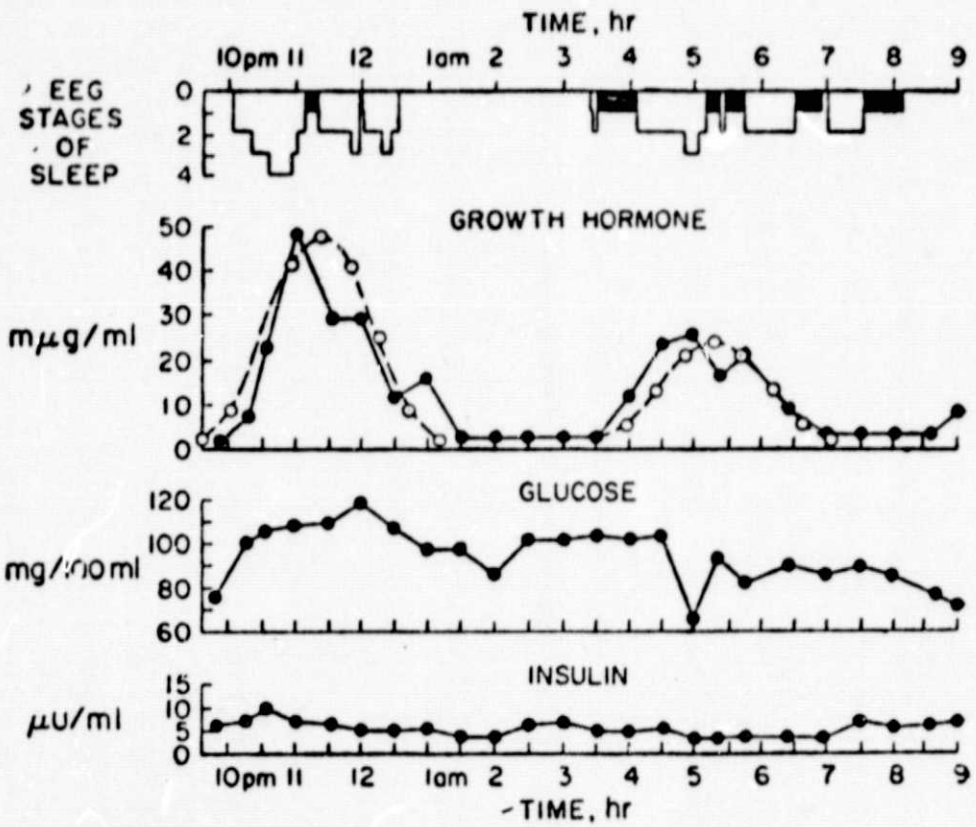
Note: Solid line denotes observed results.
Broken line denotes theoretical values.

Figure 1. – The plasma growth hormone, glucose, insulin, and EEG-EOG monitored CNS activity during a normal night's sleep in a 27 yr old man. In this and subsequent figures the levels of sleep are indicated at the top of the figure. Blank areas are periods of rapid eye movement.



Note: Solid line denotes observed results.
Broken line denotes theoretical values.

Figure 2. – Reproducibility of plasma growth hormone responses during sleep. This control study was carried out on the same individual as shown in Fig. 1, 2.5 mo later.



Note: Solid line denotes observed results.
Broken line denotes theoretical values.

Figure 3. – The effect of a prolonged interruption of sleep (3 hr) on the plasma growth hormone secretory pattern.