A MATHEMATICAL MODEL
FOR HYPOTHALAMUS-HYPOPHYSIS-ADRENAL CORTEX SYSTEM

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ABSTRACT

Under certain assumptions we set up a mathematical model for the hypothalamus-hypophysis-adrenal cortex system as a self-regulative system to study the dynamics of this system and to explain the clinical observations by the model equations. Some predictions of this model will be checked by future experiments.

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kinds of hormones. Thus, we consider the part of functions concerned
with secreting adrenal hormones in the hypothalamus and hypo-
physis as a relatively independent subsystem in the internal system. We shall call it the hypothalamus-hypophysis-adrenal cortex system.

c) The activation of the hypothalamus is controlled by the nerve
centre. At present, we do not know the details of this control pro-
cess. In our discussion we consider this control as an external fac-
tor to the subsystem under discussion.

2. Equations and Solutions

In a normal human body, the plasma ACTH and OHCS, metabolic product
of the cortisol, show a periodic pattern. The period is twenty-four
hours. During the period there are few peaks. Usually the plasma
ACTH and OHCS levels demonstrate the highest peak which begins a few
hours after the onset of sleep. Following this peak, there is a
gradual downward trend in the plasma ACTH and OHCS levels with the
other peaks occurring between 11:30 AM to 2:00 PM and 4:30 to 6:00
PM. The quiescent periods usually occur between these intervals.
The clinical observations show that there are obvious differences
in the values and occurring times of the peaks for different indi-
viduals. But, generally speaking, the periodic pattern is similar
for a normal person [2],[3].

To discuss this system quantitatively, we define:

\[ x' = \text{the concentration of the plasma CRF} \]
\[ y' = \text{the concentration of the plasma ACTH} \]
\[ z' = \text{the concentration of the plasma F} \]

with the \( x_0, y_0, z_0 \) as the daily averaged values of these quanti-
ties.

Let \( x - x'/x_0, y - y'/y_0, z - z'/z_0 \)

Following the clinical observations and the three assumptions given
above we obtain three equations which describe the dynamics of this
system:

\[
\begin{align*}
\frac{dx}{dt} &= g_1 e^{(a_1 t)} + g_2 e^{(b_1 t)} - \alpha x + g_3 e^{(c_1 t)} w t \\
\frac{dy}{dt} &= g_1 e^{(a_1 t)} + g_2 e^{(b_1 t)} - \beta y \\
\frac{dz}{dt} &= g_1 e^{(a_1 t)} + g_2 e^{(b_1 t)} - \gamma z \\
\end{align*}
\]

where \( g_1, g_2, g_3, \alpha, \beta, \gamma, \alpha, \beta, \gamma, \omega \) indicate the capacity of secreting corresponding hormones. The value of parameter \( g_4 \) indicates the con-
trol capacity of the nerve centre.

Referring to the clinical observations [2] we choose the following
parameter values:

\( g_1 = 0.4488, g_2 = 0.7478, g_3 = 0.6732, g_4 = 0.8228 \)

\( \alpha = 7.6, \beta = 0.45, \gamma = 0.374, \omega = 0.5086, c = 0.1646, \omega = 1.0472 \)

Let \( u = \cos \omega t, v = \sin \omega t \), we transform the equations into the
following form:

\[
\begin{align*}
\frac{dx}{dt} &= g_1 e^{(a_1 t)} + g_2 e^{(b_1 t)} - \alpha x + g_3 e^{(c_1 t)} w t \\
\frac{dy}{dt} &= g_1 e^{(a_1 t)} + g_2 e^{(b_1 t)} - \beta y \\
\frac{dz}{dt} &= g_1 e^{(a_1 t)} + g_2 e^{(b_1 t)} - \gamma z \\
\end{align*}
\]

This is a system of nonlinear autonomous differential equations
with bifurcation and chaos phenomena. With the chosen parameters we
obtain periodic solutions with the period length of twenty-four hours (Fig.2) [4].
We call this solution the period 4 solution. These solutions \( x(t), \)
\( y(t) \) and \( z(t) \) give the normal 24 hour pattern of the plasma CRF,
ACTH and F levels. Fig. 3 gives the comparison between the theoret-
ical values and the experimental results.

Within a certain range of parameters, the system is characterized
by the stable periodic solutions. When the parameters are too large
or too small, the period of the solutions will change. This would
indicate the occurrence of the various diseases from endocnopathy.

It is found that when the function of the adrenal cortex is degradation the quantity of OHCS decreases and the periodic pattern of OHCS changes from a normal pattern into form "M". Corresponding to this situation we set \( g_3 < 0.567 \) in equations (2), and the solution \( z(t) \) is changed from period 4 into period 2 and the amplitude is less than the normal pattern (Fig. 4). The transformation of the plasma OHCS level is the same as the cortisol one. The pattern of the theoretical curve of the cortisol agrees with the experimental results (Fig. 5) [5].

The pattern of a patient with active Cushing's syndrome is described by a seemingly random pattern of oscillations. There are no periodic phenomena and the average value of the plasma ACTH and OHCS levels is obviously bigger than the normal one. When we increase the parameter \( g_3 \) so that \( g_3 > 1.42 \), we obtain the chaotic solution of equations (2) which explain the pattern of patients with active Cushing's syndrome.

3. Discussion

a) In equations (2) parameters \( g_1, g_2, g_3 \) and \( g_4 \) play a similar role. If we increase any of them to exceed some critical values, the period will change. For example, when \( g_3 < 0.567 \), the solution is period 2, then if we increase parameter \( g_2 \), we will also obtain the pattern of period 4. Fig. 6 corresponds to \( g_3 = 0.5236, g_2 = 0.8976 \) and shows a normal pattern of the plasma ACTH levels. Similarly, by changing \( g_1 \) and \( g_4 \) we can obtain the same results. Therefore, when the function of the adrenal cortex is degradation, we can recover it to normal levels by raising the function of the hypothalamus, the hypophysis or the central nervous system. This means that this model suggests some new possible ways to cure the diseases of the internal system.

b) By cancelling the last item "\( g_4 \cos(\omega t) \)" in the first formula of equations (1), we will obtain steady periodic solutions. Its pattern is like a sine wave. There are no peaks with different values during a period. This result tells us that the normal pattern of the body is mostly due to the control of the nerve centre.

c) Experimentally we have never observed the periodic pattern with the period 8 or bigger than the period 8. The reason is perhaps that the corresponding parameter range is very narrow.

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REFERENCES


Fig. 2 Periodic Solution of Eq. (2)
Fig. 3
Comparison between the theoretical and experimental values in the normal human
--- theoretical values
--- experimental values

Fig. 4 Period 2

Fig. 5
The periodic pattern of the cortisol
--- theoretical values
--- experimental values

Fig. 6 Period 4
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