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# SEASONAL CHANGES IN CARDIOVASCULAR PARAMETERS AND BRAIN MONOAMINE LEVELS IN RABBITS

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**KEY WORDS:** seasonal biorhythms; heart rate; systemic arterial pressure; cerebral blood flow; dopamine; noradrenalin; serotonin

A characteristic of the cerebral blood flow (CBF) is its mosaic pattern [2]. Previous studies [6, 7] showed not only differences in blood flow at different depths and in different cortical formations, but also differences in CBF of different experimental rabbits and in the same animal from one experiment to another. Monoamine levels in the animal brain also have been shown to be variable [4, 5]. We were interested to discover correlation between changes in CBF, the systemic arterial pressure (SAP), heart rate (HR), and brain monoamine levels, and dependence of these parameters on the time of year.

## EXPERIMENTAL METHOD

Experiments were carried out on 300 rabbits (male and female) under 1 year old over a period of 13 years. There were three series:

In series I, SAP was measured by a mercury manometer under urethane anesthesia (1 g/kg, intramuscularly), by means of a cannula introduced into the femoral artery. SAP and HR were measured in each experiment for 5 min.

In series II the local CBF (LCBF) was measured by the hydrogen clearance inhalation method. A platinum monopolar electrode was implanted stereotaxically in each of the test structures (hypothalamus, thalamus, septum) to measure LCBF, and a nichrome bipolar electrode was similarly implanted for electrical stimulation. During the postoperative period the experimental animals became adapted to the experimental conditions. The experiments began 7-10 days after the stereotaxic operation and were conducted on conscious rabbits without any premedication. The reference electrode for measurement of LCBF was an Ag/AgCl plate measuring 0.5 × 0.5 cm, secured by clips to the rabbit's ear. LCBF was measured simultaneously in one deep structure and in the neocortex, before and after stimulation. The parameters of the pulsed current used for stimulation were: 0.5 msec, 60 Hz, 2-4 V, 33 sec. Blood flow was calculated by the method based on the initial slope of the clearance curve.

In series III concentrations of biologically active monoamines were determined by the same method in 1972, 1973, 1981, and 1982. Concentrations of noradrenalin (NA), dopamine (DA), and serotonin (5-HT) were determined in the central cerebral cortex and in deep structures (hypothalamus, striatum). Concentrations of NA, of DA, and of its chief

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TABLE 1. SAP and HR in Different Months in Rabbits Anesthetized with Urethane

| Month | SAP, mm Hg | HR, beats/min |
|---|---|---|
| October | 97,5 | 216,3 |
| November | 107,6 | 220,1 |
| December | 97,0 | 210,0 |
| January | 109,1 | 208,1 |
| February | 104,0 | 205,0 |
| March | — | — |
| April | 97,9 | 212,8 |
| May | 91,5 | 220,9 |

TABLE 2. CBF of Rabbits in Different Months

| Months | CBF, ml/100 g/min | |
|---|---|---|
| | in deep structures | in neocortex |
| October | 70,7 | 97,6 |
| November | — | — |
| December | — | — |
| January | 67,7 | 87,8 |
| February | 79,7 | 103,6 |
| March | 85,6 | — |
| April | 87,3 | 91,1 |
| May | 67,1 | 46,9 |

TABLE 3. 5-HT and NA Concentrations in Central Cortex of a Rabbit in Different Months

| Month | 5-HT | NA |
|---|---|---|
| October | 0,25±0,05 | 0,19±0,03 |
| November | 0,37±0,05 | 0,13±0,02 |
| December | 0,55±0,05 | 0,25±0,04 |
| January | 0,60±0,06 | 0,16±0,01 |
| February | 0,47±0,04 | 0,17±0,01 |
| March | 0,33±0,02 | 0,17±0,02 |
| April | 0,37±0,05 | 0,19±0,03 |
| May | 0,66±0,1 | 0,31±0,04 |
| June | 0,46±0,06 | 0,24±0,02 |
| Mean | 0,45±0,04 | 0,20±0,02 |

metabolite were determined spectrofluorometrically by the method of Shellenberger and Gordon [13], in Spano and Neff's modification [14]. 5-HT was determined by a modified method of Curzon and Green [9]. For at least 2 weeks before the biochemical experiments the animals were kept on a schedule of 12 h light:12 h darkness.

All series of experiments were limited to the period from October through June. No experiments were carried out in July, August, and September. Average data for individual months were obtained by adding all data for a particular month in every year.

## EXPERIMENTAL RESULTS

The data in Table 1 show that the mean SAP and HR varied in different months. The lowest SAP (91.5 mm Hg) was observed in May, the highest (109.1 mm Hg) in January. Examination of the trend of SAP in the first half of the year reveals a tendency toward a steady fall of SAP, ending in May. Changes in HR were less marked.

The background CBF of deep (diencephalic) structures (hypothalamus, thalamus, septum) was between 67.1 and 87.3 ml/100 g/min (Table 2). The lowest CBF in the diencephalon was in January and May. Electrical stimulation of these structures caused their CBF to increase by 25-40%. The exceptions were January and May, when the increase in CBF was only 10 and 5% respectively. The cortical CBF was a little higher than in the deep structures. Changes in the cortical CBF during stimulation of diencephalic structures amounted to ±10-20%. The exception in this case was May, when the cortical CBF was much lower than in the other months and when there was no response to stimulation.

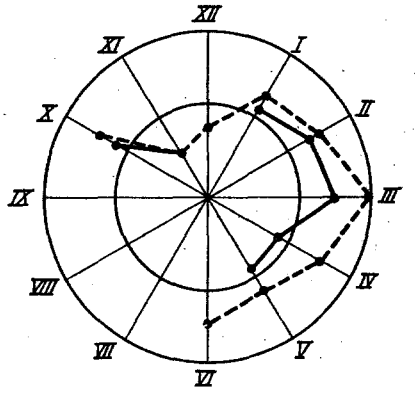


Fig. 1. Correlation of reactivity of cerebral vessels and brain DA levels of rabbits month by month. DA concentration in mg/g starting from center of circle; vascular reactivity indicated by magnitude of change in CBF in response to diencephalic stimulation, corresponding to difference of monthly change as a percentage of mean poststimulation level for the year (inner circle). Continuous line CBF, broken line DA. Roman numerals indicate months.

Table 3 gives the 5-HT and NA concentrations in the rabbit central cortex. In the deep brain structures the changes were in the same direction. The data are averaged for each month, but sometimes the peak value was observed in the middle or in the first weeks of the month. The mean level of 5-HT was 0.45 ± 0.04 mg/g, and of NA 0.20 ± 0.02 mg/g. The 5-HT concentration was highest in the spring and summer in the last weeks of May, and in winter at about the New Year. The experimental results show that the 5-HT concentration rose sharply in the second half of December, reached a maximum in the first weeks of January, and then fell steadily. A sharp rise of the 5-HT concentration also took place in May. The 5-HT concentration was minimal in October and March. The NA concentration had acute peaks in the first half of December and May. It fell to a minimum in the first quarter. A rile of the NA level apparently precedes a rise of the 5-HT level. Comparison of the brain monoamine levels and the cardiovascular parameters month by month reveals a definite parallel trend in their changes. A low HR corresponds to a low NA concentration in the winter months. The increase in HR in May correlates with an increase in the NA and 5-HT concentrations. The prolonged low NA level from January through March correlates with slowing of HR in these months.

Brain dopamine levels of the rabbits are compared month by month with the overall response of CBF (diencephalon + neocortex) to diencephalic stimulation in Fig. 1. A higher dopamine level corresponds to a greater increase in CBF. This result is in agreement with the view that vasodilatation is dopaminergic in character whereas vasoconstriction i6 the result of adrenergic activation [14]. Changes in biogenic monoamine concentrations, as the results of many investigations have shown, are genetically programed [1]. It has also been shown that changes in monoamines and in physiological parameters continue to take place under permanent animal-house conditions because of changes in activity of electromagnetic fields. Geomagnetic storms are most frequent in autumn and spring months [3]. This may be one reason for the ellipsoidal character of changes in the concentrations of all the biogenic monoamines. The ends of the axes of the ellipsoids for dopamine are March-October, for serotonin December-January and May-June, and for noradrenalin December-May (Table 3). Our data agree with the observations of other workers [10-12] and indicate that changes in brain monoamine levels may influence the state of the cardiovascular system. It can be concluded from the results of these investigations that the cerebral blood flow and reactivity of the cerebral microvessels depend on monoamine concentrations in the brain and exhibit seasonal variability.

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