Short Communication

Association between Increase in Cyclic AMP and Subsequent Induction of Tyrosine Hydroxylase in Rat Adrenal Medulla
Experiments with Swimming Stress

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Summary. After male rats (100 g body weight) have completed 7 min of swimming at 15 °C, their rectal temperature is decreased by 15 °C. As expected, the increase of cAMP and the decrease of cGMP concentrations in adrenal medulla are delayed by the time period necessary for the body temperature to return to normal. Thus, taking into consideration the delaying effect of hypothermia, the swimming stress experiments are in agreement with the view that the enhancement of cyclic AMP/cGMP concentration ratios may function as the second messengers for the induction of tyrosine hydroxylase in adrenal medulla.

Key Words: Cyclic AMP — Cyclic GMP — Swimming Stress — Hypothermia — Tyrosine Hydroxylase — Adrenal Medulla.

In rat adrenal medulla, the induction of tyrosine hydroxylase activity (TH) by cold exposure or drugs is always preceded by an increase of 3',5'-cyclic adenosine monophosphate (cAMP) concentration (Costa and Guidotti 1972, Guidotti et al., 1973). Thoenen and his collaborators (Thoenen et al., 1974) found in 100 g rats, after swimming to exhaustion in 15° C water (3 swimming periods of 5—7 min in 1 h), that TH of adrenal medulla is increased 48 h later, however these stresses "... lead to an unexpectedly small increase in cyclic AMP". They reported that each environmental stress was terminated by exhaustion which occurred after 5—7 min of swimming. Other reports have previously shown that in similar experimental conditions exhaustion coincides with a decrease of body temperature by 10—15° C (Dawson et al., 1969). In the present experiments, the water temperature (15° C), the weight of the animals and the degree of the stress were a replication of the conditions reported by Thoenen et al. (1974). To avoid interferences by the enduring and profound hypothermia caused by repeated swimming stress the activity of medullary TH in
100-g rats was studied 24 h after one swimming session of 7 min. The TH activity was measured by the method of Waymire et al. (1971) and expressed in nmol of 3,4-dihydroxyphenylalanine formed/h/gland. In control rats, the enzyme activity was 4.8 ± 0.2 (SEM) (n = 5) and in rats exposed to swimming stress it increased to 6.3 ± 0.3 SEM (n = 5) (P < 0.02). The rectal temperature of these rats was profoundly decreased at the end of the swimming session as reported by Dawson et al. (1969). The data of Fig. 1 show that the rectal temperature persists below 30°C for about 30 min after the termination of the environmental stress and gradually returns to normal in about 90 min. cAMP and 3',5' cyclic guanosine monophosphate (cGMP) were separated and purified from the same adrenal medulla according to Mao and Guidotti (1974) and then measured according to Kuo et al. (1972) and Mao and Guidotti (1974). Proteins were assayed with the method of Lowry et al. (1951).

In agreement with Thoenen et al. (1974) and Otten et al. (1973) the data of Fig. 2 shows that immediately after the swimming stress, the cyclic AMP concentrations of adrenal medulla are not increased. The data of Fig. 1 show that at this time the body temperature was lowered to 22°C. However as soon as the body temperature reached 30°C, the cyclic AMP concentrations of adrenal medulla are increased while the cyclic GMP concentrations are decreased. As previously reported for cold exposure (Guidotti et al., 1973, 1974), the data of Fig. 2 show that in adrenal medulla the second messenger response persist longer than 90 min after one swimming stress.

The measurement of cyclic AMP concentrations at 30 min (Fig. 2) were performed 23 min after the termination of one swimming stress, whereas the 30-min measurements reported by Otten et al. (1973) were performed after two swimming stress and 7 min after the last stress. Extrapolating from the data of Fig. 1 one might infer that the body temperature

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**Fig. 1.** Rectal temperature in rats (Sprague Dawley 100 g body weight) swimming in 15°C water for 7 min and then placed at 22°C. Each point refers to the average temperature of 4 rats. Black bar in abscissa: swimming time in 15°C water.