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EFFECT OF SUSTAINED EXERCISE ON CONCENTRATIONS OF PLASMA AROMATIC AND BRANCHED-CHAIN AMINO ACIDS AND BRAIN AMINES

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SUMMARY: In both trained and untrained rats, exercise increased the plasma concentration ratio of aromatic amino acids to branched-chain amino acids which might favour entry of the aromatic amino acids into the brain. Exercise in trained rats did not change the brain concentration of 5-hydroxytryptamine but increased that of 5-hydroxyindole acetic acid. Exercise in the untrained rat increased the concentration of brain tryptophan and that of 5-hydroxytryptamine but that of 5-hydroxyindole acetic acid was unchanged. The increased concentration of 5-hydroxytryptamine in untrained rats might be involved in central fatigue.

INTRODUCTION: Continuous exercise eventually results in fatigue, that is, an inability to maintain the same power output (1). Although there is no doubt that this fatigue occurs due to changes within the active muscle (2,3), there is evidence that factors within the CNS may also be partially responsible: this is known as central fatigue (4,5). One specific amine, 5-hydroxytryptamine (5HT), is known to be involved in the CNS in the regulation of sleep (6,7). It seemed possible therefore that sleep and fatigue caused by endurance exercise could be brought about, in part, by an increase in the brain concentration of 5HT. The question arises as to the mechanism by which endurance exercise could influence the concentration of 5HT in the brain. The following hypothesis can be put forward. Since none of the enzymes involved in the synthesis

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of 5HT in the brain approaches saturation with substrate, an increase in the concentration of tryptophan in the brain could lead to an increase in the rate of formation and hence possibly in the concentration of 5HT (8) and, in addition, the rate of transport of tryptophan across the blood brain barrier controls the brain concentration of tryptophan (6,7,9). Of considerable importance is the fact that the carrier responsible for the transport of tryptophan and tyrosine across the blood brain barrier also transports the branched-chain amino acids, leucine, isoleucine and valine (10) which are taken up primarily by the muscle (8,9). These amino acids in the plasma will compete against each other for binding to this carrier and hence for transport into the brain. There is some evidence that the rate of branched-chain amino acid uptake by muscle is increased during sustained exercise (11) so that their plasma concentrations should be decreased and this will lead to an increase in the plasma ratio of concentrations, aromatic amino acids/branched chain amino acids. This should favour the entry of aromatic amino acids into the brain and the increased brain concentration of tryptophan should cause an increase in the concentration of 5HT resulting in central fatigue. This hypothesis has been tested in the rat by studying the effect of sustained exercise in untrained and trained rats on the plasma concentrations of aromatic and branched-chain amino acids and brain concentrations of aromatic amino acids and some amines including 5HT.

METHODS: Male rats were obtained from Olac 76 Ltd., Bicester, Oxon, U.K. Rats were exercised on a rodent treadmill. For the untrained rats, animals were exposed to the treadmill for three days prior to sacrifice; for two days, rats were allowed to run for only 5-10 min but, on the final day, they were run for 75-100 mins with the treadmill at an angle of 1°. Trained rats were run for 60 min each day, six days a week for five weeks and during this time the angle of the treadmill was increased from 1° to 4°. On the final day, rats were run for 90 mins at 25 m/min with the treadmill at an angle of 4°. Immediately after the run was finished, rats were killed by cervical dislocation, the brain was quickly dissected out and freeze-clamped. At the same time, samples of blood were taken from the heart, centrifuged at 9000 g and samples of plasma frozen and kept at -70°C for subsequent analysis. The concentration of tyrosine was measured by the method of Undenfriend & Cooper (12), that of tryptophan by the method of Denkla & Dewey (13), as modified by Bloxam & Warren (14), and that of branched-chain amino acids by the method of Livesey & Lund

(15). The brain monoamine concentrations were measured by a method based on that of Mefford (16).

RESULTS: Sustained treadmill running in both trained and untrained rats caused an increase in the plasma concentration of tryptophan, and decreases in those of tyrosine and branched-chain amino acids (Table 1). Treadmill running in trained rats increased the ratio of concentrations, aromatic amino acid/branched-chain amino acids, from 54 to 71% and in untrained rats the ratio was increased from 26 to 37%; the ratio of concentrations, tryptophan/branched-chain amino acids, was increased from 29 to 45% and 12 to 21% in trained and untrained rats respectively (Table 1). Treadmill running in untrained rats increased the concentration of brain 5HT (10%) but there was no change in that of other amines or that

TABLE 1: Effect of exercise on the plasma concentrations of tyrosine, tryptophan, branched-chain amino acids and the brain concentrations of noradrenaline, dopamine, and 5-hydroxytryptamine in trained and untrained rats

	Conditions			
	Sedentary control (5)	Exercise (untrained) (5)	Sedentary control (5)	Exercise (untrained) (8)
Plasma concentration (μM)				
Tyrosine	74 ± 2.0	59 ± 2.0***	100 ± 4.0	80 ± 6.0*
Tryptophan	59 ± 0.6	76 ± 2.0***	120 ± 8.0	140 ± 8.0*
Branched-chain amino acids	502 ± 26	344 ± 33***	410 ± 2	310 ± 20***
Brain concentration (nmol/g fresh wt.)				
Tryptophan	18 ± 0.1	21 ± 0.9**	-	-
Tyrosine	152 ± 10	160 ± 36	-	-
Brain content (ng/g fresh wt.)				
Noradrenaline	293 ± 20	313 ± 10	314 ± 10	379 ± 20*
Dopamin	805 ± 30	803 ± 21	832 ± 30	862 ± 40
5-Hydroxy tryptamine	685 ± 10	748 ± 10***	684 ± 10	646 ± 30
5-Hydroxyindole acetic acid	314 ± 13	314 ± 13	253 ± 9	338 ± 10***
Concn. ratio (%) plasma aromatic plasma aromatic amino acids/ branched-chain amino acids	26	37	54	71

Results are presented as means ± S.E.M. with the number of different animals used in each group given in parenthesis. The statistical significance was determined using Student's t test and significant differences from the appropriate control are denoted as follows: *P < 0.05;**P < 0.01 ***P < 0.005.

of 5-hydroxyindoleacetic acid (Table 1). Treadmill running in trained rats increased the concentrations of noradrenaline (21%) and 5-hydroxyindoleacetic acid (34%) but there was no change in those of 5HT or dopamine.

DISCUSSION: The rate of uptake of branched-chain amino acids by muscle increases during and/or after exercise (11). This would be expected to lower the plasma concentration of these amino acids so that the ratio of concentrations, aromatic amino acids/branched-chain amino acids should increase: this has been observed in the present work (Table 1). Endurance exercise also raises the plasma fatty acid concentration, which is known to displace tryptophan from albumin (17), so that the free concentration of tryptophan may be markedly increased in the plasma of exercised rats. Hence the ratio of concentrations, free tryptophan/branched-chain amino acids, should increase dramatically and this might explain why the brain concentration of tryptophan but not that of tyrosine is increased by exercise in the untrained animal (Table 1). The increased concentration of tryptophan should lead to an increased activity of tryptophan 5-monooxygenase, increasing the concentration of 5-hydroxytryptophan which, in turn, should increase the activity of the aromatic L-amini acid decarboxylase leading to an increased concentration of 5HT (see Introduction). The latter is observed as a result of treadmill running of untrained rats in the present work (Table 1) and it might account, in part, for the fatigue in these animals. However, in untrained rats, treadmill running did not increase the concentration of brain 5HT but increased that of the degradation compound 5-hydroxyindoleacetic acid; this suggests that training increases not only the rate of formation of 5HT in the brain but also its rate of breakdown. A failure to increase the concentration of brain 5HT in trained rats might explain, in part, how training can increase the time of onset of fatigue and hence increase endurance. It would be of considerable interest to know if physical training leads to an increase in the acti-

vities of amine oxidase and aldehyde dehydrogenase in the brain.

In the present work, treadmill running in trained rats increased the concentration of nor-adrenaline (Table 1). If a similar increase in the concentration of brain nor-adrenaline occurs in man, it could account for the improvement in mood claimed to be produced by exercise (18,19,20) and, in particular, suggests that such an improvement will be dependent upon the state of training of the individual.

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