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Tocopherol mobilization during dynamic exercise after beta-adrenergic blockade

BY

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(3 figures)

This study addresses the question of whether tocopherol mobilization during exercise could be explained by a lipolysis effect. Nine healthy male subjects were submitted to dynamic exercise of graded intensity (45, 60, 75% $\dot{V}O_{2max}$) on a cycle ergometer after ingestion of either a placebo or 40 mg propranolol as β -blocker. Plasma tocopherol concentration increased toward a peak value reached during or at the end of exercise. The magnitude of this increase did not differ in the two experimental conditions while plasma free fatty acids concentration was lowered under β -adrenergic blockade by propranolol. From these results, we conclude that tocopherol mobilization during dynamic exercise does not depend on lipolysis.

Introduction

During the course of dynamic exercise corresponding to an energy requirement (\dot{E}) equal to the maximal aerobic power ($\dot{E}_{ox max}$), plasma tocopherol concentration (TH) is significantly increased. (PINCEMAIL *et al.*, 1988). Given the strong interaction of tocopherol with free fatty acids (FFA), given the release of FFA under the action of lipolytic hormones during intense exercise - especially catecholamines - it has been hypothesized that this increase of TH could be explained by a mobilization of tocopherol from adipose tissue during lipolysis. The aim of this study was to test this hypothesis. For this purpose, we have measured TH in 9 healthy male subjects during and after dynamic exercise, with and without acute β -adrenergic blockade by a single oral dose of propranolol.

Methods

Nine healthy male subjects (mean age : 23 years; mean body weight : 75,2 kg) participated in this study. Prior to the experiments, their maximum oxygen uptake ($\dot{V}O_{2max}$) was measured during graded cycling exercise at 80 r.p.m. on a cycle ergometer (*Monark*). The initial power of exercise (P) was 78W and was increased by 39W every 4 minutes until exhaustion. Expired air samples exhaled during the last minute of each work stage were analyzed for steady state oxygen consumption ($\dot{V}O_2$) measured using an automatic gas analyzer (*Ergo-oxyscreen*, JAEGER). $\dot{V}O_{2max}$

was determined from these measurements according to the levelling off criterion. The individual relationships between $\dot{V}O_2$ and P were used to calculate the mechanical powers corresponding to 45, 60 and 75% $\dot{V}O_2$ max. After this first test, the subjects reported two times to the laboratory in the fasting state. Each time, they were administered in random order either 40 mg propranolol (*Inderal*, ICI) or a placebo. One hour later, a teflon catheter was introduced percutaneously into an antecubital vein. A first blood sample (E_1) was drawn 10 minutes after catheter insertion. Immediately after blood withdrawal, exercise was started in the seated position on the cycle ergometer. The subjects performed continuous submaximal exercise of graded intensity. They were working 10 minutes at a work load corresponding to 45% $\dot{V}O_2$ max and 5 minutes at work loads corresponding to 60 and 75% $\dot{V}O_2$ max. Heart rate (HR) was measured at rest and during exercise. Two blood samples were taken during exercise: E_2 at the end of the first work stage, and E_3 at the end of exercise. Three additional blood samples were obtained during recovery as follows: E_4 , E_5 and E_6 , 5, 15 and 25 min after the end of exercise respectively.

Plasma tocopherol concentration [TH] was determined after extraction with hexane, by high pressure liquid chromatography (BIERI *et al.*, 1979).

After extraction with a chloroform-methanol mixture (FOLCH *et al.*, 1957), plasma non esterified fatty acids (NEFA) were determined according to the method described by DEBY *et al.* (1978).

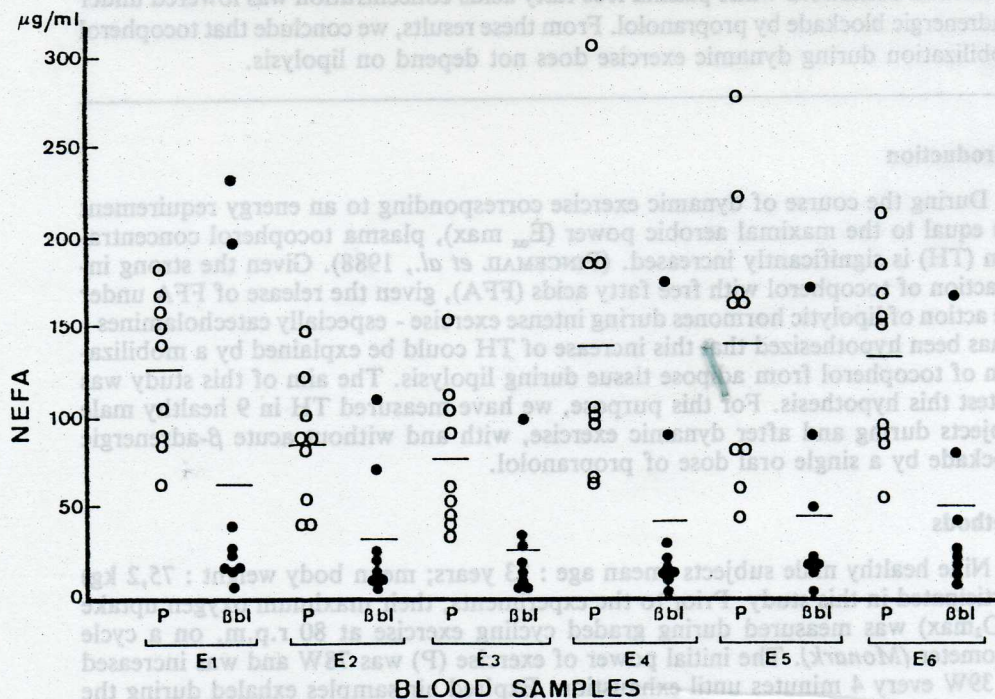


FIG. 1. Plasma non esterified fatty acids concentration [NEFA], at rest, during exercise (E_1 , E_2) and recovery (E_4 , E_5 , E_6) after placebo (○) and after propranolol (●). Horizontal bars indicate mean [NEFA] values.

Results

In our subjects, $\dot{V}O_2$ max, measured during the course of incremental exercise, averaged $53 \text{ ml O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Mean mechanical powers eliciting energy expenditures of 45, 60 and 75% of $\dot{V}O_2$ max were 120, 160, 190 W respectively.

The effects of propranolol and exercise on HR are well known. At rest, HR after placebo averaged $74 \pm 16 \text{ beats min}^{-1}$; after propranolol, $63 \pm 10 \text{ beats min}^{-1}$. During exercise, HR increased as a function of time in the two experimental conditions but the increase of HR was significantly reduced by about 20% under β -adrenoceptor blockade ($P < 0.02$).

The individual values of plasma NEFA concentration measured in blood samples taken in the two experimental conditions are plotted in Figure 1. Horizontal bars indicate mean NEFA. At rest (E_1) and 25 min after exercise (E_6), mean NEFA was lowered by propranolol but the difference with placebo was not significant. In contrast, propranolol significantly reduced mean NEFA during exercise (E_2, E_3) and during the first 15 min of recovery (E_4, E_5) ($P < 0.01$). This decrease was followed by an increase of NEFA towards resting values. These variations of NEFA after exercise were less pronounced under β -adrenoceptor blockade. On the average, NEFA were lower with propranolol than with placebo throughout this study.

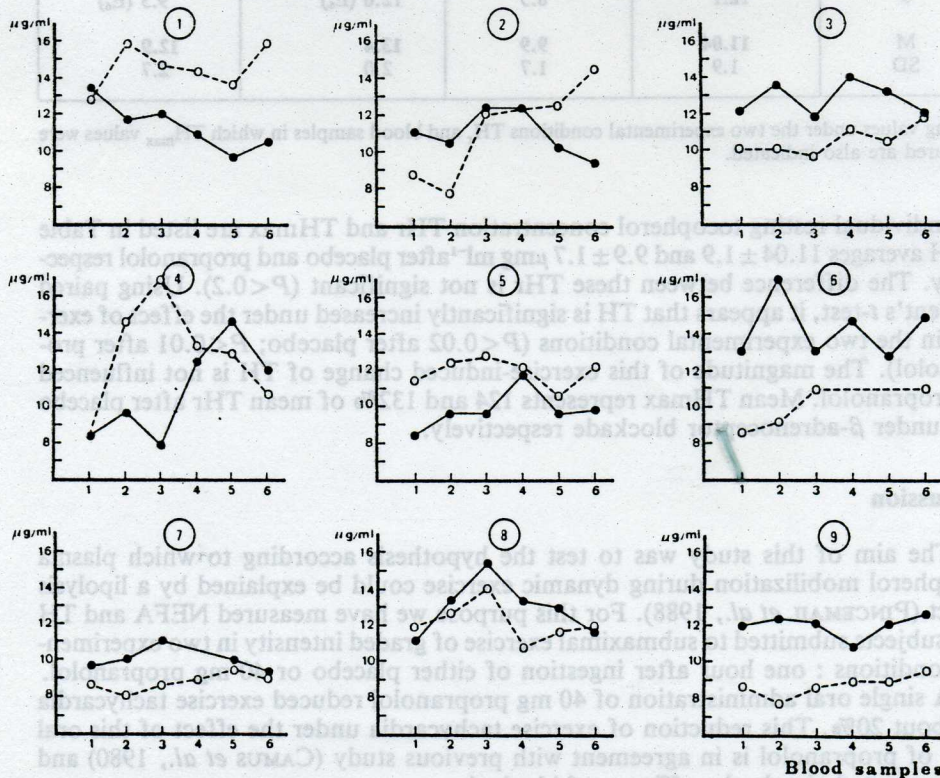


Fig. 2. Individual values of plasma tocopherol concentration at rest, during exercise and recovery after placebo (●—●) and after propranolol (○- - -○)

For each subject, exercise-induced changes of TH in the two experimental conditions are shown in Figure 2.

Except for subjects 1 and 9 exercising after placebo ingestion, TH changed as a function of time and reached a peak value TH_{max} in the two experimental conditions. The blood samples in which TH_{max} values were measured differ from one subject to another. In most cases, TH_{max} were observed in blood samples taken at the end of exercise (Table I).

TABLE I. Peak plasma tocopherol concentration ($[TH]_{max}$) after placebo and propranolol.

Subjects	TH ($\mu\text{g}\cdot\text{ml}^{-1}$)		TH _{max} ($\mu\text{g}\cdot\text{ml}^{-1}$)	
	Placebo	Propranolol	Placebo	Propranolol
1	13.4	12.7	12.0 (E ₃ , E ₄)	15.9 (E ₂)
2	11.0	8.7	12.4 (E ₃ , E ₄)	14.5 (E ₆)
3	12.2	10.1	14.0 (E ₄)	11.8 (E ₆)
4	8.3	8.4	14.7 (E ₅)	16.9 (E ₃)
5	8.4	11.4	11.8 (E ₄)	12.8 (E ₃)
6	13.1	8.5	17.0 (E ₂)	10.9 (E ₃)
7	9.7	8.6	11.0 (E ₃)	9.5 (E ₅)
8	11.2	11.9	15.4 (E ₃)	14.0 (E ₃)
9	12.1	8.5	12.6 (E ₆)	9.5 (E ₆)
M	11.04	9.9	13.4	12.9
SD	1.9	1.7	2.0	2.7

Resting values under the two experimental conditions TH_r and blood samples in which TH_{max} values were measured are also indicated.

Individual resting tocopherol concentration TH_r and TH_{max} are listed in Table I. TH averages 11.04 ± 1.9 and $9.9 \pm 1.7 \mu\text{mg ml}^{-1}$ after placebo and propranolol respectively. The difference between these TH_r is not significant ($P < 0.2$). Using paired Student's *t*-test, it appears that TH is significantly increased under the effect of exercise in the two experimental conditions ($P < 0.02$ after placebo; $P < 0.01$ after propranolol). The magnitude of this exercise-induced change of TH is not influenced by propranolol. Mean TH_{max} represents 124 and 132% of mean TH_r after placebo and under β -adrenoceptor blockade respectively.

Discussion

The aim of this study was to test the hypothesis according to which plasma tocopherol mobilization during dynamic exercise could be explained by a lipolysis effect (PINCEMAIL *et al.*, 1988). For this purpose we have measured NEFA and TH in 9 subjects submitted to submaximal exercise of graded intensity in two experimental conditions: one hour after ingestion of either placebo or 40 mg propranolol.

A single oral administration of 40 mg propranolol reduced exercise tachycardia of about 20%. This reduction of exercise tachycardia under the effect of this oral dose of propranolol is in agreement with previous study (CAMUS *et al.*, 1980) and demonstrated clearly the efficacy of blockade.

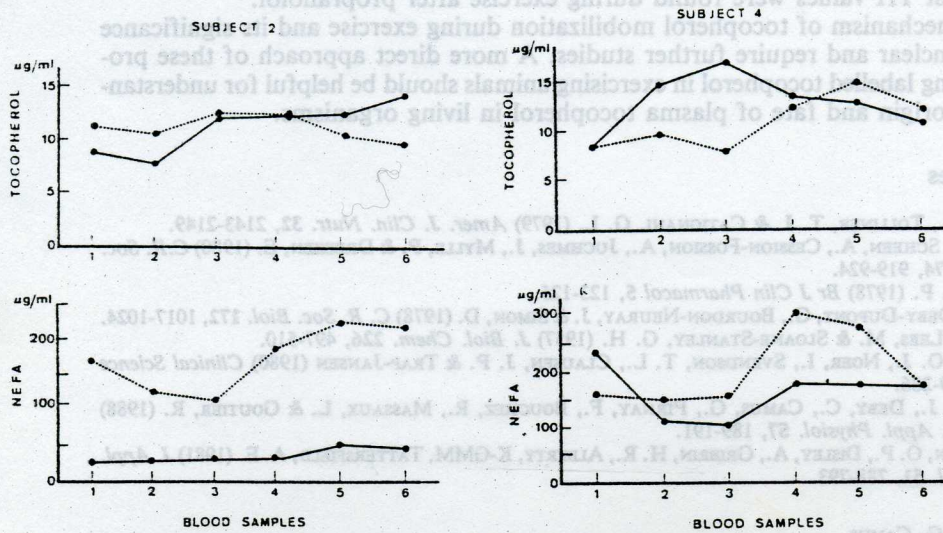


FIG. 3. Upper part : plasma tocopherol concentration at rest (E_1), during exercise (E_2 , E_3) and recovery in subjects 2 and 4 after placebo (●—●) and after β -adrenergic blockade (●—●). Lower part : plasma non esterified fatty acids concentration at rest (E_1), during exercise (E_2 , E_3) and recovery in subjects 2 and 4 after placebo (●—●) and after β -adrenergic (●—●).

Despite the wide scatter of NEFA values, our results clearly show that free fatty acids mobilization was reduced by propranolol, not only at rest and during exercise but also during recovery. Since plasma glycerol concentration was not measured, it cannot be concluded that the effect of propranolol on NEFA results only from inhibition of β -adrenoceptor-mediated lipolysis. This effect could also be explained by an increase of FFA uptake by skeletal muscles (HARTLING *et al.*, 1980) or by a combination of the two mechanisms. Nevertheless, on the basis of other studies showing a concomitant decrease of plasma glycerol and NEFA under β -adrenergic blockade (DEACON, 1978; TWENYTMAN *et al.*, 1981), it seems reasonable to state that lipolysis has been effectively reduced by propranolol in our subjects.

Mean TH measured at rest in the two conditions are in agreement with previous values published by BIERI *et al.* (1979) and PINCEMAIL *et al.* (1988). The significant increase of TH levels close to the end of exercise also confirms the previously reported tocopherol mobilization during intensive exercise (PINCEMAIL *et al.*, 1988). As TH was not reduced under β -adrenergic blockade despite a large decrease of mean NEFA, it can be concluded that tocopherol mobilization during exercise does not depend on lipolysis. This conclusion is still more obvious when the results obtained in subjects 2 and 4 are considered. These results are illustrated in Figure 3. As shown in the lower part of this figure, NEFA is considerably lowered by propranolol in comparison to control condition, especially in subject 2. In this subject, TH is slightly higher at rest and after 10 min exercise under control condition. At the end of exercise, TH are practically equal in the two conditions but reach higher values after β -adrenoceptor blockade during recovery. In subject 4, NEFA is higher at rest after propranolol but TH are equal. During exercise and recovery, NEFA are higher after

placebo except in the last blood sample. As shown in the upper part of Figure 3, the highest TH values were found during exercise after propranolol.

The mechanism of tocopherol mobilization during exercise and its significance remain unclear and require further studies. A more direct approach of these problems using labelled tocopherol in exercising animals should be helpful for understanding the origin and fate of plasma tocopherol in living organisms.

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