Effects of coca chewing on metabolic and hormonal changes during graded incremental exercise to maximum

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Spielvogel, Hilde, Esperanza Caceres, Harry Koubi, Brigitte Sempore, Michel Sauvain, and Roland Favier. Effects of coca chewing on metabolic and hormonal changes during graded incremental exercise to maximum. *J. Appl. Physiol.* 80(2): 643–649, 1996.—We examined the effects of 1 h of coca chewing on metabolic and hormonal responses during incremental exercise to exhaustion in traditional coca chewers (C; n = 8), and the results were compared with a group of nonchewers (n = 13). For 1 h, C chewed ~12 g of coca leaves that resulted in the apparition of cocaine in blood that reached 72 ± 9 ng/ml. In resting conditions, even though sympathoadrenergic activity (as assessed by norepinephrine and epinephrine plasma levels) was similar in both groups, C displayed a higher level of plasma free fatty acids. Oxygen uptake measured at exhaustion and delta work efficiency during exercise were similar in both groups. During the incremental exercise, C displayed a significantly lower arterial oxygen saturation that cannot be explained by a reduced ventilatory response after coca chewing. In fact, even at maximal exercise, both ventilatory output and ventilatory equivalent were higher in C compared with nonchewers. It is concluded that the beneficial effects of coca chewing on exercise tolerance reported frequently by traditional coca users is not related to either an improved maximal exercise capacity or an increased work efficiency. However, during incremental exercise, coca chewing appeared to result in an increased free fatty acid availability that could be beneficial for prolonged submaximal exercise.

arterial oxygen saturation; epinephrine; fat metabolism; lactate; norepinephrine; oxygen uptake; respiratory exchange ratio; work efficiency

CHEWING COCA LEAVES is known to be frequent among the Andean populations, and this practice has existed for at least 4,000 yr (6). One of the most frequent reasons evoked by the traditional users is that coca chewing helps to increase work capacity and to reduce fatigability. There may be a physiological basis for these claims but so far scientific research information on the ergogenic benefits of coca chewing is scarce (15, 16) and does not permit us to conclude whether coca chewing leads to an improved tolerance to work. Indeed, in his pioneer study, Hanna (15) reported that maximal oxygen uptake ($\dot{V}O_{2max}$) was similar in four habitual coca users compared with four nonusers but concluded that "during the coca use trials there was a propensity toward a longer exercising time." He attributed this effect to cocaine. Subsequently, Kerhsner et al. (19) reported that cocaine injection improved $\dot{V}O_{2max}$ and endurance time of running rats, but this conclusion was recently called into question again by Bracken and co-workers (3, 4) and Conlee et al. (8). In those latter studies with rats, cocaine was found, during exercise, to exaggerate catecholamine response (8), to enhance the rates of glycogen breakdown and blood lactate accumulation (3, 4, 8), and to reduce exercise endurance (3, 4). It is not known, however, whether the effects of coca chewing are similar to or different from those observed after cocaine injection. In addition, the influence of coca use on exercise performance can be multiple [i.e., on aerobic capacity, on work efficiency (η), and on endurance during submaximal exercise].

In this first paper, we report on a study that was designed to assess the effects of coca chewing on peak oxygen uptake ($\dot{V}O_{2peak}$), η, and plasma hormonal (catecholamines) and metabolic responses during graded incremental exercise leading to exhaustion. For this purpose, we selected subjects from two rural communities from the Altiplano in which we were able to recruit traditional coca chewers (C) and nonchewers (NC). The two groups were examined according to their habit only. In other words, the C will be examined after coca chewing, whereas the NC will be tested without chewing. Even though we realize that such an experimental design will not allow us to distinguish the acute from the chronic effects of coca chewing, we hypothesized that we should be able to appreciate the impact, if any, of coca chewing on hormonal and metabolic adaptations during graded exercise.

METHODS

Subjects. The study was performed on 22 men, high-altitude natives from the Altiplano (Bolivia; 3,800 m altitude). Genetically, the subjects were Mestizos with predominantly an Indian (Aymara) admixture. The subjects were instructed about possible risks involved in this study before they gave their informed consent for participation. Before the initiation of the protocol, each volunteer was examined by a physician and was deemed to be free of any cardiovascular or pulmonary disease. The subjects were divided into two groups: the first (n = 14) consisted of NC (i.e., subjects chewing <3 times/yr), whereas the second (C; n = 8) was composed of traditional coca users (i.e., subjects chewing >3–4 times/wk during work in the field). Body mass and height were measured with a standard scale and an anthropometer, respectively. Skinfolds were measured with a caliper (Holtain), body composition was estimated from percent body fat, and lean body mass was calculated from skinfolds and body weight (10). All measurements were performed at the Instituto Boliviano de Biologia de Altura (IBBA, La Paz, Bolivia; mean altitude 3,600 m).

The subjects reported to the IBBA 1 day before the first trial and were asked to abstain from coca chewing. To minimize factors of learning that could affect maximal performance, each subject performed an incremental test on a bicycle ergometer with a mechanical braking system. The C were asked to abstain from coca chewing until the next day when they reported to the laboratory, and all the subjects were provided with a light standardized breakfast (mainly bread without fats). They were allowed to drink agua de cañawa (cañawa juice). Cañawa is an Andean grain like quinoa. They were prohibited from having tea or coffee. A small catheter was introduced into an antecubital vein, and the subject rested in a chair for 1 h. During this period, the coca users were invited to chew their customary quantity of coca leaves. The chewer takes a few leaves from a small pouch, usually removes the midribs, and places the leaves into the mouth and chews until a compact quid is formed. The quid is then placed in one cheek and periodically rechewed to extract the juice. Coca leaves are chewed with a bit of alkali (lejia) that users claim "sweetens" the quid. Quids are usually replenished with new leaves, and the juice and up to 70% of the leaves are swallowed (17). Coca leaves contain a few alkaloids, among which cocaine is present in greatest quantities. Extraction of this narcotic is most efficient, and it is estimated that 80% of the cocaine in the leaves is removed by chewing (17). The amount of leaves chewed was determined by weighing the bag containing the coca leaves before and after 1 h of chewing. Thereafter, $\dot{V}O_{2peak}$ was measured the same way as on the day of familiarization.

$\dot{V}O_{2peak}$. Oxygen uptake ($\dot{V}O_2$) was determined with a continuous progressive protocol. The seat height on the ergometer was adjusted before exercise so that each leg was in a position of slight flexion at the nadir of the downstroke. The exercise test began with a 4-min warm-up at a power output of 60 W (70 rpm). Thereafter, the power output was increased by 30 W every 4 min until the subject could not maintain the desired revolutions per minute. The subjects were verbally encouraged to continue exercise as long as possible.

Respiratory gas exchange parameters were measured with an open-circuit system. Timed collections of expired air were obtained as the subject breathed through a low-resistance nonrebreathing valve (Hans Rudolph 2700) into Douglas bags. Expired gas was analyzed with a paramagnetic oxygen analyzer (Servomex 570A) and an infrared carbon dioxide analyzer (Capnograph Mark III, Gould). Expired air volume was measured by withdrawing the contents of the Douglas bag into a Tissot spirometer. Thus discrete measurements of $\dot{V}O_2$, carbon dioxide production, respiratory exchange ratio (RER), and ventilation ($\dot{V}E$; BTPS) were obtained. We calculated delta work efficiency (η) as the ratio of Δwork accomplished over Δenergy expended, as originally defined by Gaesser and Brooks (13).

Heart rate (HR) was monitored continuously by bipolar electrocardiographic telemetry (Sport Tester). Arterial oxygen saturation (Sa_{O_2}) was measured continuously with an ear oximeter (Biox 3000, Ohmeda). The ear lobe was cleansed and massaged vigorously to increase perfusion before ear-clip attachment.

Blood sampling. Two blood samples were obtained at rest from before and after coca chewing in coca chewers. The same sampling protocol was used for NC. In this latter case, the two blood samples were separated by 1 h during which the subjects rested quietly in a chair. During exercise, three samples were withdrawn, two at submaximal workloads (E1, 80 ± 4 W, 43.7 ± 1.3% $\dot{V}O_{2peak}$; E2, 137 ± 5 W, 75.9 ± 1.3% $\dot{V}O_{2peak}$), and one during the last minute of maximal exercise (E3, 184 ± 7 W; 100% $\dot{V}O_{2peak}$). The total blood volume withdrawal averaged 20 ml (5 × 4 ml).

A 0.5-ml blood sample was deproteinized by adding 1.0 ml of ice-cold 10% $HClO_4$. The acid extract was separated by centrifugation and neutralized with KOH. Two milliliters of blood were added to a second iced tube containing EDTA for the catecholamine assays. The remaining blood was collected into heparinized tubes and centrifuged for 10 min at 800 *g*.

Biochemical assays. Plasma glucose concentration was determined with a Boerhinger kit (Meylan). Free fatty acids (FFAs) were determined by the acyl CoA synthase-acyl oxidase method with a kit (nonesterified fatty acids test, Biolyon). Glycerol concentration was evaluated by an enzymatic method (Boerhinger, Meylan). Lactate was fluorometrically assayed by a method derived from Lowry and Passonneau (21). Blood cocaine level was determined by liquid chromatography (24).

Epinephrine (Epi) and norepinephrine (NE) were assayed by high-performance liquid chromatography with electrochemical detection (20).

Statistical analysis. Variables are presented as means ± SE. For statistical comparisons of group means, a two-way analysis of variance was used followed by a post hoc test (Fisher's protected least significant difference). The level of significance was set at 5%.

RESULTS

Among all the subjects, one of the subjects from the nonchewing group was very stressed by the study environment and displayed a sympathoadrenergic response (increased NE and Epi) at rest greater than the mean + 2 SD and thus was excluded from the study. The anthropometric data from the two groups of subjects are reported in Table 1. They are comparable to those obtained in our laboratory in an urban population. The amount of cocaine in the blood averaged 72 ± 9 ng/ml after chewing before exercise and remained elevated (74 ± 9 ng/ml) at exhaustion.

From before to after chewing, C displayed a significant increase in plasma FFAs, whereas plasma FFA levels in the NC remained unchanged. There was a significant increase in plasma NE from before to after chewing in both groups (Table 2), whereas plasma Epi remained unchanged from before to after chewing.

At maximal exercise, $\dot{V}O_2$, HR, RER, Sa_{O_2}, mea arterial blood pressure, circulating catecholamines (Epi and NE), and plasma metabolites (glucose, FFAs, glycerol, and lactate) were similar in NC and C (Table 3). In addition, we found that $\dot{V}O_{2peak}$ decreased with the

Table 1. *Anthropometric characteristics of subjects*

	Nonchewers	Chewers
Age, yr	31.6 ± 2.7	33.9 ± 1.4
Body weight, kg	60.5 ± 3.2	59.3 ± 1.9
Body height, cm	162.1 ± 1.1	160.7 ± 0.8
Body mass index, kg/m^2	22.9 ± 1.1	22.9 ± 0.6
Body surface area, m^2	1.64 ± 0.04	1.62 ± 0.03
%Fat	16.7 ± 1.0	16.7 ± 1.4
Body density	1.06 ± 0.02	1.06 ± 0.03
Amount of coca leaves, g		12.9 ± 1.3
Amount of lejia, g		0.8 ± 0.2
Coca use duration, yr		8.8 ± 2.6

Values are means ± SE.

Table 2. *Metabolic and plasma metabolite and catecholamine values before and after coca chewing*

	Nonchewers		Chewers	
	R1	R2	R1	R2
$\dot{V}O_2$, ml·kg^{-1}·min^{-1}		5.3 ± 0.2		5.0 ± 0.3
$\dot{V}E$, l/min		10.2 ± 0.4		9.3 ± 0.8
RER		0.92 ± 0.03		0.86 ± 0.08
HR, beats/min		61 ± 2		63 ± 3
Sa_{O_2}, %		94.7 ± 0.5		94.4 ± 0.5
MABP, Torr		107.1 ± 3.2		108.3 ± 4.0
Glucose, mM	4.6 ± 0.2	4.6 ± 0.8	4.9 ± 0.6	5.7 ± 0.9
FFA, mM	0.147 ± 0.028	0.153 ± 0.027	0.080 ± 0.027	0.203 ± 0.039*
Glycerol, μM	150 ± 12	147 ± 7	136 ± 12	159 ± 20
Lactate, mM	1.4 ± 0.1	1.6 ± 0.1	1.3 ± 0.1	1.6 ± 0.1
Epinephrine, pg/ml	47 ± 6	51 ± 5	49 ± 9	59 ± 3
Norepinephrine, pg/ml	528 ± 41	690 ± 43*	499 ± 62	748 ± 63*

Values are means ± SE. $\dot{V}O_2$, O_2 uptake; $\dot{V}E$, ventilation; RER, respiratory exchange ratio; HR, heart rate; Sa_{O_2}, arterial O_2 saturation; MABP, mean arterial blood pressure; FFA, free fatty acids; R1, before chewing; R2, after chewing. In nonchewers, R1 and R2 correspond to 1 h of rest during which subjects remained seated. See METHODS for further details. * Significantly different from R1.

duration of coca use ($P < 0.05$; data not shown). It has to be mentioned that at exhaustion, C displayed a higher $\dot{V}E$ and ventilatory equivalent ($\dot{V}E/\dot{V}O_2$).

During submaximal workloads, $\dot{V}O_2$ was identical at each level of exercise (Fig. 1) and delta η averaged 26.4 ± 0.7 and 27.0 ± 0.8% in NC and C, respectively.

The effects of coca use on plasma metabolites are reported in Fig. 2. Plasma glucose was significantly higher in C than in NC, whereas blood lactate accumulation was unaffected by coca chewing (Fig. 2). Both exercise intensity ($P < 0.01$) and coca use ($P < 0.05$) affect the plasma FFA levels and, in addition, there was a significant interaction between the two factors ($P < 0.005$). Thus, plasma FFAs were increased by coca chewing, and the levels of FFAs decreased throughout the exercise test (Fig. 2). By contrast, the plasma FFA levels in the NC were slightly decreased at a low work intensity and returned to resting levels when exercise intensity was maximal (Table 3). Of note is that plasma glycerol levels increased with exercise but to a similar extent in C and NC.

There was no significant effect of coca chewing on plasma Epi and NE kinetics during exercise (Fig. 3), although there was a tendency to a higher sympathoadrenergic response in C during exercise at high intensity (Fig. 3, Table 3).

Table 3. *Metabolic and plasma metabolite and catecholamine values*

	Nonchewers	Chewers
$\dot{V}O_2$, ml·min^{-1}·kg^{-1}	41.9 ± 1.9	41.2 ± 2.0
$\dot{V}E$, l/min	98.9 ± 5.0	123.9 ± 4.9*
$\dot{V}E/\dot{V}O_2$, l BTPS/l STPD	40.9 ± 0.8	47.9 ± 2.4*
RER	1.05 ± 0.03	1.06 ± 0.03
HR, beats/min	168 ± 3	176 ± 3
Sa_{O_2}, %	88.9 ± 0.7	89.4 ± 1.0
MABP, Torr	104.8 ± 2.1	100.6 ± 3.1
Glucose, mM	4.7 ± 0.2	4.7 ± 0.2
FFA, mM	0.153 ± 0.032	0.162 ± 0.040
Glycerol, μM	176 ± 12	171 ± 27
Lactate, mM	7.1 ± 0.8	7.4 ± 0.5
Epinephrine, pg/ml	291 ± 72	411 ± 67
Norepinephrine, pg/ml	2,423 ± 367	3,310 ± 578

Data are means ± SE. $\dot{V}E/\dot{V}O_2$, ventilatory equivalent. See METHODS for further details. * Significantly different from nonchewers.

DISCUSSION

Before discussing the effects of coca use on exercise performance, we must analyze the anthropometric data

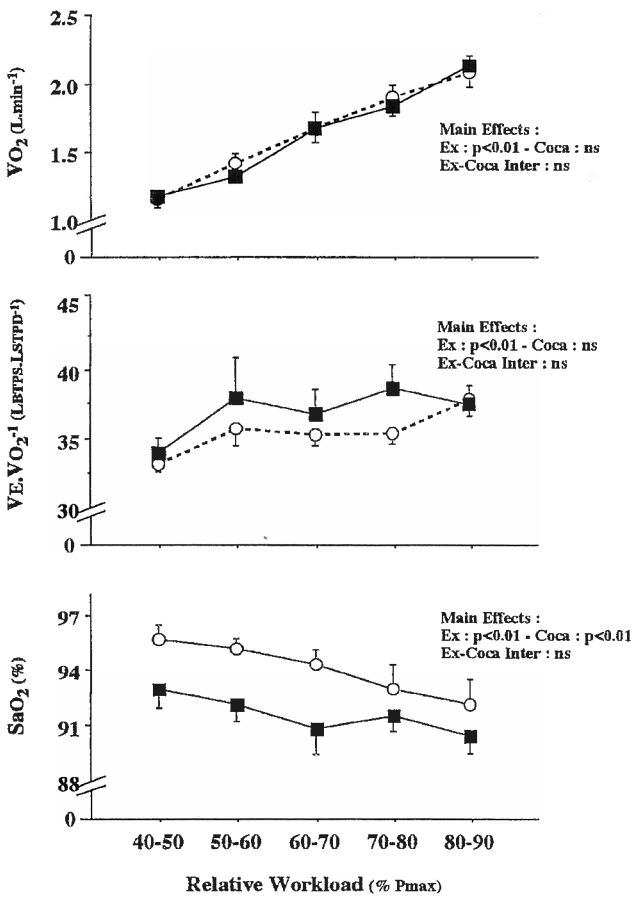

Fig. 1. Oxygen uptake ($\dot{V}O_2$), ventilatory equivalent ($\dot{V}E/\dot{V}O_2$), and arterial O_2 saturation (Sa_{O_2}) responses during incremental exercise in coca chewers (■) and nonchewers (○). Ex, exercise; ns, not significant; Inter, interaction; %Pmax, relative percentage of maximal aerobic power. Data are means ± SE.

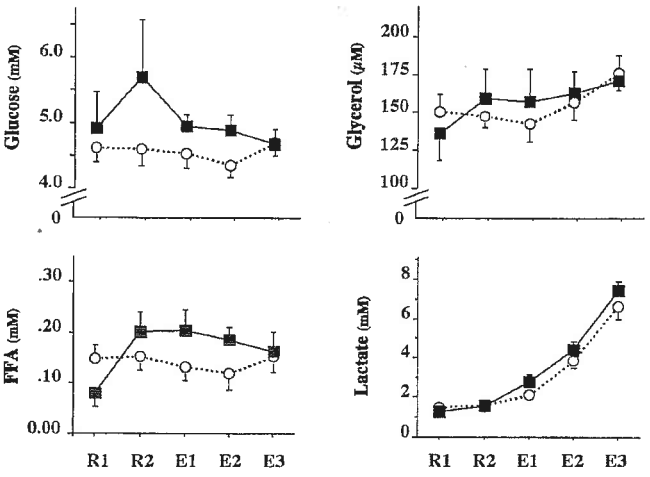

Fig. 2. Plasma glucose, free fatty acid (FFA), glycerol, and lactate concentrations at rest before (R1) and after (R2) 1 h of coca chewing during submaximal exercise [E1, 43.7 ± 1.3% peak O_2 uptake ($\dot{V}O_{2peak}$); E2, 75.9 ± 1.3% $\dot{V}O_{2peak}$] and at exhaustion (E3) in chewers (■) and nonchewers (○). Data are means ± SE. For further explanation, see METHODS.

of the two populations to establish whether they are comparable in NC and C and are within normal range. Indeed, it has been suggested that rural high-altitude residents may be marginally undernourished (22), a situation that could affect work performance (2). Furthermore, Picon-Reátegui (22) has reported that coca chewing resulted in an increased negative energy balance.

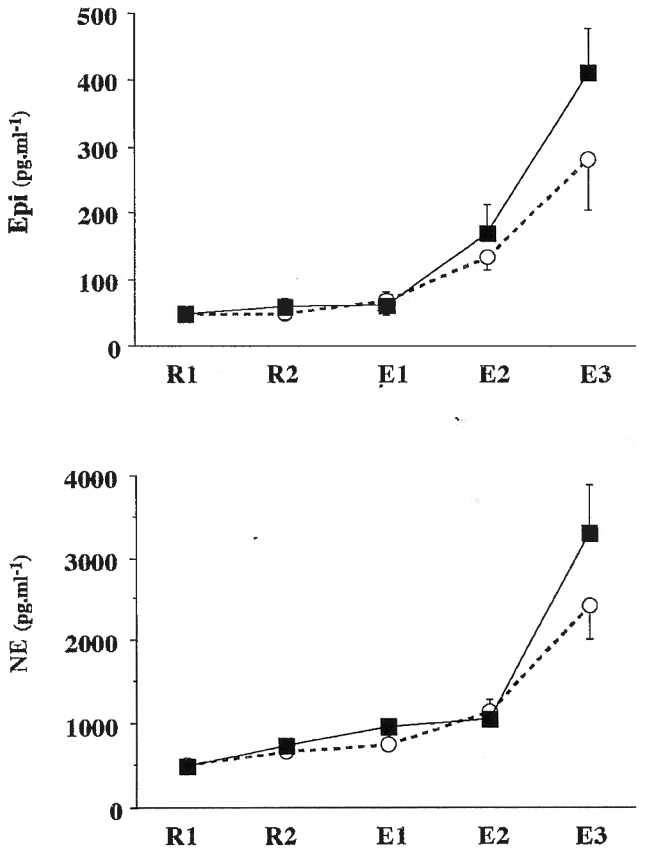

Fig. 3. Plasma epinephrine (Epi) and norepinephrine (NE) concentrations at rest before and after 1 h of coca chewing during submaximal exercise (E1, 43.7 ± 1.3% $\dot{V}O_{2peak}$; E2, 75.9 ± 1.3% $\dot{V}O_{2peak}$) and at exhaustion in chewers (■) and nonchewers (○). Data are means ± SE. For further explanation, see METHODS.

The nutritional survey performed in our two populations showed that the C and NC had the same qualitative and quantitative food intake (C. Lujan and J. C. San Miguel, personal communication). In addition, it has been shown that the body mass index [weight (kg)/height (m^2)] can be considered as a relatively good measure of nutritional status (12). From the data reported in Table 1, it appears that both C and NC are within the normal range of anthropometric standards (12).

Effects of coca chewing at rest. From the available data of the literature, it is known that coca chewing results immediately in a detectable amount of cocaine in blood, which reaches peak concentration at ~1 h and persists in the plasma for >7 h (17). Therefore, we asked the C to take the desired amount of coca leaves that they could chew in 1 h, which allowed us to suppose that, after chewing, the plasma cocaine level was at its maximum and remained at this level throughout the graded incremental exercise. This assumption was confirmed by cocaine level determination in blood, which averaged ~70 ng/ml and remained at this level up to exhaustion.

In resting conditions, coca chewing appears to result in an increase in plasma FFAs (Table 2). Plasma FFA levels are determined by the rates of *1*) lipolysis, *2*) lipid oxidation, and *3*) reesterification of FFAs (5). With respect to the rate of lipolysis, it is considered that it can be estimated from glycerol release in the bloodstream because glycerol formed by lipolysis cannot be reutilized in adipose tissue due to a low concentration of α-glycerokinase. It can be calculated that approximately one-third (45 μM) of the increase in FFAs after coca chewing was related to an increased rate of lipolysis. Classically, lipid oxidation is estimated in vivo from the RER. From the RER data measured at rest in the NC and C (Table 2), it can be estimated that fat oxidation was ~50% higher in the C compared with the NC. In regard to reesterification of FFAs, the present study cannot provide any valuable estimation because triglyceride-FFA recycling can be calculated only by infusion of stable isotopes (27). On the basis of a sympathoadrenergic activation from before to after chewing, it is possible to hypothesize a modification of FFA delivery to the tissues (e.g., liver) due to NE-induced vasoconstriction causing decreased blood flow. Indeed, changes in blood flow during exercise have been shown to contribute to both lipid mobilization and utilization (5). It did not seem that the effect of coca chewing on circulating FFAs was related only to an increased sympathoadrenergic response because the plasma NE was higher after chewing in the NC as well as in the C and circulating FFAs were elevated only in the C (Table 2). The difference in circulating NE from before to after chewing in NC was likely due to postural changes. Indeed, before chewing, blood was withdrawn from subjects in the supine position, whereas after chewing blood was recollected while the subjects were

sitting on the bicycle, and such postural changes have been shown to result in a doubling of NE concentration (9). It is also possible that chronic coca chewing has resulted in an increased tissue sensitivity to β-adrenergic stimulation because plasma FFAs were increased in the C, whereas they did not change in the NC.

Although not directly comparable to our study, Bracken and co-workers (3, 4) and Conlee et al. (8) have shown that acute injection of cocaine hydrochloride in resting rats resulted in a sympathoadrenergic activation and an increased level of plasma FFAs. However, in these latter studies, the dose of alkaloids used was at least 10 times higher than the maximum amount of cocaine that could be extracted by coca chewing. Furthermore, it was reported that plasma Epi was significantly elevated in rats (4, 8), whereas our C did not display any adrenal activation after coca chewing (Table 2). It can thus be considered that the cocaine level in the C was low when compared with the quantities used in topical anesthesia or intravenously injected by cocaine addicts, who may use up to 10 g in a day (17).

Effect of coca chewing on subsequent exercise-induced hormonal and metabolic responses. The $\dot{V}O_{2peak}$ of the NC (Table 2) was slightly lower (~10%) than the values reported for native Aymara men from the same altitude (14). However, although the subjects in this latter study were of similar ethnic and occupational backgrounds as our subjects, they were younger, and aging during adulthood is normally associated with a decrease in the functional capacity of the oxygen transport system. $\dot{V}O_{2peak}$ was similar in the NC and C (Table 3), but it was found that it decreased in the C as coca chewing was prolonged over years ($P < 0.05$; data not shown). However, this effect was related to aging and not to prolonged coca use because the decline in $\dot{V}O_{2peak}$ with age was similar in C and NC (data not shown). The lack of effects of coca chewing on maximal exercise capacity observed in the present study confirms the data obtained in the few C examined by Hanna (15, 16) but contrasts with those of Kershner et al. (19), who showed that cocaine injection (25 mg/kg) can improve $\dot{V}O_{2max}$. Whether these discrepant results are related to differences in species or in the amount of circulating cocaine cannot be ascertained, but recently Bracken et al. (4) have reported that rats injected with 20 mg/kg of cocaine displayed a dramatic reduction (−75%) in endurance capacity. Even though our study was not aimed at comparing maximal exercise capacity after acute or chronic use of coca chewing, it must be underlined that $\dot{V}O_{2peak}$, maximal HR, and Sa_{O_2} measured in C without chewing and blood sampling on the day of familiarization were identical to those obtained in these subjects after chewing and with blood sampling ($\dot{V}O_2$ 41.9 ± 1.9 and 41.2 ± 1.4 ml·min^{-1}·kg^{-1}, maximal HR 168 ± 3 and 172 ± 6 beats/min, and Sa_{O_2} 88.9 ± 0.7 and 90.1 ± 1.5% for trials with and without coca, respectively).

Another way to explain the supposedly ergogenic effect of coca use could be linked to an increased η, which is defined as the work accomplished divided by the energy expended to do that work (13). Several exercise efficiencies (gross, net, work, apparent, delta, and instantaneous) have been proposed, but the problem is interpreting the meaning of such efficiencies (25). However, these authors mentioned that any one of them can be used safely for comparative purposes providing the conditions of the experiments are matched as well as possible, which was our case. In the present study, delta η was identical in both groups (26.4 ± 0.7 and 27.0 ± 0.8% for NC and C, respectively), indicating that changes in η are not a plausible explanation for the benefits claimed by habitual coca users.

Although coca use was not shown to affect either maximal exercise capacity or η, coca chewing was accompanied by some physiological changes during submaximal exercise. Thus we found that C displayed an increased plasma FFA level (Fig. 3), which could favor fat oxidation during exercise in C (5, 7). The mechanism(s) by which coca increases FFA availability during exercise is not readily apparent but could be due either to an increased rate of lipolysis or to a decreased rate of fat oxidation and/or FFA reesterification. From the glycerol (Fig. 2) and RER (Fig. 4) data, it can be concluded that both lipolysis and fat oxidation were similar in NC and C. As in resting conditions, it can hypothesized that FFA reesterification during exercise was lower in C in relation to changes in sympathoadrenergic activation. However, during submaximal exercise,

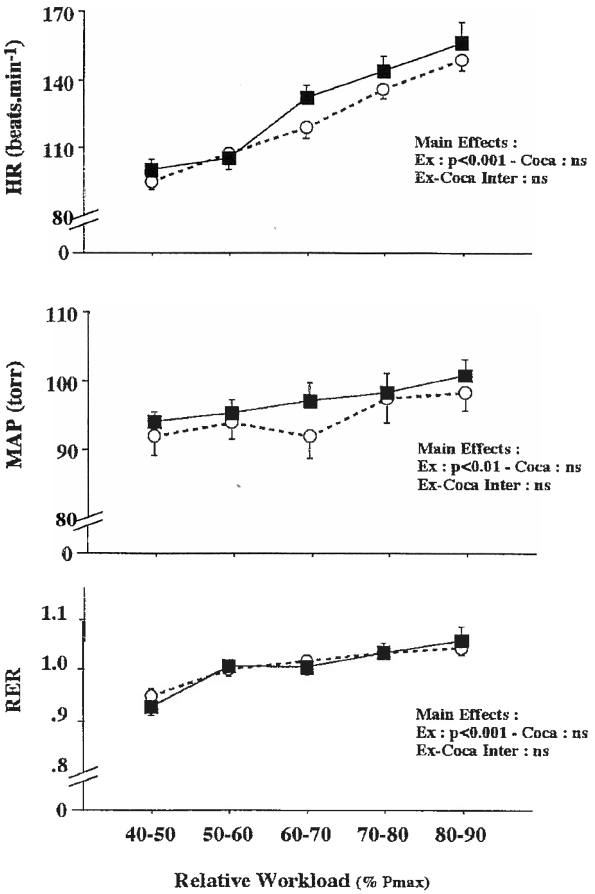

Fig. 4. Heart rate (HR), mean arterial pressure (MAP), and respiratory exchange ratio (RER) responses during incremental exercise in coca chewers (■) and nonchewers (○). Data are means ± SE.

plasma catecholamine levels were similar in NC and C, whereas plasma Epi and NE tended to be higher in C at exhaustion (Fig. 3). This marginal sympathoadrenergic activation might play a role in controlling FFA reesterification, but this possibility needs to be evaluated by an infusion of stable isotopes (27).

It has to be remarked that the metabolic and hormonal effects of coca chewing are reminiscent of what is observed after caffeine ingestion (see, e.g., Ref. 18). Indeed, several studies have shown that caffeine increases plasma FFAs and enhances endurance performance (for a review see Ref. 1). The key aspect of the response to caffeine ingestion is an elevation of plasma catecholamines (1). During exercise, however, the increase in plasma catecholamines was similar in NC and C (Fig. 3), but plasma FFAs remained higher in C compared with NC (Fig. 2). However, it has to be mentioned that plasma FFAs decreased from rest to maximal exercise (Fig. 3) in the C, whereas in the NC the circulating level of FFAs was maintained at its resting level up to exhaustion. This suggests an greater utilization of FFAs during exercise in C compared with NC.

In addition, Sa_{O_2} was significantly lower in the C throughout the incremental exercise test (Fig. 1). Arterial desaturation can result from one of or the combination of the following factors: *1*) ventilation-perfusion inequality, *2*) arteriovenous shunt, and *3*) diffusion limitation. From the results reported in the present study, it appeared that coca chewers did not display any sign of hypoventilation during submaximal (Fig. 1) and maximal exercise (Table 3). We are not aware of any pulmonary and circulatory studies after coca chewing, but recently Wilkins (26) has shown that the lung is a major site for tissue sequestration of cocaine, which is known to block the reuptake of catecholamines at adrenergic nerve endings (23) and may possibly also potentiate catecholamine-receptor sensitivity (26). Although plasma catecholamine levels were not different in the C compared with the NC during exercise (Fig. 3), it is not possible to exclude that coca chewing was followed by pulmonary vasoconstriction in relation to the predominant sequestration of cocaine by the lungs (26). This effect of coca chewing on pulmonary hemodynamics needs, however, to be evaluated in greater details in future studies.

In conclusion, the present study demonstrated that coca chewing at rest resulted in an increased fat availability. During incremental exercise, FFAs remained elevated even though sympathoadrenergic activation was similar in the NC and C. Although increased FFA availability did not result in either an enhanced maximal aerobic capacity or an increased η in the C, it is possible that it could be beneficial in improving tolerance to endurance exercise. The effect of coca chewing on prolonged submaximal exercise performance is reported in a companion paper (11).

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