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Running Endurance in 27-hour Fasted Humans

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Abstract

RUNNING ENDURANCE IN 27-HOUR FASTED HUMANS

by

Kristin A. Carlson

Nine male marathon runners were exercised to exhaustion to determine the effects of a 27-hour fast on endurance performance. Each subject completed two exercise tests at 72% peak oxygen uptake (VO_2 max), one following a 27-hour fast and one three hours after a pre-exercise meal, in random order. Fasting caused a $44.7 \pm 5.8\%$ (\pm SE) decrease in endurance performance ($p < 0.01$). Blood, muscle, psychological, and ventilatory data were examined to determine the cause of the decreased performance. Fasting caused significant increases in VO_2 ($9.3 \pm 2.0\%$), heart rate ($8.4 \pm 2.4\%$), rating of perceived exertion (RPE), and psychological fatigue, evident within the first 60 minutes of exercise. There was no difference in plasma glucose or epinephrine levels. Muscle glycogen degraded at the same rate (0.48 ± 0.15 vs $0.47 \pm 0.28 \mu\text{moles} \cdot \text{g}^{-1} \cdot \text{min}^{-1}$ in the non-fasted and fasted tests, respectively) despite lower respiratory exchange ratio (R) and elevated free fatty acid (FFA) levels. Lactate, insulin, norepinephrine (NE), and 3,4-dihydroxyphenylacetic acid (dopac) were all increased in the fasted test ($p < 0.05$). The increase in NE ($r = 0.79$, $p < 0.01$), the diameter of type I muscle fibers ($r = 0.70$, $p < 0.05$), and ending insulin levels ($r = -0.88$, $p < 0.01$) were correlated with endurance time in the fasted state.

Fatigue in endurance running for 27-hour fasted humans appears to be related to a combination of physiological, psychological, metabolic, and hormonal changes.

LOMA LINDA UNIVERSITY

Graduate School

RUNNING ENDURANCE IN 27-HOUR FASTED HUMANS

by

Kristin A. Carlson

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of the Requirements for the Degree Master of Science
in Nutrition

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Each person whose signature appears below certifies that this manuscript in his opinion is adequate, in scope and quality, in lieu of a thesis for the degree Master of Science.

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Introduction

The effects of fasting on resting human metabolism have been studied extensively (53). Only recently, however, have the effects of fasting on the exercising human been explored. These studies have been one of two types--either involving a long term fast (59 hours or more) (4,7,22,28,40) or a short term overnight fast (15-16 hour) (11,12,48).

Work performance in both submaximal (28,40) and maximal exercise (1,28,36) has been found to be decreased by long-term fasting. The studies have had contradictory conclusions, however, on the cause of this decreased performance. Henschel et al. (28) determined that the decreased efficiency in grade walking of 60 to 120-hour fasted subjects contributed to their diminished work capacity. In a 7-day semistarvation study by Bender and Martin (1), decreased time to exhaustion in maximal treadmill tests was attributed to a variety of unmeasured factors, including hypohydration and a decrease in muscle glycogen.

The conclusions of short term fasts have been mixed, also. Pequignot et al. (48) investigated sedentary men after a 15-hour fast, cycling at 80% VO_2 max. Work performance was decreased 23% by the fast. He attributed this to elevated counterregulatory hormones that may have led to an early depletion of muscle glycogen. Coyle et al. (11) examined trained cyclers after a 16-hour fast with and without carbohydrate (CHO) feedings during exercise. The CHO fed

subjects were able to cycle 33% longer. In contrast to Pequignot, however, muscle glycogen degraded at the same rate in both trials.

Recently Dohm et al. (18) examined the effect of a 24-hour fast on endurance performance in the rat. He found a significant increase in treadmill time to exhaustion in fasted rats compared to non-fasted rats. This study led to the investigation by Loy et al. (38) to determine if this effect was evident in human cyclers. In this recently published paper, he concluded that a 24-hour fast was detrimental to endurance performance as the cyclists fatigued significantly earlier after the fast.

Although Loy studied the effect of fasting and factors contributing to fatigue in trained cyclers, this has not been studied in human endurance runners. It is possible that fatigue may occur from different causes for the trained cyclist compared to the trained runner. In non-fasted exercise, it has been seen that hypoglycemia and the depletion of muscle glycogen appear to be the prime causes of fatigue for the cyclist while in the runner these seem to be less important (12,13,38). Therefore, we thought it important to examine the effects of a 27-hour fast on endurance performance in the human runner and the metabolic, psychological, and physiological causes of fatigue.

Methods

Subjects. Nine healthy male subjects volunteered for this study. Each subject voluntarily signed an informed consent statement approved by the Loma Linda University Institutional Review Board for Human Studies. All were involved competitively in marathon running, running an average of 42.1 ± 4.5 miles per week. Subjects had been running seriously for an average of 7.6 ± 0.48 years with best marathon performances averaging 3.03 ± 0.09 hours.

Subject information is presented in Table 1. Peak oxygen uptake (VO_2 max) was determined for each subject utilizing a multistage graded exercise test with continuous metabolic measurement employing the Sensor Medics MMC Horizon System 4400 metabolic cart (Sensor Medics, 1630 S. State College Blvd., Anaheim CA). Treadmill speeds corresponding to 70% of the subjects' VO_2 max were estimated from this test.

Exercise Design. Each subject completed two exercise tests, one following a 27-hour fast and one 3 hours after a pre-exercise meal, in random order. The two tests were separated by a minimum of 2 weeks, with an average separation of 30 ± 6.4 days. Subjects maintained their normal training regimen between the tests. In order to avoid diurnal variation, each of the two tests was conducted on the same day of the week at the same time of the day.

Test 1. Subjects were instructed by a nutritionist to eat a high carbohydrate diet. Food intake was monitored through 4-

day food records completed prior to each test by each subject. The last meal consumed consisted of a liquid meal, Ensure Plus (52.8% CHO, 32.0% fat, 15.2% pro), given at 7 Kcal/kg at 7:00am on the morning of the test. Subjects did not exercise vigorously for 48 hours prior to the test. Upon arriving at the exercise lab at 10:00am, subjects completed the Profile of Mood States (POMS) inventory, a measure of six mood states (39), using the "right now" rating period. Pre-exercise blood and muscle samples were collected as described below. Subjects then exercised on the treadmill at a speed corresponding to 70% VO_2 max. The average room temperature for each test period was 22.00 ± 0.24 C and subjects were cooled by a fan throughout their exercise period. Subjects had a progressive warm-up, reaching their calculated test speed within 7.14 ± 1.20 minutes. The warm-up time was included in their total time on the treadmill to exhaustion. Oxygen uptake, ventilation, and respiratory exchange ratio (R) were measured throughout the exercise period with 30-second average values recorded every 10 minutes using the Sensor Medics metabolic cart. Heart rate was recorded every 10 minutes. Subjects reported the rating of perceived exertion using a 10 point scale every 10 minutes (44). Subjects drank an average of 452 ± 22 ml water each 30 minutes on the treadmill. After 90 minutes on the treadmill, subjects were stopped for another muscle biopsy and blood sample. Average time off the treadmill was 6.13 ± 0.91 minutes which

was not included in the total treadmill time. Subjects then returned to the treadmill and continued running until exhaustion, defined by their inability to continue running at the set treadmill speed and a reported RPE of 10. Immediately following exhaustion, final blood samples and a muscle biopsy were collected. Average time to complete sample collection was 7.60 ± 1.16 minutes.

Subjects were encouraged to perform maximally through stipends and monetary bonuses based on maximal inter- and intra- individual performances. Subjects were not allowed to know their time on the treadmill and were not given any information on other subjects' treadmill times in order to encourage full efforts for each subject.

Test 2. Subjects followed the same protocol of Test 1 except for the replacement of the last day of the high CHO diet with a 24-hour fast. As in Test 1 the last meal consisted of Ensure Plus at 7:00am, 27 hours prior to the test. Subjects drank at least 3 quarts of water on the day of their fast to assure adequate hydration prior to their test. Six of the nine subjects became exhausted before 90 minutes, thus only 2 biopsies and blood samples were collected on these subjects.

Sampling and Analytical Procedures. Percent body fat was determined from a seven site skinfold test (32).

Blood was collected immediately prior to exercise, after 90 minutes of exercise, and immediately after exhaustion from a catheter with a heparin lock placed in an

antecubital vein.

Five milliliters of blood were collected into a tube containing ethylenediaminetetraacetate (EDTA) and placed on ice until the addition of 0.5 ml aprotinin. The sample was then centrifuged and the plasma used for the determination of glucagon based on the assays of Sperling et al. (54) and Henquin et al. (27) (Serano Diagnostics, Braintree, MA, catalogue code 5910000). Another 5 milliliters of blood were collected into an evacuated tube and allowed to clot at room temperature. The sample was then centrifuged to separate the serum which was used to determine insulin (23) (Immuno Nuclear Corp., Stillwater, MN, catalogue no. 0600). Blood for catecholamine determination was collected into tubes with sodium heparin and immediately centrifuged. The modified (37) methods of Davis et al. (14) and Moyer et al. (42) were used in the determination.

Another five milliliters of blood were collected in tubes containing EDTA. A 1 ml aliquot was separated and kept on ice for the determination of hematocrit (analyzed by microcentrifugation) and hemoglobin (19) (Sigma Diagnostics, St. Louis, MO, catalogue no. 525). The remaining blood was centrifuged immediately and the plasma separated for the determination of glucose (5) (Sigma Diagnostics, catalogue no., 115), free fatty acids (FFA) (46), and triglycerides (43) (Sigma Diagnostics, catalogue no., 405). Lastly, 2 milliliters of blood were collected in a tube containing 7.5 mg

sodium fluoride and 6.0 mg potassium oxalate and kept on ice. 1 ml of this was then added to 2 ml cold 8% perchloric acid to deproteinize the blood. This was then centrifuged and the supernatant collected for the determination of lactate based on the method of Gutman and Wahlefeld (25) (Sigma Diagnostics, catalogue no. 726).

Muscle biopsies were obtained from the medial head of the gastrocnemius muscle using the method of Bergstrom (2) and the modification of Evans et al. (20). Samples were immediately frozen in liquid nitrogen and stored at -70 C until analysis. The methods of Hassid and Abraham (26) were used to determine muscle glycogen content. One sample from each subject was mounted in embedding medium, frozen and stored for later histochemical analysis. Muscle samples were analyzed for type I and type II muscle fibers after incubating at pH 10.3 and 4.3 and staining for myofibrillar ATPase activity (35).

Plasma volume decrease was determined through the calculations of Dill and Costill (16).

Diets were analyzed through the Nutritionist III program (47).

Results are presented as means \pm SE using the Statistical Package for the Social Sciences computer program (45). Pearson Correlations were used to determine the association between variables. Changes within and between Test 1 and Test 2 were evaluated by paired t-test.

Results

Time to Exhaustion

Average time to fatigue is presented in Figure 1. Fasting caused an average $44.7 \pm 5.8\%$ decrease ($p < 0.01$) in endurance performance.

Treadmill Performance Data

Treadmill performance data are presented in Figure 2. The first 60 minutes and ending values for each variable were compared between the two tests. The values for the variables beyond 60 minutes were not compared because 33% of the fasted subjects had already completed their run at this time.

Fasting caused a significant increase in VO_2 , averaging $9.3 \pm 2.0\%$ for the first 60 minutes of exercise. At exhaustion, however, this difference was decreased to $6.7 \pm 3.6\%$ (NS). Heart rate was also significantly elevated during the first 60 minutes of exercise by an average of $8.4 \pm 2.4\%$. At exhaustion, heart rate was elevated $2.8 \pm 1.3\%$ above the non-fasted test (NS). R was significantly decreased, averaging $6.5 \pm 2.1\%$ for the first 60 minutes and $4.2 \pm 1.2\%$ at exhaustion. For the first 30 minutes of exercise, there was no significant difference in RPE but by 40 minutes, RPE was significantly elevated in the fasted test. All subjects reached an RPE rating of 10, indicating exhaustion, except one subject in the fasted test who only reported a 9. Despite the differences in VO_2 , heart rate, R, and RPE between the fasted

and non-fasted tests, there was no significant differences between the two tests in ventilation rate (VE) and breath rate (BR) with the exception of VE at 10 and 40 minutes.

Heart rate, VO_2 , BR, and VE increased significantly throughout the exercise period in both tests. Heart rate increased $21.7 \pm 1.8\%$ and $15.6 \pm 1.7\%$ while VO_2 increased $17.6 \pm 7.8\%$ and $10.0 \pm 3.1\%$ in the non-fasted and fasted tests, respectively. R decreased significantly through exercise in the non-fasted test but not in the fasted test.

Metabolic Variables

Metabolic variables are presented in Table 2. The 27-hour fast decreased pre-exercise muscle glycogen values 17% (NS). Glycogen decreased $71.9 \pm 16.0\%$ from pre-exercise to exhaustion in the non-fasted test ($p < 0.01$) and $28.3 \pm 13.0\%$ in the fasted test (NS). Despite the greater percent decrease of glycogen in the non-fasted test, in both tests muscle glycogen degraded by the same rate. Glycogen decreased $0.48 \pm 0.15 \mu\text{moles glycogen} \cdot \text{g}^{-1} \cdot \text{min}^{-1}$ in the non-fasted test and $0.47 \pm 0.28 \mu\text{moles glycogen} \cdot \text{g}^{-1} \cdot \text{min}^{-1}$ in the fasted test. One subject in the fasted test and one subject in the non-fasted test had glycogen levels less than $15 \mu\text{moles} \cdot \text{g}^{-1}$.

Lactate increased significantly with exercise in both tests. At fatigue, fasted lactate levels were elevated $76.2 \pm 21.0\%$ above the non-fasted group ($p < 0.05$). Two subjects in the fasted test had lactate levels above $6 \text{mmole} \cdot \text{l}^{-1}$. There was no significant correlation, however, with lactate

level and endurance time.

Plasma glucose levels remained constant throughout exercise in both groups with no difference between the groups. Two subjects in the fasted test demonstrated signs of hypoglycemia (plasma glucose $< 2.5 \text{ mmole} \cdot \text{l}^{-1}$) while no subjects in the non-fasted test demonstrated hypoglycemia.

Plasma FFA increased from pre-exercise to fatigue in both groups. The values for the fasted test were elevated $80.3 \pm 28.7\%$ ($p < 0.05$) before exercise and $31.0 \pm 14.6\%$ (NS) at fatigue compared to the non-fasted test.

Pre-exercise plasma triglyceride levels in the non-fasted test were $49.3 \pm 6.7\%$ lower than in the fasted test ($p < 0.01$). At fatigue, however, there was no significant difference between the groups.

Fasting versus non-fasting did not cause a significant elevation in catecholamines at rest. After exhaustion, norepinephrine (NE) and 3,4-dihydroxyphenylacetic acid (dopac) in the fasting state were significantly elevated $43.3 \pm 20.5\%$ and $132.7 \pm 49.0\%$ above the non-fasting levels, respectively, while epinephrine (E) was not elevated significantly. During exercise in both states, NE and dopac but not E increased significantly. A positive correlation was demonstrated between time to fatigue and increase in NE in the fasted test ($r = 0.79$, $p < 0.01$). Changes in NE ($r = 0.72$, $p < 0.05$) and dopac ($r = 0.70$, $p < 0.05$) were correlated with endurance time in the non-fasted test. Glycogen degradation

and catecholamine levels were not correlated.

Resting insulin was $55.6 \pm 27.8\%$ lower ($p=0.07$) in the fasted test. The insulin-to-glucagon ratio was significantly lower for the fasted test prior to exercise but not after exercise. Through exercise in the fasted test, insulin (NS) and glucagon increased ($p<0.05$). The change in the ratio from rest to fatigue was not significant, however. In the non-fasted test, the insulin-to-glucagon ratio tended to decrease from pre-exercise to fatigue ($p=0.09$) as insulin decreased (NS) and glucagon increased (NS) through exercise. There was a significant difference between the change in the insulin-to-glucagon ratio from pre-exercise to fatigue in the fasted and non-fasted test. Time to fatigue in the fasted test was negatively correlated with ending insulin levels ($r=-0.88$, $p<0.01$).

Psychological Data

The POMS test results demonstrated the characteristic iceberg pattern for competitive marathon runners (41), revealing low values for tension, depression, fatigue, and confusion and high values for vigor (figure 3). In comparing the results from each of the two tests, a significant increase in T-score for fatigue of approximately 11% was found in the fasted group compared to the non-fasted group. There was also a correlation between time to exhaustion and vigor rating in the non-fasted group ($r=.80$, $p<0.01$).

Miscellaneous

Subjects ran at the same speed in each test. This speed was an average of $72.9 \pm 3.0\%$ VO_2 max in the fasted test and $71.4 \pm 3.1\%$ VO_2 max in the non-fasted test. This average was computed from their VO_2 values for the entire run in each test.

The percentage of type I muscle fibers was not correlated with endurance time in the fasted and non-fasted test. The diameter of type I muscle fibers was correlated with endurance time in the fasted test ($r=0.70$, $p<0.05$).

Subjects' recorded diets before each of the tests did not differ significantly in percent of calories from CHO, fat, protein, and alcohol. Averages were $14.3 \pm 0.6\%$ protein, $53.9 \pm 5.4\%$ CHO, $22.7 \pm 2.4\%$ fat, and $4.2 \pm 2.4\%$ alcohol before the non-fasted test and $11.9 \pm 1.5\%$ protein, $61.5 \pm 4.4\%$ CHO, $23.5 \pm 3.8\%$ fat, and $3.6 \pm 2.2\%$ alcohol before the fasted test. Subjects did consume an average of 281 more calories per day in the days prior to the fasted test ($p<0.05$) but arrived at the exercise lab an average of 1.69 kg lower in weight compared to the non-fasted test ($p<0.01$).

Average decrease in plasma volume for the fasted test was $13.5 \pm 4.2\%$ and $14.0 \pm 6.4\%$ for the non-fasted test. Average percent of body weight lost through the exercise period in the non-fasted test was $2.8 \pm 0.4\%$ and $1.5 \pm 0.2\%$ in the fasted test ($p<0.01$).

Discussion

It is evident that a 27-hour fast is detrimental to endurance performance in experienced marathon runners. This agrees with the findings of Loy et al. (38) who reported a marked reduction in performance time in trained cyclers, fasted 24 hours. It can be concluded, then, that fasting, whether overnight (11,48), one day (38), or long term (28) is detrimental to work performance in both human cyclers and runners.

This is contrary to the findings of Dohm et al. (18) where it was evident that a 24-hour fast was beneficial to endurance performance on the treadmill. In this study the fasted rats experienced a significant increase in blood FFA and a decreased carbohydrate utilization. The authors concluded that the 24-fast spared muscle glycogen, increasing endurance time.

Our study revealed an increase in fat oxidation as a result of the 27-hour fast. This was evident from the significant depression in R at rest and during exercise in the fasted test. In addition, resting plasma FFA levels were significantly elevated and TG levels significantly decreased in the fasted test. Despite the higher fat oxidation, muscle glycogen decreased at the same rate (μ moles glycogen degraded/minute) in both tests. Theoretically, the higher fat oxidation should have led to a decrease in the rate of muscle glycogen usage and an increase in endurance time through the Randle effect (49). While this has been found to be true in

rats (18,51,52) and short term exercise at 70% VO_2 max in humans (8), during long endurance exercise a physiologically significant Randle effect does not appear to be present (15,31). Ravussin et al. (50) reported that elevated plasma FFA levels prior to exercise in man through heparin and intralipid infusions did not decrease the rate of CHO oxidation significantly during prolonged exercise at 44% VO_2 max. Our results suggest that the fasting-induced elevation of FFA does not produce a physiologically significant Randle effect.

The cause of fatigue during prolonged endurance running is not readily apparent (13). Although this study demonstrated some of the usual metabolic, physiological, and psychological changes associated with fasting and endurance exercise, no clear cause of fatigue could be determined.

The fatigue experienced in our study appears not to be related to metabolic factors in either the fasted or non-fasted state for most of the subjects. The post-exercise muscle glycogen levels were not representative of "depletion". Cyclists have been reported to have glycogen values as low as zero at exhaustion (30). Runners on the other hand, do not experience the same degree of depletion because of the larger number of muscle groups involved in running (33). Costill et al. (9) has proposed, however, that runners' slow twitch muscle fibers may become selectively depleted of glycogen. The depletion of glycogen in these

fibers may be the cause of fatigue in runners while fatigue in cyclers may be due to the total depletion of glycogen. Since we did not measure glycogen content in the different fiber types this is a matter of speculation in this study.

In fasted subjects a positive correlation between the diameter of type I muscle fibers and endurance time was demonstrated. Gollnick et al. (24) has reported that training increases the diameter of type I muscle fibers. These enlarged fibers possess a higher oxidative capacity which may explain the enhanced endurance of those subjects with larger type I fibers.

Blood glucose remained constant throughout exercise in both the fasted and non-fasted tests. Although two subjects in the fasted test were hypoglycemic at exhaustion, no other subjects in either test had low plasma glucose. Other treadmill studies have also concluded that hypoglycemia does not occur frequently with running (10,13,17). This is in contrast to cycling investigations where many subjects have been reported to become hypoglycemic (3,11,21). Loy et al. (38) reported that both hypoglycemia and low muscle glycogen levels were the cause of fatigue for most of the 24-hour fasted and non-fasted cycling subjects.

The serum insulin-to-glucagon ratio is an important determinant of glucose homeostasis during exercise (55). During exercise this ratio has been demonstrated to decrease, with fasting leading to a further depression (38,40). The

insulin-to-glucagon ratio did not change significantly with exercise in either state. There was, however, a significant difference in the change of the ratios from pre-exercise to fatigue between the fasted and non-fasted state. The reason for this is unclear and necessitates further investigation. In the fasted test, serum glucagon levels increased with exercise, as expected. Unexpectedly, serum insulin levels also increased with exercise. Ending insulin levels correlated negatively with endurance time in the fasted test.

Increased plasma catecholamines associated with fasting have been cited as a cause for the early fatigue of fasted subjects in a study by Pequignot et al. (48). He noted a negative correlation between the change in plasma NE levels and endurance time with fasted cyclers exercising at 80% VO_2 max. In our study, however, we found a positive correlation with the change in NE levels during exercise and endurance time in the fasted test. Furthermore, there was no correlation between increased catecholamine levels and muscle glycogen depletion. Therefore, it appears that the increased catecholamines did not lead to the earlier fatigue of the fasted subjects but this is a matter for further investigation.

Blood lactate increased during both tests, and was significantly elevated in the fasted state. Higher exercise blood lactate levels have been found to be associated with fasting (4,6,22,38). The higher level of lactate appears to

be due either to the inhibition of pyruvate oxidation by FFA, ketones, and leucine (4,6,22) or a change in pyruvate metabolism favoring the production of lactate in the muscles (22). Lactate levels experienced by our subjects have been reported in endurance events with little effect on performance (34). Thus, lactate probably was not a significant contributor to fatigue in our study.

Dehydration did not appear to contribute substantially to the early fatigue of the fasted subjects. Subjects consumed approximately 0.9 liters/hour. The percent decrease in plasma volume and the percent decrease in body weight were not of sufficient magnitude to be associated with fatigue (29). In addition, the percent of body weight lost in the non-fasted test was significantly greater than the fasted test.

Although often unmeasured and ignored, the psychological state of the subjects in each of the tests may be an important factor in fatigue. In comparing the results from the POMS inventory between the fasted and non-fasted states, the fasted subjects rated significantly higher in fatigue than the non-fasted subjects prior to exercise. By minute 40 of exercise, this increased fatigue was evident in the significantly elevated RPE values. The positive correlation between time to fatigue and level of vigor was also significant. Whether this actually influenced performance is a matter of speculation although it is probable that psycho-

logical state can influence performance (41).

Lastly the increase in VO_2 may contribute to an explanation of fatigue. Throughout the treadmill bout, VO_2 was significantly increased for the fasted subjects compared to the non-fasted, indicating increased energy output. This was reflected in elevated RPE values for the fasted subjects after 40 minutes. In addition, in both non-fasted and fasted states VO_2 steadily increased during the run. In contrast, VO_2 has been reported to remain constant during prolonged cycling (11). Davies and Thompson (13) recently reported that ultramarathon subjects running 4 hours to exhaustion on the treadmill experienced a 9.1% increase in VO_2 , slightly lower than our subjects experienced in both states. Davies attributed this increase in VO_2 to a decreased central neural drive to exercising muscles leading to the need to recruit muscle fibers to maintain necessary muscle tension. Central nervous fatigue may be a contributing factor of fatigue in our subjects in both states. It may also be a factor in the early fatigue of the fasted subjects who experienced an increase in VO_2 throughout exercise.

In conclusion, fasting caused a 44.7% decrease in endurance time. Although fasting resulted in an increase in VO_2 , heart rate, RPE, and psychological fatigue, the earlier fatigue in the fasted subjects is not clearly reflected in the metabolic measurements. Muscle glycogen degraded at the same rate despite increases in fat oxidation both at rest and

during exercise. Normoglycemia was maintained in all but two subjects. Dehydration was not a factor in fatigue. Although some subjects were affected by high blood lactate levels, low muscle glycogen levels, and low blood glucose levels, these metabolic variables did not correlate with fatigue. Serum norepinephrine, dopac, insulin and lactate were all increased in the fasted state. The increase in NE and the diameter of type I muscle fibers correlated positively and ending insulin levels correlated negatively with endurance time in the fasted state. Fatigue in endurance running for 27-hour fasted subjects, therefore, appears to be related to the combination of physiological, psychological, metabolic, and hormonal changes.

TABLE 1. Average subject characteristics.

Number	Sex	Age, years	Ht, cm	Wt, kg	% Fat	HR max, beats/min	VE max, l/min	BR max, breaths/min	VO2 max ml/kg.min	R max	% Type 1	D, type 1 m
9	M	41.2±2.0	181.9±1.8	79.4±1.7	14.1±1.8	181.0±2.0	159.7±8.2	55.4±2.2	59.2±2.7	1.16±.03	66.6±2.8	7.2±0.4

Values are means ± SE. HR, heart rate; VE, ventilation rate; BR, breath rate; VO2 max, maximum oxygen uptake; R, respiratory exchange ratio; type 1, type 1 muscle fibers; D, diameter.

TABLE 2. Effects of exercise on blood and muscle metabolite and hormone levels in fasted and non-fasted human runners.

VARIABLE	NON-FASTED			FASTED	
	PRE-EX	90 MINUTES	EXHAUSTION	PRE-EX	EXHAUSTION
GLYCOGEN, μmoles/g	114.1±21.5	84.8±22.1	42.1±9.0 [†]	98.7±21.6	70.4±14.4
GLUCOSE, mmoles/l	4.86±0.27	5.88±0.57 [†]	5.12±0.45	4.62±0.27	4.76±0.85
LACTATE, mmoles/l	1.56±0.19	1.66±0.30	2.60±0.44 [*]	1.83±0.23	4.14±0.58 ^{†‡}
FFA, mmoles/l	0.04±0.02	0.12±0.03 [*]	0.19±0.0 [†]	0.12±0.03 [‡]	0.23±0.04 [*]
TG, mg/dl	95.0±8.4	89.4±9.3	73.0±11.3	45.7±6.4 [§]	54.6±6.9
INSULIN, μU/ml	8.4±1.5		6.0±1.0	5.2±0.6	8.9±1.6 [‡]
GLUCAGON, pg/ml	286±45		374±40	371±62 [‡]	509±84 [*]
NE, pg/ml	544±86		1603±184 [†]	591±66	2160±282 ^{†‡}
DOPAC, ng/ml	3.9±0.7		12.2±1.8 [†]	6.5±1.5	27.4±6.7 ^{†‡}
EPI, pg/ml	178±42		313±34	250±72	417±138

Values are means ± SE. Pre-ex, pre-exercise; FFA, free fatty acid; NE, norepinephrine; DOPAC, 3,4-dihydroxyphenylacetic acid; EPI, epinephrine. * Significant difference from pre-exercise values, p<0.05. † Significant difference from pre-exercise, p<0.01. ‡ Significant difference between fasting and non-fasting diet groups, p<0.05. § Significant difference between fasting and non-fasting diet groups, p<0.01.

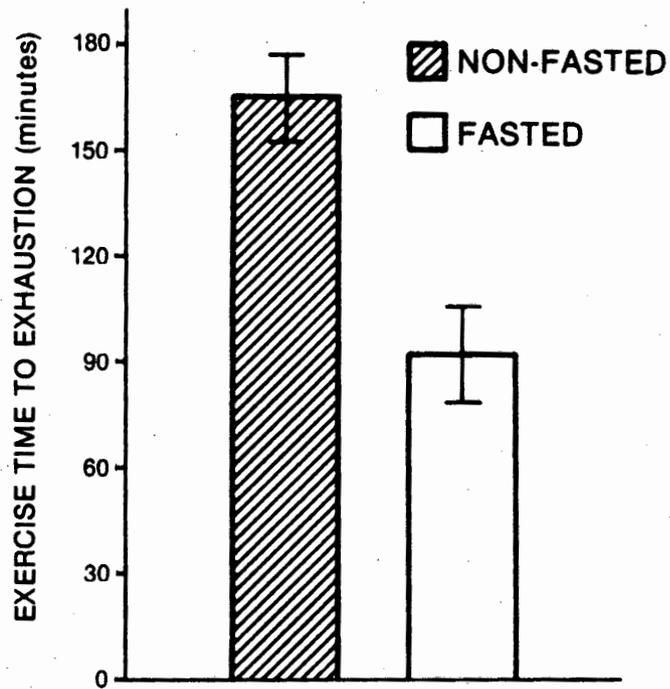


Figure 1. Mean changes in endurance time between the fasted and non-fasted tests, $p < 0.01$.

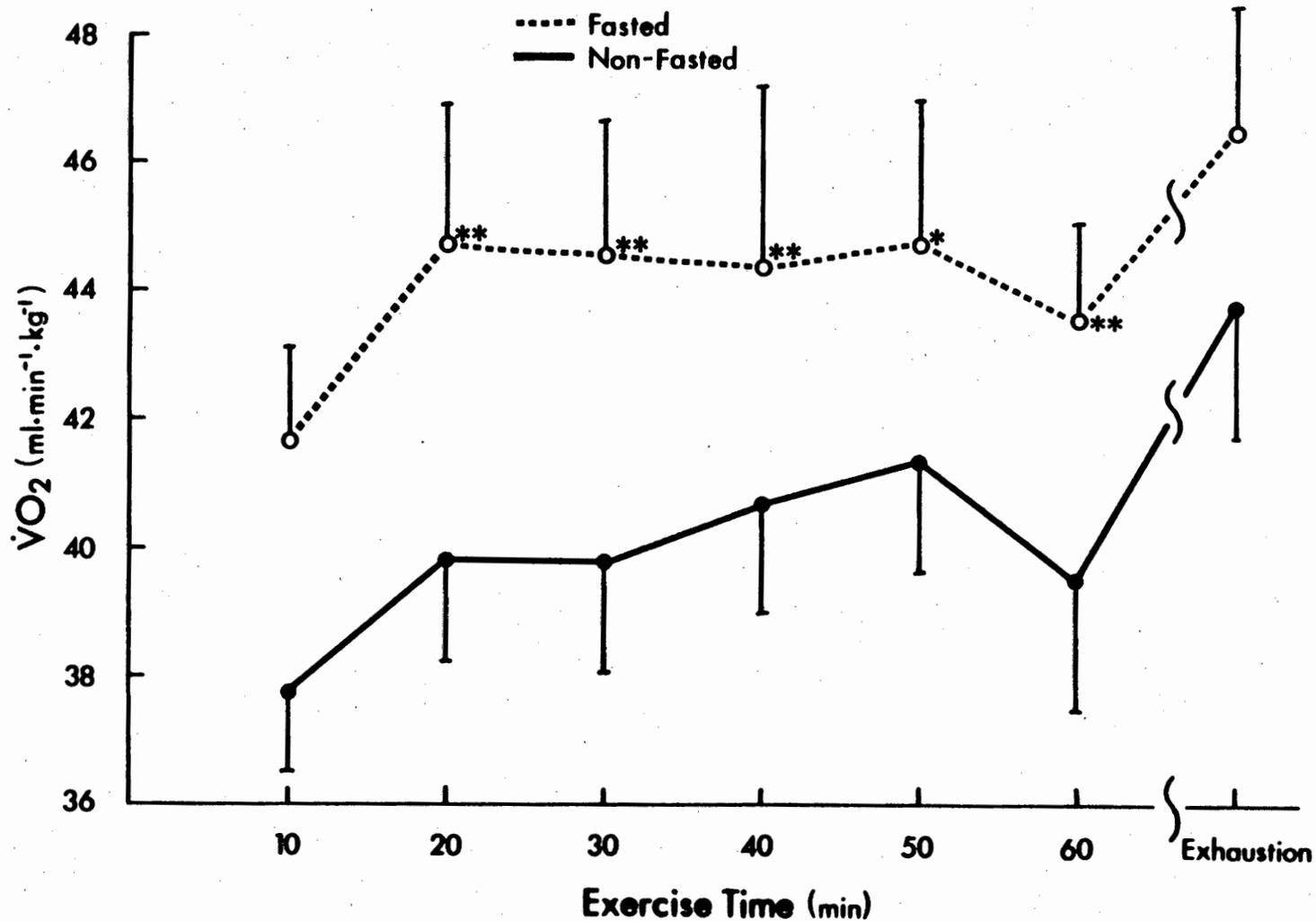


Figure 2a. Effect of a 27-hour fast on oxygen uptake ($\dot{V}O_2$).
 * Significant difference ($p < 0.05$) between fasted and non-fasted test. ** Significant difference ($p < 0.01$) between fasted and non-fasted test.

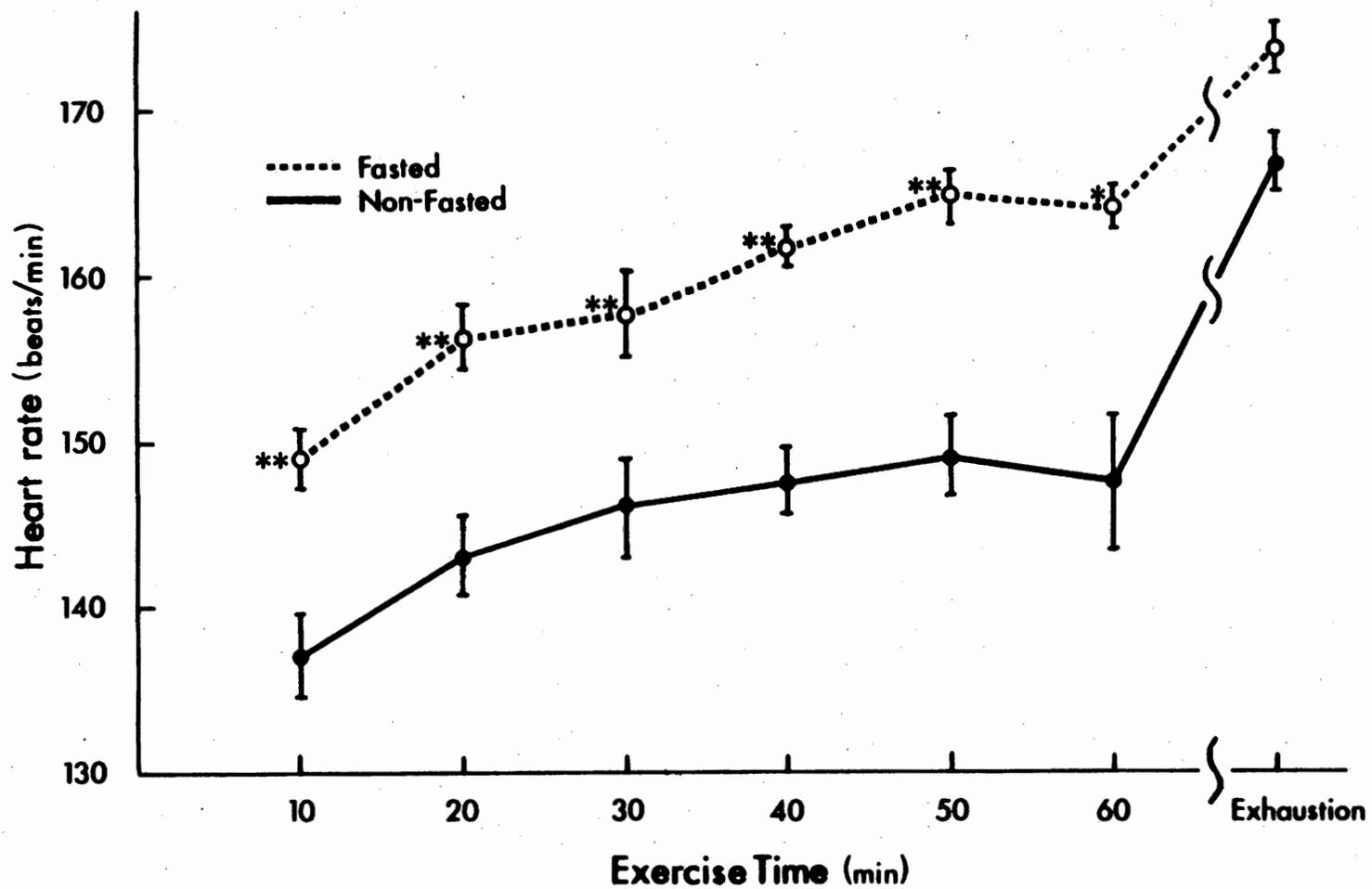


Figure 2b. Effect of a 27-hour fast on heart rate.
 * Significant difference ($p < 0.05$) between fasted and non-fasted test. ** Significant difference ($p < 0.01$) between fasted and non-fasted test.

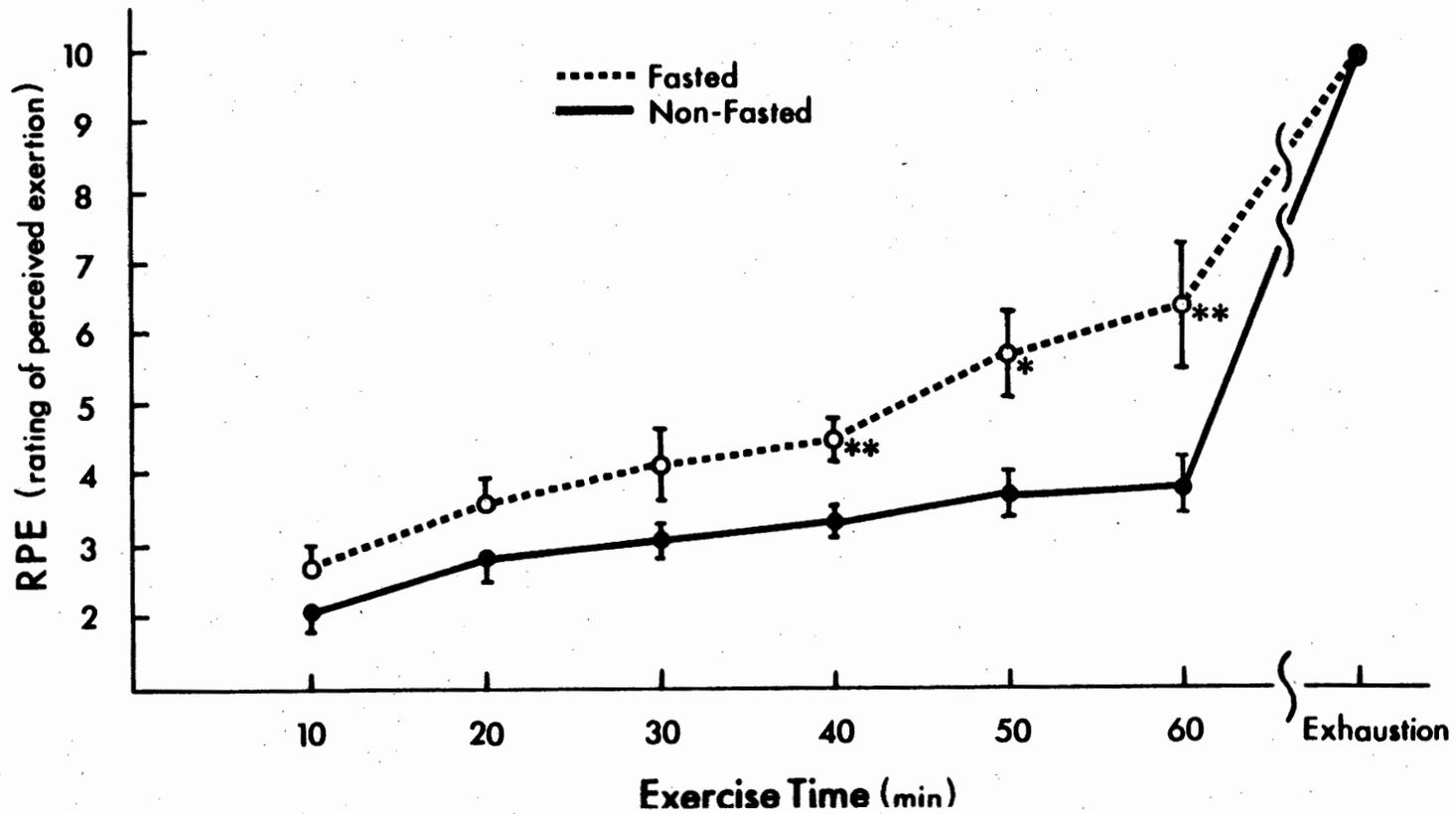


Figure 2c. Effect of a 27-hour fast on rate of perceived exertion (RPE). * Significant difference ($p < 0.05$) between fasted and non-fasted test. ** Significant difference ($p < 0.01$) between fasted and non-fasted test.

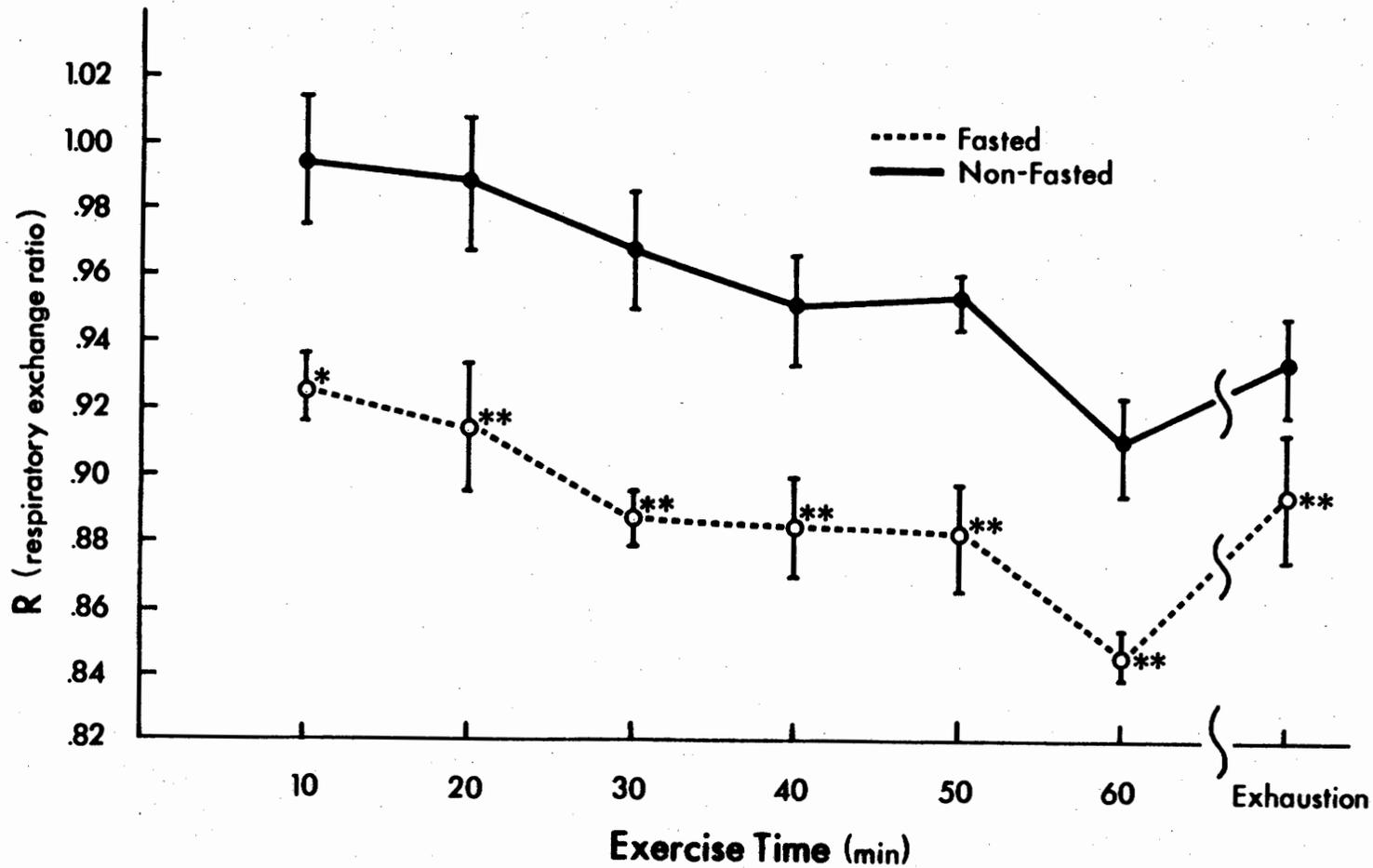


Figure 2d. Effect of a 27-hour fast on respiratory exchange ratio (R). * Significant difference ($p < 0.05$) between fasted and non-fasted test. ** Significant difference ($p < 0.01$) between fasted and non-fasted test.

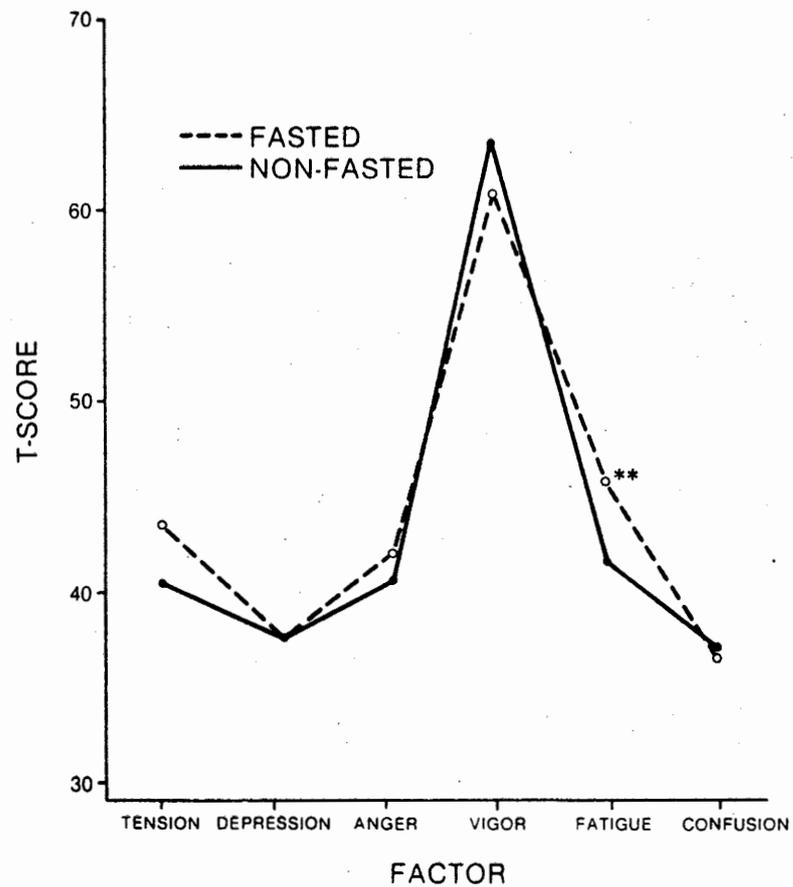


Figure 3. Effect of a 27-hour fast on Profile of Mood States (POMS) for fasted and non-fasted subjects. * Significant difference ($p < 0.05$) between fasted and non-fasted test.

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