collection and assessments. Strenuous physical exercise that was judged to be near maximal in intensity or longer than 60 min in duration was not allowed while participants were active in the EX and CON protocols, i.e., not on the day of or the day before research activities took place. To avoid the influence of ill-ness on inflammatory parameters, participants were only tested if they were free of known infection for at least 1 wk. The EX protocol consisted of baseline assessments at 7:00 a.m., followed by a bout of high-force eccentric resistance exer-cise using the elbow flexor muscles of the nonpreferred limb (according to self-reported handedness), and follow-up assessments 4, 8, 12, 24, 48, 96, and 120 h postexercise. Assessments included muscle soreness, blood collection for blood-borne variables, and maximal force production. During the EX condition, the nonexercised arm was measured as a CON for maximal force production. A time-matched CON condition identical with the experimental condition but with-out the high-force eccentric exercise was performed for blood-borne variables. The experimental and control protocols were separated by at least 3 and no more than 6 wk.

High-force eccentric exercise. The protocol for in-ducing muscle damage in the flexor muscles (primarily *m. biceps brachii and m. brachialis) of the nonpreferred* arm was performed using a computer-controlled, isokinetic dynamometer (Kin Com125 E+; Chattecx Corporation, Chattanooga, TN). The dynamometer was adjusted to the body height and limb length of the individual. The arm was supported by a padded bench at approximately 0.79 rad of shoulder abduction, the axis of rotation of the dynamometer was aligned with the axis of rotation of the elbow, and the forearm was secured to the lever arm of the dynamometer with padded support just proximal to the wrist joint. Three sets of 15 repetitions of eccentric elbow flexion were per-formed with maximal effort at a rate of one repetition per 15 s and 5 min of rest between sets. Repetitions began with the elbow fully flexed and ended with the elbow fully ex-tended. Using maximal effort, participants attempted to keep the elbow in the fully flexed position as the dynamometer pulled the arm to a fully extended position at an angular velocity of 0.79 radIsj1. The dynamometer returned the arm to the fully flexed position and paused for 10 s before beginning the next repetition. Participants were verbally encouraged to give a maximal effort with each repetition.

Maximal force production. Maximal isometric force production for elbow flexion at an enclosed elbow angle of 1.57 rad was measured before exercise, immediately after exercise (to identify the amount of fatigue induced by the exercise), and 24, 48, 96, and 120 h postexercise (to identify prolonged strength loss, which is an indicator of muscle damage [24]). To perform the isometric strength measurement, the dynamometer and subject position were adjusted as for the high-force eccentric exercise, and the lever arm was fixed such that the elbow was positioned with a 1.57 rad angle. Participants were instructed to pull (flex) for 3 s using maximal effort. Three maximal efforts were performed with 30-s rest between repetitions. To ensure uniformity of measurements from day to day, all dynamometer position settings for each subject were recorded and reproduced at each testing session To eliminate variation due to initial strength levels, data were converted to percentages of the initial strength measurement before analysis.

TABLE 1. Characteristics and resting serum or plasma concentrations of blood lipid and inflammation variables for normal and overweight BMI groups.

	Normal BMI Group	Overweight BMI Group	*P*-Value
Age (yr)	20.6 ± 3.9	19.9 ± 1.9	0.588
BMI ($kg \cdot m^{-2}$)	22.4 ± 1.3	27.1 ± 5.1*	<0.001
TGs ($mg \cdot dL^{-1}$)	94.9 ± 31.0	113.9 ± 46.0	0.196
Cholesterol ($mg \cdot dL^{-1}$)	154.6 ± 25.4	161.5 ± 25.0	0.493
sTNFR1 ($pg \cdot mL^{-1}$)	1210.1 ± 144.8	1244.2 ± 193.2	0.596
IL-6 ($pg \cdot mL^{-1}$)	1.310 ± 0.760	2.053 ± 1.568	0.185
sgp130 ($ng \cdot mL^{-1}$)	251.0 ± 38.3	268.9 ± 50.3	0.238
CRP ($mg \cdot L^{-1}$)	0.542 ± 0.593	1.395 ± 1.040*	0.020
IL-10 ($pg \cdot mL^{-1}$)	1.27 ± 0.78	1.21 ± 0.86	0.860
sICAM-1 ($ng \cdot mL^{-1}$)	202.3 ± 44.9	197.4 ± 29.3	0.760
Cortisol ($\mu g \cdot dL^{-1}$)	33.3 ± 8.2	31.9 ± 6.1	0.642
CK activity ($IU \cdot L^{-1}$)	155.1 ± 59.4	201.9 ± 114.7	0.263
CON/EX condition 1st	11/8	4/6	0.359

Values are presented as mean ± SD unless stated otherwise.
* $P < 0.05$ compared with normal weight BMI group.

Muscle soreness. A subjective assessment of muscle soreness was made by participants using a 100-mm visual analog scale anchored at one end with ''no soreness'' and at the other end with ''very, very sore.'' Participants were instructed to fully flex and extend the elbow while holding a 1-kg weight and gently squeezing the elbow flexor muscles and then to place a tick mark on the analog scale that rep-resented the degree of soreness. Participants also were instructed to think of their ratings in terms of muscle sore-ness, not of fatigue or relative to other types of pain, e.g., a broken bone.

Blood collection and analysis. Participants sat for 10–15 min before blood was collected from an antecubital vein into evacuated tubes using a standard venipuncture technique. Blood was collected in a vacuum tube without additive for analysis of CRP, cortisol, and CK, and containing ethylenediaminetetraacetic acid for IL-6 and sTNFR1. After clotting, serum was separated from cells using a refrigerated 21000R Marathon centrifuge (Fisher Scientific, Pittsburgh, PA). All samples were stored at j80-C until analysis. Fasting, basal, serum cholesterol, and triglyceride (TG) concentrations were measured in duplicate by standard laboratory techniques using an VitrosDT60 Ektachem analyzer (Eastman Kodak Co., Rochester, NY) and the procedures described by Lie et al.(19). Serum CRP (high sensitivity assay; MP Biomedicals, Irvine, CA), plasma IL-6 (high sensitivity assay; R&D Sys-tems, Minneapolis, MN), plasma sTNFR1 (R&D Systems), serum sICAM (R&D Systems), serum IL-10 (R&D Sys-tems), and serum cortisol (Diagnostic Systems Laboratories, Inc., Webster, TX) concentrations were measured using com-mercially available enzyme-linked immunosorbent assay kits according to the instructions of the manufacturers. Absor-bance of 96-well assay plates was read using a KQuant Uni-versal microplate spectrophotometer (Bio-Tek Instruments, Winooski, VT). All samples were run in duplicate. Average intraassay coefficients of variation for CRP, IL-6, sTNFR1, and cortisol were 11.0%, 7.6%, 3.8%, and 3.4%, respectively. On the basis of the anticipated time course for changes in these variables and the need to identify potential circadian variations throughout

of circadian rhythms) and obesity, diabetes mellitus, and hypertension incidence (6). It also has been demonstrated in animal models that inducing obesity with a high-fat diet disrupts circadian patterns for insulin resistance andmediators of inflammation including TNF-α and IL-6 (3). Thus, there is evidence not only that disruption of circadian patterns, for example, by altering sleep patterns, in-creases the likelihood of becoming obese or acquiring some diseases, but also that becoming obese disrupts circadian variation and influences development of some diseases. In humans, a flattening of the circadian variation in cortisol occurred in the highest (>31 $kg \cdot m^{-2}$) and lowest(<21 $kg \cdot m^{-2}$) BMI groups, a U-shaped association, and for men (n = 2915) and women (n = 1041) in the Whitehall II study (16). Other researchers found flattening of cortisol var-iation with increasing abdominal obesity in women but not in men (18). Our finding that circadian patterns in cortisol, sTNFR1, and IL-6 were similar for normal and overweight men may be an indication that men are not sensitive enough to body mass–related flattening of circadian patterns for this to be measured in nonobese, over-weight men. Alternatively, it may be that overweight men fall within the same region of the U-shaped association as normal weight men and do not have circadian disruptions. Regardless, we found no evidence that normal and over-weight men differed in circadian patterns for the endocrine and immune variables measured.

We conclude that the elements of the pro-inflammatory state characteristic of obesity that can be detected in over-weight men are an increase basal concentrations of CRP and a modest enhancement of the acute inflammation response. This enhancement was most evident for sTNFR1 than other mediators of inflammation. Whether the enhanced response is a result of a greater TNF-α response or the result of the sTNFR1-specific role in obesity and insulin resistance requires further investigation. Circadian patterns of cortisol and mediators of inflammation are unchanged in young, healthy, overweight men. This finding adds to the body of evidence suggesting that being overweight, not just obese, influences the risk of diseases associated with inflammation and can do so at a relatively early age. Furthermore, our findings suggest that body mass–associated increases in in-flammation include both basal levels of mediators of in-flammation and the magnitude of the acute inflammation response. It is possible that additional differences between groups are present but too small to detect with our experi-mental methods and samples size; thus, it may be most reasonable to conclude that the differences we measured are the most pronounced and additional differences were not of sufficient magnitude for reliable detection. Accordingly, the trends for circadian differences in sTNFR1 and greater IL-6 and CRP during acute inflammation may be emerging differences that will become more pronounced as BMI in-creases further. The primary limitations of this study are that cardiovascular fitness, chronic physical activity levels, and body composition were not measured. These variables in-fluence inflammation, and adjustment for their influence would allow for greater discrimination between BMI groups. Future research that includes these measurements to aid in interpretation of inflammation differences is recommended.

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