Aged men display blunted biorhythmic variation of muscle performance and physiological responses

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Aged men display blunted biorhythmic variation of muscle performance and physiological responses. J Appl Physiol 92: 2319–2325, 2002. First published February 1, 2002; 10.1152/japplphysiol.01116.2001.—Aging is known to disrupt the “biological clock” that governs physiological variables at rest. This study sought to determine whether aged men demonstrated biorhythmic variation in muscle performance during resistance exercise and physiological responses to that stimulus. Ten aged (75.6 ± 1.6 yr; mean ± SE) men completed an isokinetic testing protocol of knee extensors and flexors at 0800, 1200, 1600, and 2000 h. Although time of day variation in peak torque was detectable, significant (P < 0.05) oscillation was established only in the knee flexors at 3.14 rad/s. Heart rate, blood pressure, and rectal temperature displayed no significant variation, but trends (P < 0.10) in oscillation of postexercise blood pressure and rectal temperature were noted. Temporal patterns in biorhythmic variation of muscle performance, as well as thermal and cardiovascular measures, emulated those observed in a previous study involving young men where the magnitude of variation was sufficient to achieve statistical significance. Similar to our earlier findings in young men, however, pre- and postexercise testosterone and cortisol concentrations demonstrated significant variation among aged men. These data confirm the blunting of biorhythmic variation in muscle performance and physiological variables, except for circulating hormones, in aged men.

Biorhythmic variation refers to the predictable, and internally programmed fluctuation that occurs within all organisms during the day. Such variation when studied throughout the course of the 24-h solar day is termed a circadian rhythm. Under resting conditions, virtually all physiological variables, including heart rate (5, 10, 20, 29), blood pressure (21, 30), core temperature (27, 28, 41), and circulating hormones (1, 12, 14, 35), display unique circadian rhythms, peaking and ebbing at different times of the day.

Exercise-induced physiological responses have also been found to vary according to the time of day at which physical exertion occurs (26, 43). This is true even when the hours of investigation are restricted to those in which exercise is typically performed (7, 8). In a previous study involving college-age men, our laboratory established that muscle performance during isokinetic resistance exercise exhibited significant (P < 0.05) fluctuation between the hours of 0800–2000 (7). Similarly, pre- and/or postexercise values for physiological parameters, i.e., blood pressure, rectal temperature, plasma testosterone, and cortisol, varied significantly in that study as well as an earlier one examining responses to maximal aerobic exercise, also featuring young adult males (8).

The process of normal, biological aging has been the focus of much recent investigation. As part of this research effort, it has been found that aging disturbs the patterns of biorhythmic variation observed in juveniles and younger adults. This disturbance is apparent in the circadian rhythms of cardiovascular parameters (24), core temperature (23, 42), and circulating hormones (18, 34, 38). That is, statistically significant or stable, predictable changes in these variables during the day are no longer evident among the aged. In general, it can be said that there is a senescence-related tempering, or blunting, in the biorhythmicity of physiological parameters under resting, or basal, conditions. However, the effects of aging on the biorhythmic variation of maximal muscle capacity during resistance exercise, as well as the physiological responses to that stress, remain undefined. This issue is important in view of the fact that high-intensity resistance training is recommended as an effective preventative and palliative health measure among the aged (19). In the present study, we hypothesized that the biorhythmic variation of muscle performance and accompanying physiological responses previously noted in young men would be blunted in aged men.

METHODS

Subjects

Ten aged [75.6 ± 1.6 yr (mean ± SE), range = 66–81 yr] men that were absent of contradicting medical conditions, as determined by a physician, served as subjects. One subject, however, was taking a β-adrenergic blocker; cardiovascular

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data from this individual were excluded from analysis. All subjects were habitually active, but none were engaged in a formal exercise training program. Mean height of the 10 subjects was 179.0 ± 1.6 cm and weight was 86.0 ± 2.5 kg.

After receiving a verbal description of the study, its potential risks, and the experimental procedures to be employed, the participants provided written, informed consent. All experimental procedures were approved by the Committee for the Protection of Human Subjects at The College of William and Mary.

Experimental Design

Subjects were initially provided with two familiarization trials using the muscle dynamometer 1–2 wk before the onset of data collection. During the actual testing sessions, each subject completed a maximal-effort resistance exercise protocol of isokinetic knee extensions and flexions at 0800, 1200, 1600, and 2000 h in a randomized sequence. At least 48 h separated any two consecutive data collection sessions. Subjects were instructed to avoid exercise for a minimum of 12 h before testing and to consume only water for 4–12 h before test sessions. Each subject completed all testing within a 4-wk period, and normal sleeping and activity patterns were maintained throughout the experimental period.

At the first test session, subjects’ body mass, height, and age were recorded. On arriving at the laboratory for each test, subjects first inserted a rectal temperature probe ~150 mm beyond the external sphincter (32), and a heart rate monitor was secured around their chests. Subsequently, subjects sat quietly in a chair for 5–10 min; after this equilibration period, a blood sample (2–3 ml) was obtained from an antecubital vein, and other preexercise physiological data were recorded. Subjects then completed a 5-min warm-up on an electrically braked cycle ergometer (Excaliber, Lode, Groningen, The Netherlands) at 50 W.

Exercise Testing

The exercise protocol consisted of alternating concentric muscle actions of the knee extensors and flexors performed on an isokinetic dynamometer (model 900-350, Biodex, Shirley, NY) by using the right and then the left leg. A 5-min interval separated testing of the right and left legs. For each leg, five repetitions were executed at 0.52, 1.05, and 2.09 rad/s, with a final set of 30 repetitions at 3.14 rad/s. Within each leg, sets were dispersed by 3-min rest intervals. Because time of day was the main independent variable of interest, the sequence of movement velocities was held constant for each test session.

To control for confounding movements, the inactive leg was secured on a chair during testing, a subject’s contracting leg and torso were stabilized with Velcro straps, and arms were crossed in front of the chest. The back rest was maintained in a position resulting in hip flexion of 80°, and the knee joint was aligned with the axis of the dynamometer. The weight of the tested limb was assessed by the dynamometer so that performance variables could be corrected for that resistance. At each subject’s first test session, the subject selected a range of motion that was adhered to for each subsequent test session. Verbal encouragement was provided throughout each exercise protocol. Immediately (<15 s) after completion of the exercise regimen, physiological variables were quantified, and a second blood sample was drawn.

Quantitation

Heart rates were measured with a portable telemetry unit (Polar Electro, Woodbury, NY). Rectal temperature was monitored with a thermistor connected to a digital thermometer (model 400, VWR Scientific, Bridgeport, NJ). Blood pressure was assessed via a sphygmomanometer (Welch Allyn Tycos, Tycos Instruments, Arden, NC) and a stethoscope (Littmann Select, 3M Health Care, St. Paul, MN). Mean arterial blood pressure was calculated as the diastolic pressure plus 33% of the difference between the systolic and diastolic pressures. This value represents the average pressure driving blood into the tissue over the entire cardiac cycle (39).

Blood samples were collected into heparin-treated tubes (Vacutainer, Becton Dickinson, Franklin Lakes, NJ). Aliquots of whole blood were used immediately for hemoglobin and hematocrit analyses. Hematocrit was assayed in triplicate by using microcapillary tubes after centrifugation at 4,000 g for 5 min, whereas hemoglobin values were determined with the cyanmethemoglobin method. Exercise-induced changes in plasma volume were calculated from hematocrit and hemoglobin values according to Dill and Costill (9). The remaining whole blood was then centrifuged at 3,000 g for 15 min at 4°C. The resultant plasma fraction was stored at −75°C until hormone analyses were conducted.

Plasma testosterone and cortisol levels were assessed with enzyme immunoassays (Diagnostic Systems Laboratories, Webster, TX) in conjunction with an automated microplate reader (MultiSkan RC, Labsystems, Helsinki, Finland). For each hormone, all samples were measured on a single microplate well plate to avoid interassay variation. Selected samples were run in duplicate; intra-assay variation for each hormone was <10%. Assay sensitivities for testosterone and cortisol were 0.04 ng/ml and 0.1 μg/dl, respectively.

Muscle performance variables, i.e., peak torque, total work, and fatigability, were determined by the Biodex Advantage software accompanying the dynamometer. Fatigability was calculated as the difference in work performed between the first and last 10 repetitions of the 30-repetition set completed at 3.14 rad/s.

Statistical Analysis

All data are reported as means ± SE. Repeated-measures analyses of variance (ANOVA) were used to evaluate biorythmicity in muscle performance variables, as well as pre- and postexercise muscle physiological parameters, across the four time points (0800, 1200, 1600, and 2000). When ANOVAs revealed significant F ratios, appropriate post hoc analyses were used to identify pairwise differences. In addition, dependent t-tests (pre- to postexercise) were conducted to determine the effects of maximal exertion on physiological variables. In all cases, statistical significance was established at P ≤ 0.05.

RESULTS

Muscle Function

Statistical analysis indicated that, in general, our aged subjects failed to demonstrate significant variation in muscle performance across the four time points examined. This was true of both legs, during both knee extensions and flexions, for each performance variable quantified (peak torque, total work, fatigability) and for each velocity of movement tested. The lone exception was knee flexions of the right leg at the fastest movement velocity, i.e., 3.14 rad/s. In that case, peak torque was significantly less at 0800 than at all other times investigated, and greater at 2000 than at any other time point. Yet this was the lone statistically...
significant result among a total of 36 muscle-performance variables analyzed for biorhythmic variability (data not shown).

**Physiological Parameters**

**Cardiovascular variables.** Neither pre- nor postexercise heart rates fluctuated significantly over the segment of the day studied. As a result, heart rate response (% change pre- to postexercise) to resistance exercise also remained stable between 0800 and 2000. As expected, however, heart rates were significantly elevated by maximal muscle exertion at each of the time points of interest. Heart rate results are presented in Fig. 1.

Similar to heart rate, there was no significant variation in preexercise mean arterial pressure values or in the response of blood pressure to the exercise stimulus. However, there was a trend \((P = 0.10)\) for oscillation in mean arterial pressure after resistance exercise. Specifically, postexercise blood pressure demonstrated its lowest values at 0800 and peaked at 2000. Maximal muscle efforts resulted in significant increments in blood pressure regardless of the time of day at which they were conducted. Data on mean arterial pressure are shown in Fig. 2.

**Temperature.** Although preexercise rectal temperature progressively increased throughout the time frame studied, no significant variation was observed. And although the responsiveness of rectal temperature also failed to exhibit notable oscillation, postexercise temperature demonstrated variability that approached statistical significance \((P = 0.06)\), being lowest at 0800 and greatest at 2000. These findings are illustrated in Fig. 3.

**Circulating hormones.** No significant biorhythmic effects on plasma volume shifts were identified. Consequently, hormone values were not corrected for plasma volume changes, which averaged only \(\sim 2\%\). Our data revealed significant time of day variation in plasma total testosterone values both before and after the muscle performance protocol. That is, pre- and postex-
Table 1. Plasma testosterone and cortisol concentrations before and immediately after resistance exercise

<table>
<thead>
<tr>
<th></th>
<th>0800 h</th>
<th>1200 h</th>
<th>1600 h</th>
<th>2000 h</th>
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<tr>
<td><strong>Concentration, nmol/l</strong></td>
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<tr>
<td><strong>Testosterone</strong></td>
<td></td>
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<tr>
<td>Preexercise</td>
<td>8.9 ± 1.1a</td>
<td>7.8 ± 0.5a</td>
<td>6.5 ± 0.2</td>
<td>5.9 ± 0.2</td>
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<tr>
<td>Postexercise</td>
<td>8.8 ± 0.9b</td>
<td>8.1 ± 0.6b</td>
<td>6.7 ± 0.6</td>
<td>6.7 ± 0.6c</td>
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<tr>
<td><strong>Cortisol</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Preexercise</td>
<td>546.5 ± 65.6d</td>
<td>318.0 ± 38.7d</td>
<td>255.9 ± 37.3d</td>
<td>139.4 ± 15.4d</td>
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<tr>
<td>Postexercise</td>
<td>507.8 ± 72.0d</td>
<td>257.5 ± 23.6d</td>
<td>254.2 ± 49.6d</td>
<td>154.8 ± 16.8d *</td>
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Coefficients of variation

|               |        |        |        |        |
| Testosterone   | 38.4 | 17.4 | 33.3 | 29.4 |
| Postexercise   | 32.0 | 21.7 | 26.3 | 31.5 |
| Cortisol       | 38.3 | 39.1 | 46.2 | 36.0 |
| Postexercise   | 45.1 | 29.0 | 61.9 | 33.9 |

Values are means ± SE, n = 10. a Significance difference (P ≤ 0.05) from preexercise testosterone values at 1600 and 2000. b Significant difference (P ≤ 0.05) from postexercise testosterone values at 1600 and 2000. c Significant difference (P ≤ 0.05) from preexercise cortisol value at same time point. d Significant difference (P ≤ 0.05) from preexercise cortisol values at all other time points. * Significant difference (P ≤ 0.05) from postexercise cortisol values at all other time points.

Exercise testosterone concentrations were highest in the morning (0800) and lowest in the evening (2000). It was also determined that significant exercise-induced elevations in testosterone occurred only at 2000, which was consistent with our ANOVA results, which indicated that the responsiveness of testosterone to exercise was significantly higher at that same time point.

Plasma cortisol demonstrated a significant biorhythmicity that paralleled that of testosterone. Again, concentrations were greatest in the morning and lowest at 2000. This was evident in blood samples taken both before and after the muscle-testing protocol. But unlike testosterone, exercise failed to elicit significant increases in cortisol at any interval of time examined. Data regarding plasma testosterone and cortisol concentrations are presented in Table 1.

Plasma testosterone-to-cortisol ratios, both pre- and postexercise, were also calculated and compared across the four time points studied. Significant variation was exhibited in this putative indicator of anabolic endocrine status (11, 15). Both before and after exercise, plasma testosterone-to-cortisol ratios ebbed at 0800 and peaked at 2000 (Fig. 4). At no time point did exercise significantly alter this ratio. Accordingly, the responsiveness of the testosterone-to-cortisol ratio failed to display significant biorhythmic variation.

DISCUSSION

A circadian rhythm is the natural, predictable variation that occurs within a biological system over the course of the 24-h solar day. This biorhythmicity occurs in all living entities and within virtually every physiological component within an organism. However, within a single organism each system displays its own unique rhythm or timing pattern where low points and high points are observed. The temporal pattern, synchronicity, and severity of these rhythms are governed by a biological clock located in the suprachiasmatic nucleus region of the brain’s hypothalamus (33, 44).

Several studies have determined that exercise performance and physiological responses to exercise also demonstrate significant time of day oscillation. This is true whether exercise tests were conducted at regular intervals throughout the 24-h day [a true circadian rhythm (20, 29, 30)] or were restricted to the segment of the day when exercise is typically performed, i.e.,...
0800–2000, more appropriately described as biorhythmic variation (7, 8).

It has been established that aging disrupts the biorhythm of most, if not all, physiological variables measured under resting, or basal, conditions. This is true of circulating hormones, heart rate, blood pressure, and core temperature (36, 40). The disruption of the normal variation of temperature is of particular concern because it appears that the fluctuation of many other variables is predicated on that of core temperature (17, 27, 28). Thus an age-related disturbance in the normal biorhythmic variation of core temperature may result in anomalous rhythms of other physiological parameters.

Although the effects of aging on the circadian rhythms of physiological variables have been well studied under resting conditions, the impact of senescence on the biorhythm of physiological responses to exercise has yet to be identified. Indeed, the question of whether exercise performance itself varies throughout the day in the aged has yet to be answered. This is disconcerting in view of the fact that various health agencies such as the Centers for Disease Control and Prevention (25), the National Institutes of Health (37), and the American College of Sports Medicine (19) recommend regular exercise, including weight training, among the aged. Consequently, we sought to determine whether the biorhythmic variation in muscle function and physiological responses to resistance exercise previously observed in young adult men remained evident in aged men.

In general, the data reported here demonstrate that muscle performance, whether measured as peak torque, total work executed, or fatigability, does not significantly vary between the hours of 0800 and 2000. However, in one case (peak torque of the right hamstring muscle group at 3.14 rad/s), significant time of day fluctuation was noted. Additionally, two other performance measures (total work completed by the right quadriceps at 2.09 and 3.14 rad/s) displayed biorhythmic variation that approached statistical significance (0.10 > P > 0.05). In all three of these cases, muscle performance was lowest at 0800 and peaked in the early evening hours. Indeed, out of a total of 36 muscle function tests quantified in our aged subjects, performance was least impressive at 0800 in 26 instances.

This temporal pattern of muscle performance is similar to that observed in our previous study utilizing an essentially identical testing protocol (7). Among college-age men, it had been determined that muscle function waned in the morning and gradually improved until reaching a peak in the early evening hours. But in contrast to our aged subjects, this variation in young men regularly achieved statistical significance, particularly at the fastest movement velocity employed, i.e., 3.14 rad/s. Our studies investigating young and aged men employed the same number of subjects, 10, and variability, as measured by standard error, was actually less in our aged subjects than in our young participants. Accordingly, the lack of significant biorhythmicity demonstrated among our older subjects must be accounted for by physiological and not statistical factors.

Our findings on muscle performance support recent evidence regarding the effects of aging on biorhythmic variation. Earlier research indicated that aging disrupted the timing, or synchronicity, of the brain’s biological clock, resulting in unpredictable variation and decreased stability of circadian rhythms (3, 13, 36, 40). However, a recent elegant and tightly controlled study (6) demonstrated that the synchronicity of the biological clock remains intact among the aged. Rather, aging was found to simply moderate the degree of the oscillation of any particular variable throughout the day. Simply stated, in an aged system, the peaks and nadirs occur at the same times as they do in a younger system, but these highs and lows are not as pronounced as those observed among the young. Indeed, biorhythmic variation in muscle function was noted among our aged subjects, particularly at the faster velocities of contraction, but it was not sufficiently distinct to achieve statistical significance.

Rectal temperature was measured because it accurately reflects core temperature, which in turn impacts muscle performance (32). Moreover, temperature is considered to act as a secondary pacemaker for the periodicity of numerous other physiological variables (27, 28). Across the time points studied here, preexercise temperature did not significantly fluctuate. However, the variation observed in postexercise rectal temperature nearly achieved statistical significance (P = 0.06) and was found to gradually increase from 0800 to 2000.

Among young men, our laboratory previously documented significant time of day oscillation in temperature between 0800 and 2000 (7, 8). Both before and after exercise, temperature recorded its lowest value in the morning and gradually increased throughout the day. In one of those studies (7), a strong (r = 0.88) correlation between rectal temperature and peak torque at 3.14 rad/s was detected. It was postulated that temperature predominantly affected muscle strength at faster rates of contraction because evidence suggests that the activation (firing rate and/or recruitment) of fast-twitch motor units is preferentially enhanced at higher temperatures (2, 16, 31). Thus the significant variation in rectal temperature detected among young men might have accounted for the significant oscillation in strength ascertained only at the faster movement velocities (3.14 and 2.09 rad/s) included in the testing protocol. The blunted variability in rectal temperature exhibited by our aged subjects may help explain their equally diminished fluctuation in muscle strength, even at the fastest velocity of movement quantified. Yet the correlation between peak torque at 3.14 rad/s and rectal temperature across the time intervals examined remained fairly robust (r = 0.79) among our senescent men. This suggests that the influence of temperature on muscle function at rapid rates of contraction is well maintained among the aged.

Heart rate and blood pressure were quantified to ascertain whether the stress imparted by resistance
training to the cardiovascular system is more acute at any particular time point between 0800 and 2000. This information is especially important for the aged because, compared with young adults, they may be at greater risk for cardiovascular disease and/or injury. Neither pre- nor postexercise heart rate demonstrated significant time of day variation. The responsiveness of heart rate to exercise also failed to differentiate across the segment of the day studied. Although earlier works had indicated that both pre- and postexercise heart rates display true circadian (24-h day) rhythmicity (4, 20, 29), it was due to very low values documented in the extreme early morning hours of 0200–0600, which were not included in our investigation.

The data reported here indicate that, like our young men studied earlier (7, 8), the resting blood pressure of aged men did not oscillate between the hours of 0800 and 2000. However, the present results also reveal that postexercise blood pressure among older subjects exhibited a trend ($P = 0.10$) toward significant chronobiological variation and that the temporal pattern emulates that of young men, which we had found to be significant (7, 8). As in college-age men, mean arterial pressure after resistance exercise in the aged recorded its lowest value at 0800 h. It appears, then, that our thermal and cardiovascular data are also consistent with the recent report confirming that the synchronicity of the aged biological clock is maintained but that the degree of the oscillation is tempered by aging (6). Again, the modulation of biorhythmic fluctuation in postexercise blood pressure among the aged is best explained by physiological mechanisms and is not the result of statistical artifact because standard errors were less among our aged than our young subjects.

Testosterone and cortisol were measured to provide insight into the time of day at which endocrine status may be most favorable for anabolic responses to resistance exercise to occur. Indeed, the ratio of circulating testosterone to cortisol concentrations has been suggested to be representative of the overall anabolic endocrine milieu in men (11, 15). In the present study, plasma testosterone and cortisol displayed sharp and significant ($0.006 > P > 0.0001$) variation among the time intervals of interest. This variation was manifested both before and after resistance exercise. The magnitude and temporal pattern of variation in these anabolic (testosterone) and catabolic (cortisol) hormones were similar to those that we previously reported for young men (7). This contradicts most of this investigation’s results where aged men exhibited temporal patterns of biorhythmicity analogous to those of younger men but where the degree of variation was inadequate to achieve significance.

The difference in the severity of chronobiological variation among the different systems within our aged subjects supports the conclusions of a recently published report. Monk and Kupfer (22) have provided evidence that one of the causes of age-related disturbances in circadian rhythms is the failure of target organs “downstream” from the brain to respond properly to cues provided by the suprachiasmatic nucleus. In fact, because different organs age at their own unique rates, some systems continue to display intact biorhythmicity whereas other systems show a blunted response to time of day signals provided by the brain’s biological clock. Our findings suggest that the neuroendocrine system, at least during the segment of the day studied, remained more sensitive to signals generated by the suprachiasmatic nucleus than the other systems monitored.

In summary, the data generated by this investigation confirmed our initial hypothesis. We have determined that, among aged men, muscle function and selected physiological variables display muted biorhythmic variation that in temporal pattern, but not in magnitude, emulates biorhythmic variation noted in young men. From a mechanistic standpoint, our findings suggest that modifications in target tissue rather than in the biological clock itself are primarily responsible for this attenuation of biorhythmicity, at least during the segment of the day studied. From an applied standpoint, the data reported here indicate that older men may perform resistance exercise at any time of day between the hours of 0800 and 2000, with expectations of roughly equivalent performance and stress imparted to the cardiovascular and thermoregulatory systems. Hormonal data, however, reveal that a more favorable anabolic environment exists in the early evening hours and that testosterone levels are most responsive to resistance exercise during those same hours.

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