Relations between muscle soreness and biochemical and functional outcomes of eccentric exercise

J. B. RODENBURG, P. R. BÄR, AND R. W. DE BOER
Department of Medical Physiology and Sports Medicine and Department of Neurology, Janus Jongbloed Research Centre, Utrecht University, 3521 GG Utrecht, The Netherlands

RODENBURG, J. B., P. R. BÄR, AND R. W. DE BOER. *Relations between muscle soreness and biochemical and functional outcomes of eccentric exercise.* J. Appl. Physiol. 74(6): 2976–2983, 1993.—Correlations between functional and biochemical outcomes of eccentric exercise and between these outcomes and "delayed-onset muscle soreness" (DOMS) were studied. Maximal isotonic force, extension and flexion angle of the elbow, creatine kinase activity, and myoglobin concentration in serum were measured in 27 male subjects during 5 days after 120 maximal eccentric contractions of the forearm flexors. Significant correlations were found between values at 1 to 96 h after exercise for force (r = 0.55 to 0.96), flexion (0.52 to 0.94), extension (0.41 to 0.95), and myoglobin (0.55 to 0.97) and at 24 to 96 h for creatine kinase (0.67 to 0.96) and DOMS (0.45 to 0.72). Clusters of significant correlations (0.32 to 0.91) were found among all functional and biochemical measures. DOMS, however, showed only few and lower correlations with the other parameters (0.34 to 0.63). These results can practically be interpreted as follows: *1*) subjects need more time to recover completely when early deviations after eccentric exercise are large, *2*) a large change in one measure is accompanied by large deviations in other measures, and *3*) objective outcomes of eccentric exercise are more accurate parameters than a DOMS score for use in effect studies.

functional changes; myoglobin; creatine kinase; muscle damage; correlations

MANY STUDIES IN APPLIED PHYSIOLOGY have been dedicated to a search for the cause of "delayed-onset muscle soreness" (DOMS) in humans, a phenomenon that commonly occurs after strenuous exercise. For that purpose, several changes of the muscle have been described that concur with DOMS after eccentric work (1, 3, 9, 15).

Some studies focused on morphological muscle damage, which includes disturbances of the cross-striated band pattern and disruption of Z lines (10, 11, 18). Other studies focused on a wider collection of biochemical and functional outcomes of eccentric exercise, which are probably related to morphological damage. The use of biochemical and functional measures is quite generally accepted and indeed often the only possible noninvasive way of studying the effects of eccentric exercise. Thus the release of creatine kinase (CK) (4–6, 9, 23) and myoglobin (Mb) (4, 8) is often determined after exercise. CK release and Mb release are qualitatively different: whereas CK leakage develops slowly and reaches its maximum 3–4 days after exercise (17), Mb shows a small increase immediately after exercise (4, 8) and a large peak 3–4 days after eccentric exercise (19). Functional properties that can be measured are maximal force (7, 16, 21) and flexion and extension angle of the joint spanned by the damaged muscle (7). Force decreases and flexion angle increases immediately after eccentric exercise, whereas extension is maximally changed at 48 h.

In the studies mentioned above, the main investigation was to determine whether morphological or biochemical outcomes of eccentric exercise followed the same time course as DOMS, because a similar time course would be a first indication that a particular outcome might cause DOMS or be closely related to its cause. However, no such similarity has yet been found. This may be understood when we realize that DOMS is produced by a combination of several factors, all with different time patterns resulting in one unique time pattern for DOMS.

Before the interaction between soreness and the different outcomes relevant in the study of muscle damage can be understood completely, insight must first be gained into the relationships between the different morphological, biochemical, and functional outcomes. Until now it has been unknown whether large changes in one measure concur with large changes in other measures. Therefore the question posed in this study is whether it is sufficient to determine the changes in only one measure at only one point in time to predict the other changes occurring after eccentric exercise. This question has been divided into three parts. *1*) Do the values at different points in time correlate with each other for each measure separately? *2*) Do changes in different measures correlate with each other? *3*) Does DOMS after eccentric exercise correlate with biochemical and functional measures? Hence the focus of this study is not on the time courses of individual measures but rather on the relationships between different measures and the analysis of correlations at all points in time.

To establish these relationships, a standard eccentric exercise of the forearm flexors was used to induce muscle damage (7). Functional and biochemical outcomes of the eccentric exercise were assessed with the following measures: *1*) maximal isotonic force (force), *2*) flexion angle of the elbow (7), *3*) extension angle of the elbow (7), *4*) CK activity in blood (7), and *5*) concentration of Mb in blood (8, 14).

METHODS

Subjects

Twenty-seven male subjects (age 25 ± 5 yr, weight 73.4 ± 6.6 kg, height 1.84 ± 0.06 m) participated after

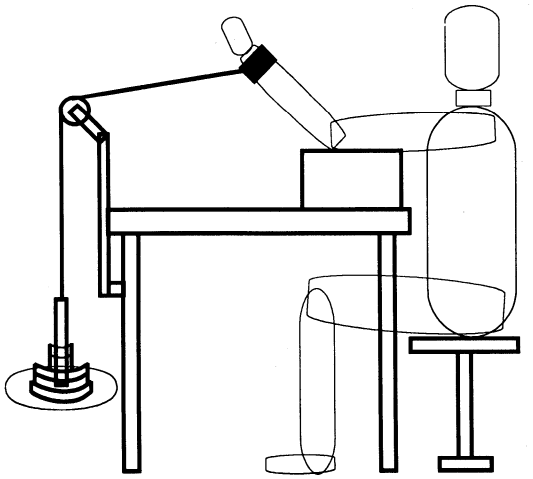

FIG. 1. Overview of experimental setup. Subjects extended their forearm in 3 s, counteracting a weight, to induce muscle damage and delayed-onset muscle soreness. Exercise time was 30 min, with 12 s of rest after each contraction.

giving informed consent. They did not perform more exercise than they were used to during the week before the tests. They had not before participated in studies involving eccentric exercise and had not been involved in sports activities requiring much arm power for the last 3 yr. The study had the approval of the Medical Ethical Committee of the University Hospital in Utrecht, The Netherlands.

Exercise

Subjects performed eccentric exercise with the left arm. The exercise protocol was similar to the one used by others (7). Briefly, the subject sat on a chair with the chest against a support. The upper arm was placed on a horizontal support at shoulder level and pointed forward in the sagittal plane. The hand was kept in a supinated position. To impose an extending momentum on the arm, a rope with a weight was attached to the wrist via a pulley system (Fig. 1).

The exercise consisted of 120 forced extensions of the forearm around the elbow joint from 45° flexion to 170° extension. The subject had to counteract the extending momentum, thus performing only lengthening contractions of the biceps brachii and brachialis muscles. Total exercise time was 30 min (4 contractions/min). At the beginning of the exercise the load equaled the subject's maximal isotonic force, but every time the subject could no longer lower a given load gradually in 3 s, the load was reduced, so that after 30 min ~30% of the initial load remained.

DOMS and Biochemical and Functional Measures

One hour before this exercise and at five time points afterward (1, 24, 48, 72, and 96 h), DOMS and the other outcomes of eccentric exercise were assessed.

DOMS. DOMS was scored on a scale ranging from 0 to 6. Each number corresponded to a verbal description of soreness (no soreness, dull feeling of soreness, light continuous soreness, more than light soreness, annoying soreness, severe soreness, and intolerable soreness). Subjects were allowed to score in half points. One score was made while the subject pressed his forearm flexors and one while he stretched the arm; both scores were summed to obtain a single score between 0 and 12 for soreness.

Force. Force was measured on the same apparatus as that used for the exercise protocol. While a load was on the tray, the subject was asked to keep the elbow flexed at 90° in a supinated position. In this position the subject had to resist the tendency for the load to stretch the muscle continually, thus performing an isotonic strength test. The maximal isotonic force was defined as the maximum weight the subject could resist for 5 s in this fixed position. To reach this maximum weight a low weight was put on the tray; when the subject could hold it, some additional weights were added. These were small (±0.80 kg) or large (±2.0 kg) depending on the ease with which the preceding trial was performed. This way of increasing the weight provided the subject a means of warm-up and adjustment to the apparatus. The subjects were allowed to rest for 2 min between the trials to avoid development of fatigue.

Flexion and extension angle. Flexion and extension angle of the elbow joint were measured with a goniometer with the subject standing. For measuring the flexion angle, each subject was asked to reach with his thumb to his shoulder as far as possible. He was asked to place the elbow along the body and to stretch his fingers. For measurement of the extension angle, the subject stood with the arm relaxed at his side. To measure elbow angles each day in the same way, the acromion, the epicondylus lateralis of the humerus, and the point halfway between the processi styloidei of the ulna and the radius were marked with semipermanent ink.

CK activity and Mb concentration. Blood was collected from an antecubital vein in a heparinized plasma separation tube to measure CK (n = 24) and in a tube without additive to measure Mb. Initially, Mb was measured only until 24 h after exercise inasmuch as only increases in Mb immediately after exercise had been known to occur (4, 8). However, after the experiments were finished, Nosaka et al. (19) published results showing that Mb also shows a large peak 3–4 days after exercise. Therefore, later on Mb was also analyzed at 48–96 h after exercise. Not enough serum was left at these time points to analyze Mb for all subjects. Depending on the time point, 20–26 values for Mb were included in the analysis. Serum or plasma was separated and stored at −20°C until analysis. CK activity in plasma was assessed by means of photospectrometry (*N*-acetyl-L-cysteine-activated kit, Boehringer Mannheim) (22). Mb concentration was assessed in serum by use of radioimmunoassay (Ria-mat, Byk-Sangtec Diagnostica).

Data Analysis

Changes in baseline levels were tested with a repeated-measures analysis of variance. The distributions of extension angle and CK were adjusted to approximate normality by means of a polynomal and logarithmic function, respectively. Only changes in DOMS (ordinal level) were assessed by means of a Friedman repeated-measures test.

Regression analysis was performed in three ways. First, for each measure separately, correlation coefficients were calculated between values at different points in time (within-measure correlations). Second, correlation coefficients were calculated for each possible pair of measures, resulting in a 6×6 correlation matrix per pair describing the interrelationship between these two measures at each point in time (between-measure correlations). Third, correlation matrices for DOMS with the biochemical and functional measures were calculated (soreness-measure correlations).

Spearman's r was used as a correlation coefficient for those matrices in which DOMS (ordinal level) or CK efflux (nonnormal distribution) was involved, because use of Pearson's r presupposes measurements at the interval level and a normal probability distribution. For calculations of the other matrices, Pearson's r was used. Because the range of values for Mb, force, and the elbow angles before exercise was large, these measures were normalized on their starting values before correlation coefficients were calculated.

The correlation coefficients were not always calculated for the same number of subjects because of missing values (especially for those concerning Mb). Therefore some coefficients were significant in some situations but not in others.

RESULTS

Significant changes from baseline were found for both DOMS and the biochemical and functional measures as a function of time ($P < 0.001$, Fig. 2). Force and flexion angle showed their largest change 1 h after exercise and recovered thereafter, whereas extension continued to decrease until 48 h and remained low. Mb showed an initial increase 1 h after exercise, like force and flexion, but showed even larger increases after 24 h. CK started to rise only after 24 h.

Within-Measure Correlations

Mb, force, flexion angle, and extension angle showed significant correlations for all cells in the within-measure correlation matrices (Fig. 3): the r values ranged from 0.55 to 0.96 for force, from 0.52 to 0.94 for flexed angle, from 0.41 to 0.95 for relaxed angle, and from 0.55 to 0.97 for Mb ($P < 0.01$). These correlations mean that subjects who showed a large change from resting level 1 h after exercise relative to other subjects also remained far from baseline levels for these measures in the subsequent days. This relation holds for all days after exercise. The CK matrix shows a different pattern: the CK values before exercise and 1 h afterward correlated with each other ($r = 0.96$), and the CK values at 24, 48, 72, and 96 h afterward correlated significantly ($0.67 < r < 0.96$, $P < 0.01$). The lack of significant correlation between the early (before and 1 h after exercise) and the later values (24–96 h) shows that the increase in CK due to muscle damage cannot be influenced by the resting CK efflux. The DOMS matrix shows a pattern similar to the CK matrix: there are no correlations for the values 1 h after exercise with later time points; only values at 24, 48, 72, 96 h significantly correlated with each other ($r = 0.45$–0.72) except for the two measurements at 24 and 96 h, which reached an r of only 0.24 (Fig. 3).

Between-Measure Correlations

For matrices including force, significant correlations were found over a whole cluster in the matrix, showing that the decrease in force after exercise was related to changes in all other biochemical and functional measures (Fig. 4). The r values for force with other measures reached the following levels: with CK, $r = -0.41$ to -0.91; with flexion, $r = -0.38$ to -0.78; with extension, $r = 0.32$–0.73; with Mb, $r = -0.40$ to -0.80. For flexion and extension angle, a more disordered pattern was found. One hour after exercise, when the flexion values were maximally increased, they did not show any correlation with CK values at 48–96 h, the points at which CK was maximally increased. In the CK-flexion matrix, significant r values ranged from 0.35 to 0.87. Furthermore, the matrix for flexion angle with extension angle showed a lack of correlation between extension at 1 h after exercise and flexion. Significant r values in this matrix ranged from -0.37 to -0.64. The same was found for flexion and Mb: no significant correlations were found for flexion with Mb at 1 h, but from 24 to 96 h correlations ranging from 0.45 to 0.72 were found. The matrix for CK with extension showed a whole cluster of significant correlations, ranging from -0.36 to -0.88. Finally, Mb values were significantly correlated with CK at 24–96 h ($r = 0.38$–0.90), but for Mb and extension angle fewer significant correlations were found (ranging from -0.40 to -0.73).

Soreness-Measure Correlations (Fig. 5)

For force only one significant correlation was found with DOMS (-0.38), showing that the DOMS score hardly was related to force. However, extension angle, flexion angle, CK, and Mb showed a few more significant correlations with DOMS: extension angle, CK, and Mb correlated with DOMS after 24 h (for extension, $-0.37 < r < -0.56$; for CK, $0.36 < r < 0.58$; for Mb, $0.34 < r < 0.55$). For extension and CK, only the values after 48 h correlated with these DOMS scores. Flexion angle showed significant correlations at all points in time with DOMS at 48 h. Also, some correlations were found for DOMS at 72 and 96 h with flexion at the later points in time. Values in this matrix ranged from 0.39 to 0.63.

DISCUSSION

The question raised in this study was whether it is sufficient to measure the changes in only one functional or biochemical measure at one point in time to predict the changes due to eccentric exercise at other points in time and in other measures. Thus, correlations were calculated for each measure between different time points, between measures, and between functional and biochemical measures and DOMS to answer this question.

Within-Measure Correlations

The analysis of the within-measure correlations shows significant correlations for DOMS between all points in time except for 1 h after exercise. This may be explained

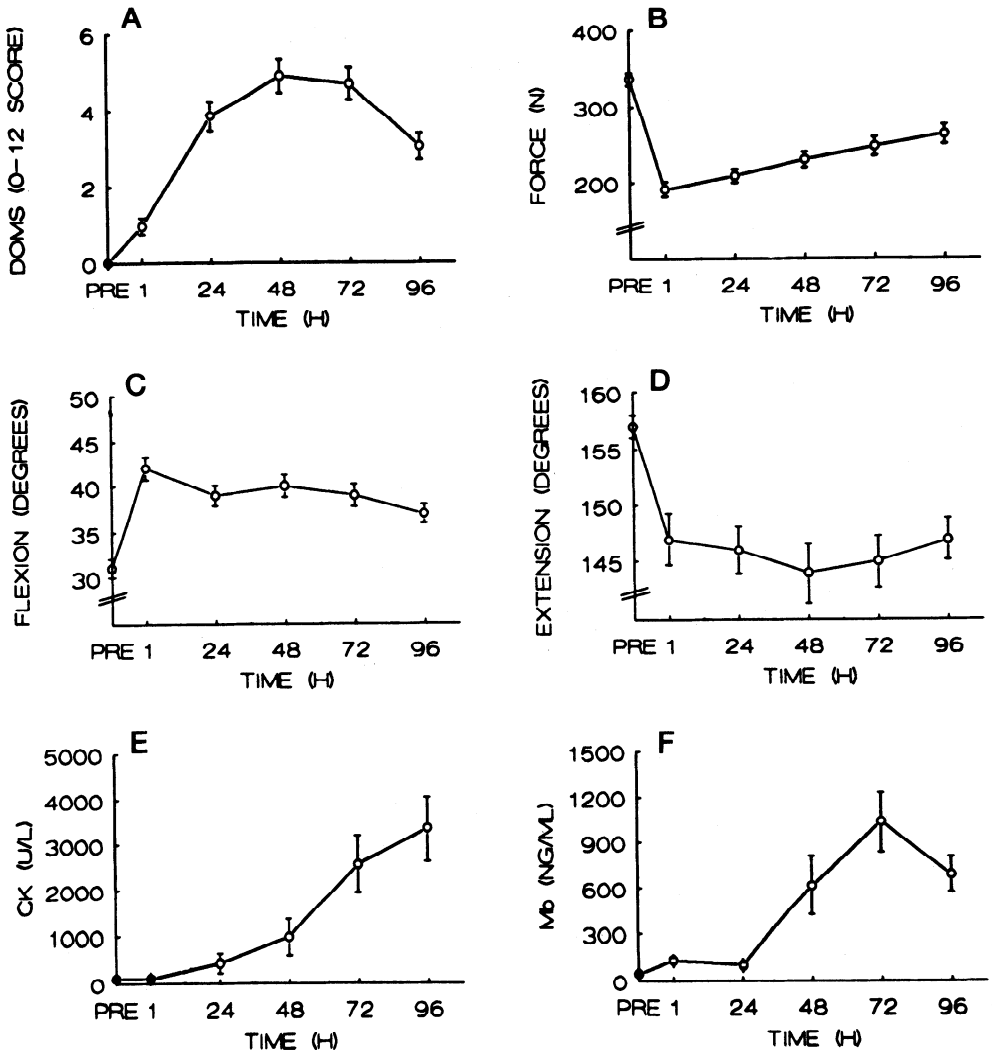

FIG. 2. Time course (means ± SE for 20–27 subjects) for all biochemical and functional measures and delayed-onset muscle soreness (DOMS) from preexercise until 96 h after exercise. *A*: DOMS; *B*: maximal isotonic force (force); *C*: flexion angle; *D*: extension angle; *E*: creatine kinase (CK); *F*: myoglobin (Mb). Changes over time were significant at $P < 0.001$ for all measures.

by the subjects' experience that soreness at 1 h after exercise is quite different from soreness later on: subjects describe a rather tired, numb feeling 1 h after exercise but hesitate to call it soreness. To discriminate between the feeling before and immediately after exercise, a score larger than zero is given. What exactly causes this feeling of tiredness is unclear. Depletion of energy supplies is not very likely because this kind of feeling is never reported to occur after concentric exercise, which requires more energy (5). Therefore the cause must be in other aspects of muscular contraction; for example, it could be that neuromuscular signal transmission is hampered, proprioception is disturbed, or the initial changes seen in morphological studies (10, 11) result in dysfunctioning of the contractile elements. On the other hand, soreness on subsequent days is described more often as an ache. Hence, DOMS is indeed "delayed," and it can be understood that subjects who have a high DOMS score 1 h after exercise do not necessarily have one on subsequent days, as is shown by a lack of correlation.

From the within-measure correlations for CK it can be deduced that a large change in CK activity at one time predicts a high CK activity later on. This does not hold for CK 1 h after exercise, because this value does not correlate with the later ones. For Mb, force, flexion angle, and extension angle, the results are uniform: all matrices show significant within-measure correlations for the whole period after exercise, reflecting that a large change immediately after exercise coincides with a large deviation later on. This means that the velocity of recovery generally is the same in all subjects but that total recovery time (in days) is longer when the initial changes are larger. The results for these within-measure correlations show that measurement at one moment after exercise suffices when two groups are compared, and it describes both groups adequately: when a high correlation exists between different points in time, subjects with high values at one point in time will also show high values at the next point in time for that particular measure. Obviously, there will be some intersubject variation, but on average a high correlation between the results at two points means that the second point hardly provides new information. Therefore, in experiments in which groups are studied, comparisons can be made at one point in time without much information being lost. In 12 of the 43 significant correlations calculated in Fig. 3, the amount of variance that was explained by the correlations between different time points was >80%. In another 14 of the 43 significant correlations, the explained variance was >50%. However, it must be realized that in some situations 55% of the variance remained unexplained (e.g., CK), so this procedure should be applied only when

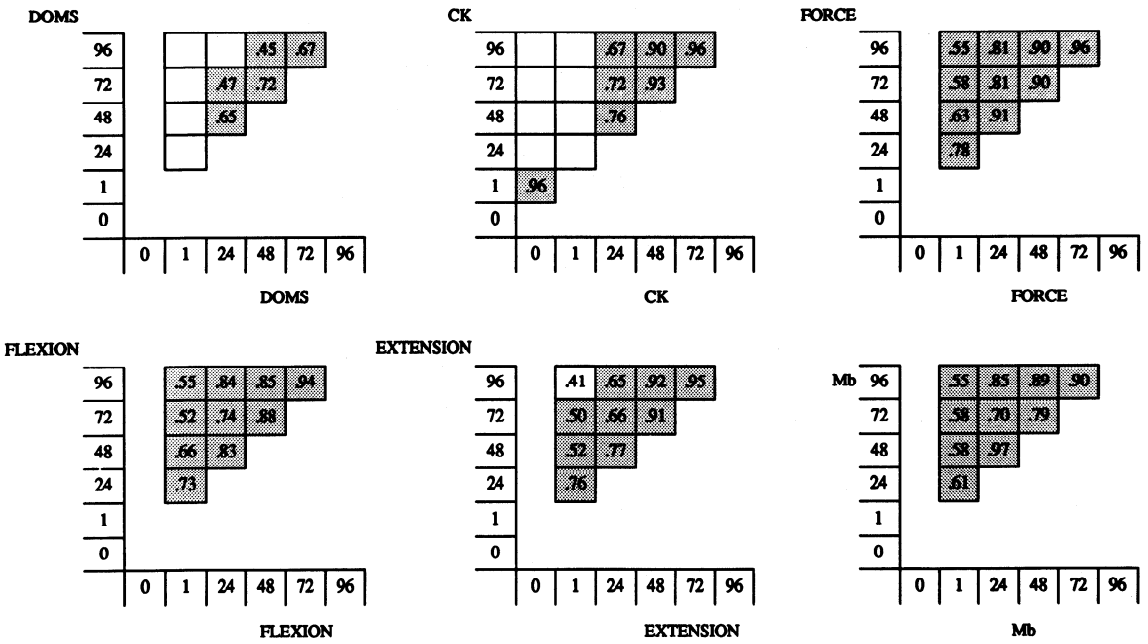

FIG. 3. Within-measure correlation matrices for biochemical and functional measures and DOMS. For CK and DOMS, Spearman's r was calculated; for other measures Pearson's r was used. Shaded areas represent correlation coefficients significant at $P < 0.01$; areas containing only a correlation coefficient are significant at $P < 0.05$. No coefficients for 1st measurement are given for matrices including Mb, force, flexion, and extension, because these parameters were normalized on 1st measurement; all preexercise values then equal 100% (Mb, force, %) or 0 (flexion, extension, difference from preexercise).

there is time constraint during measurements, and no individual predictions of later changes should be made on the basis of initial changes in these measures.

Between-Measure Correlations

It seems that there is a close relationship between the functional and biochemical outcomes of the exercise: most between-measure correlation matrices in Fig. 4 show a cluster of correlations after the exercise. This suggests that generally all measures cohere and that a large change in one measure coincides with a large change in other measures, even when they have their individual maximal change at different points in time. When groups are compared for differences in consequences of eccentric exercise, one type of measure will suffice, according to the same reasoning as that described above for measuring only one point in time instead of a whole time course. When a difference between two groups exists, testing one measure should be sufficient to establish this difference.

If we assume that early changes (e.g., in force and flexion) are indicators of an initial phase of changes within the muscle after eccentric exercise and that later changes (e.g., CK activity) are indicators of later phases, it is likely that high between-measure correlations reflect a close relationship between the different phases of changes within the muscle after eccentric exercise. In that situation, the initial phase of changes in muscle characteristics is not merely a trigger for the next phases but may even determine how large changes in the next phases will be. Then all changes in measures, and hence all phases of the development of damage, are components of one chain of events, occurring parallel and serial to each other. A model describing the events in muscle after damaging exercise has been proposed on the basis of animal experiments (1) in which initial damage to the sarcolemma and later damage due to inflammation are separate events. However, the time courses of changes described in our study and in the literature on humans (4, 7, 15, 19) do not correspond with this model, possibly reflecting species differences.

The correlations found in this study support a central role for one factor that determines the amount of change in all functional and biochemical measures. Calcium has been proposed as an important factor in the processes leading to muscle damage (2) and may have this role. However, it must be realized that a direct action of any single factor on all measures is unlikely. If there were such direct action, all measures should follow the fluctuations in this one common factor exactly and hence have the same time course. Because it has been shown by many studies, including this one, that all measures follow different time courses, calcium may be considered to trigger a chain of events in time, with each event characterized by a different measure.

It is surprising that Mb 1 h after exercise shows only correlations with force, whereas the values for Mb from 24 to 96 h correlate with all other measures. Because Mb also showed a clear rise 1 h after exercise, correlations were expected at this point in time. Collectively, data on Mb after concentric (8) and eccentric exercise (4, 19, this study) suggest that Mb is released immediately after exercise in all instances. It returns to normal because of its fast secretion when no or marginal damage has developed, but it reaches high values after damaging exercise. The latter changes follow about the same time course as

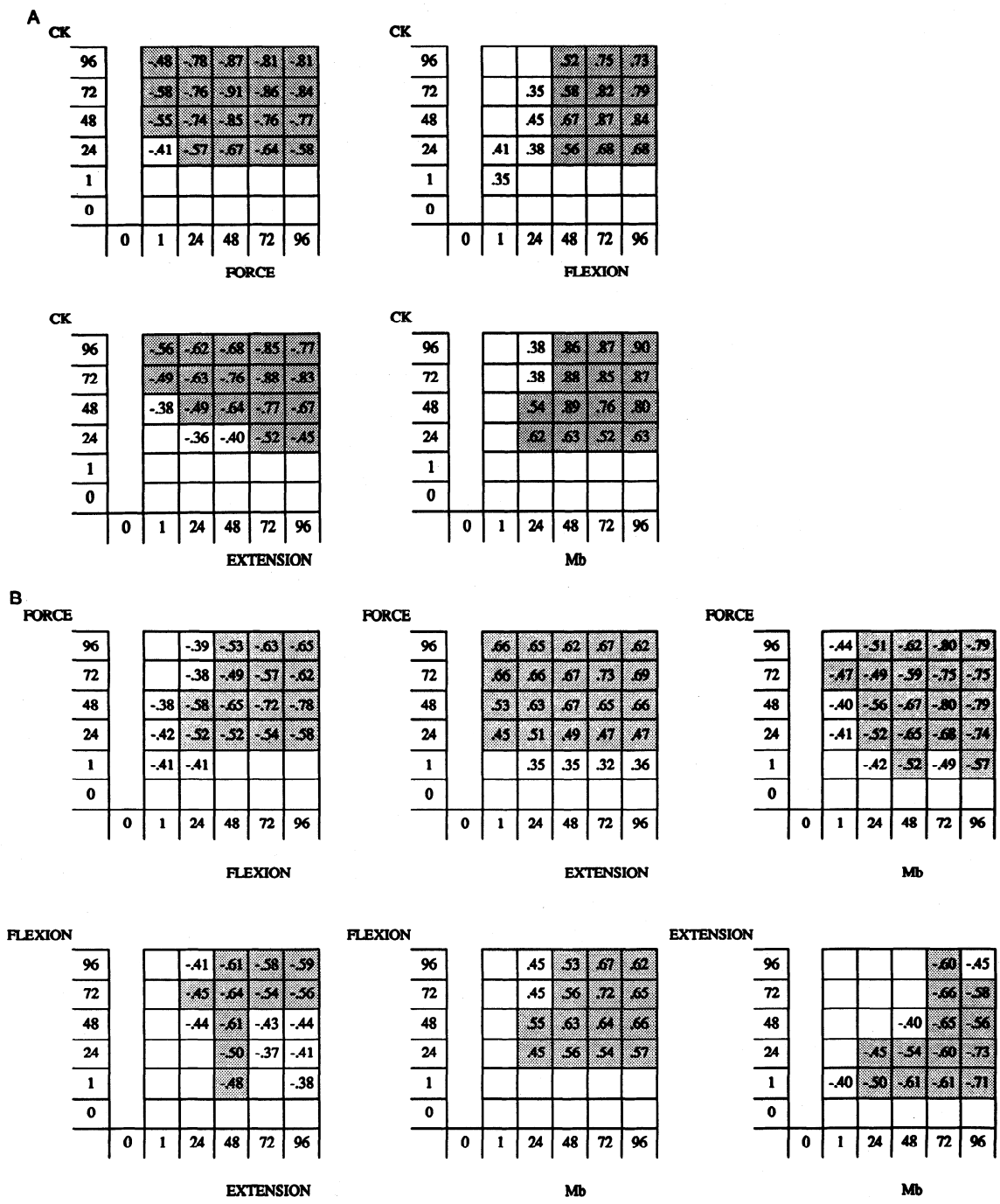

FIG. 4. *A*: between-measure correlation matrices for CK with all other biochemical and functional measures. Because CK was involved, Spearman's *r* was calculated. *B*: between-measure correlation matrices for force, extension angle, flexion angle, and Mb. For all pairs of measures Pearson's *r* was calculated. For further explanation, see Fig. 3.

CK, although CK because of its longer half-life may remain elevated for a longer period (Fig. 2, *E* and *F*).

Soreness-Measure Correlations

Interesting results occur in the matrices in which DOMS is correlated with the other outcomes of eccentric exercise (Fig. 5). The clustering of significant correlations for DOMS with CK, Mb, flexion angle, and extension angle at later points in time suggests that some DOMS can be explained by changes in other measures (Fig. 5). However, it was expected that DOMS at 24 h would correlate with the other measures inasmuch as DOMS is present at that time. For CK 1 h after exercise it can be expected that no correlations with DOMS exist, because CK at 1 h is still at the normal level. But for CK at 24 h, a correlation with DOMS would have been likely, because changes in DOMS and CK were expected to belong to the same chain of events that is described above. If both CK release and occurrence of DOMS belonged to the same chain of events, significant correlations could be expected. Also, for the matrices including DOMS with flexion or DOMS with Mb, more significant correlations were expected, such as for the correlation matrices in Fig.

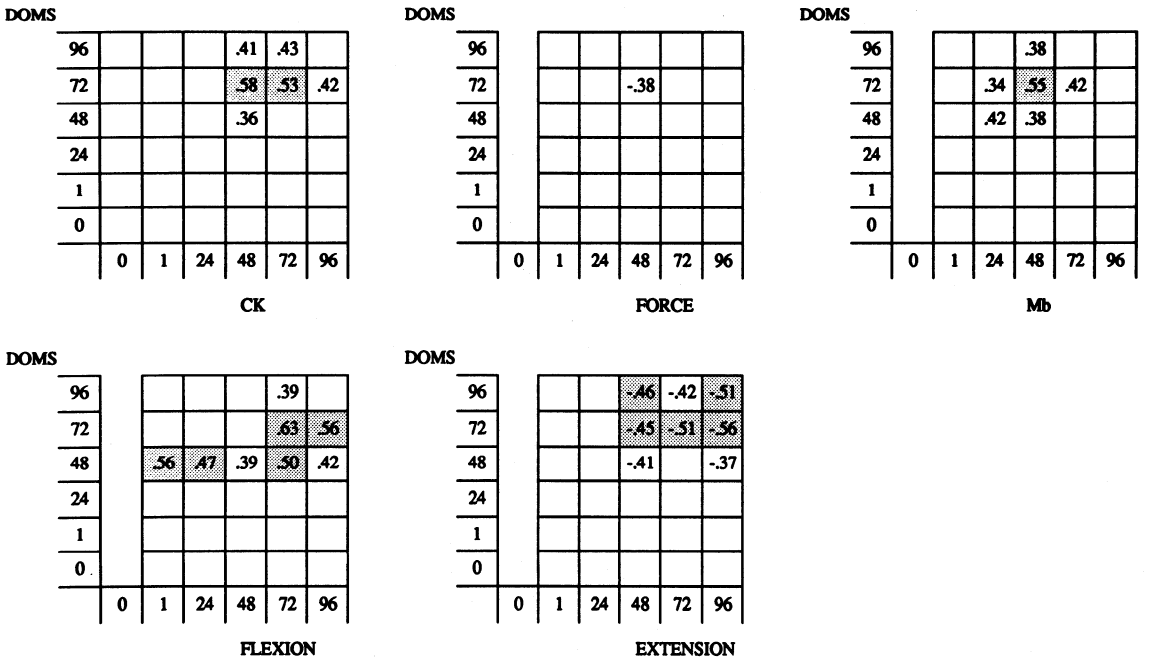

FIG. 5. Soreness-measure correlation matrices for DOMS with biochemical and functional measures on basis of Spearman's r. For further explanation, see Fig. 3.

2, *A* and *B*, on the basis of the same reasoning. It is likely that the lack of ample correlation between soreness and the other measures is caused by the subjective nature of the soreness score: although subjects can compare their own scores over days, it is difficult to compare scores of different subjects in an absolute sense. Pain scores are sometimes used in the evaluation of treatments that are supposed to prevent soreness, such as stretching and warm-up (12). The lack of correlation between DOMS and other outcomes of eccentric exercise found in the present study leads to the conclusion that some care must be taken in using the DOMS score while testing the effect of preventive treatments. Measurement of functional and biochemical measures is to be preferred above measurement of DOMS when one plans a study to investigate whether differences exist between groups.

Comparison With Previous Studies

Patterns of change (Fig. 2) are similar to those found in the literature in that the different measures start to change in the same sequence and generally follow the same time course of recovery (6, 7, 16). Therefore it is justified to suppose that the relationships that were established here systematically within measures, between measures, and between functional and biochemical measures and soreness will also hold for the data described in several other studies.

Until now, within-measure correlations have not been described, and of the between-measure correlations only a significant relation between CK and Mb release has been described (4). Soreness-measure correlations have been studied, but most authors did not find any correlation between DOMS and biochemical and functional outcomes of eccentric exercise (4–6, 16): no correlation was found between DOMS and maximal force (20). CK efflux did not correlate with DOMS in most studies (4–6, 16) but did in one (23). Finally, Jones et al. (13) observed DOMS when CK efflux was absent. In the present study some correlations were found between DOMS and CK, flexion angle, and extension angle. The difference between our results and those in the literature may have two causes. Other studies did not describe exactly in what way correlations were calculated; possibly not all points in time were included in the analysis, leaving out points that would have shown correlation with the present study. Another possibility is that the difference results from the kind of correlation coefficient used: in the studies cited, Pearson's r was used to correlate CK and DOMS, whereas in the present study Spearman's r was used, because the distribution of the CK values was rather skewed. A significant correlation of 0.80 between CK and DOMS has been reported (23). However, this correlation was based on pooled, and therefore not independently collected, data; thus this figure must be interpreted with care. When Pearson's r was used in calculating the correlation between CK and DOMS in the present study (data not shown), only significant correlations were found between CK at 72 h and DOMS at 48 and 72 h. The differences between our results and those of others cannot be explained by the fact that relative values were used for force, flexion, and extension, because absolute values also produced significant correlations (data not shown).

Conclusions

From our experiments the following conclusions can be drawn. *1*) On the basis of within-measure correlations, it can be concluded that a subject with large initial deviations for a particular measure generally also shows large deviations at later days. This means that subjects with large initial deviations follow a similar rate of recovery as subjects with smaller initial changes but need a longer

time for total recovery because the initial deviations are large.

2) On the basis of between-measure correlations, it can be concluded that all measures change to the same extent from eccentric work and reflect a chain of events. If changes in the initial phases of muscle damage are large, then changes during later phases of muscle damage are also large and vice versa.

3) On the basis of soreness-measure correlations, it can be concluded that DOMS is related to functional and biochemical outcomes of eccentric exercise, although the correlations are not as abundant as those between different functional and biochemical outcomes because of the subjective nature of the DOMS score. It is concluded that the use of objective measures of the outcome of eccentric exercise is preferred to subjective comparisons of soreness between groups in studies in which preventive treatments are to be tested.

The main question posed was whether studying one measure at one point in time is sufficient to predict the time course of all changes present after eccentric exercise. Although the within-measure and the between-measure correlations and, to a lesser extent, the soreness-measure correlations show many significant values, not all correlation coefficients reach values of 1.00. This means that information will be lost when only one measure is determined at one point in time, because values at other points in time and for other measures do not correspond with the parameter measured according to a one-to-one relation. However, when groups are compared, the additional measurements will hardly provide new information on the group average. Hence, when groups are compared, it is sufficient to use one measure at one point in time to find differences between groups. When it is necessary to assess the exact outcome of eccentric exercise in individual subjects, it is advisable to use more measures at more points in time.

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Some preliminary results have already been described in an abstract (20).

Present address of R. W. de Boer: Philips Medical Systems, Best, The Netherlands.

Address for reprint requests: P. R. Bär, Dept. of Neurology, AZU, Univ. of Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands.

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