# Changes in maximal voluntary force of human adductor pollicis muscle during the menstrual cycle

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1. Muscle strength of the adductor pollicis (AP) was studied throughout the menstrual cycle to determine whether any variation in force is similar to the known cyclical changes in ovarian hormones. Three groups of young women were studied: trained regularly menstruating athletes (trained), untrained regularly menstruating (untrained) and trained oral contraceptive pill users (OCU). In addition a group of untrained young men was studied as controls.

2. Maximum voluntary force (MVF) of AP was measured over a maximum period of 6 months. Ovulation was detected by luteinizing hormone measurements or change in basal body temperature. There was a significant increase in MVF (about 10%) during the follicular phase of the menstrual cycle when oestrogen levels are rising, in both the trained and untrained groups. This was followed by a similar drop in MVF around the time of ovulation. Neither the OCU nor the male subjects showed cyclical changes in MVF.

We have shown previously that the maximum voluntary force (MVF) which can be exerted by the adductor pollicis muscle (AP) relative to its cross-sectional area (CSA) is 28% lower in old than in young people (Phillips, Rook, Siddle, Bruce & Woledge, 1993*b*). In women this decline in MVF/CSA occurs at the time of the menopause, i.e. at the time when ovarian failure leads to a permanent decline in sex hormone secretion. In postmenopausal women using hormone replacement therapy MVF/CSA is greater than in age-matched controls and not less than that of young women (Phillips *et al.* 1993*b*). These facts suggest that oestrogen may have a muscle-strengthening action. If this is correct, and if the action is exerted within a few days, then we could expect to see changes in MVF during the menstrual cycle. It is well recognized that, during the follicular phase of the menstrual cycle, oestrogen levels rise to a peak and then fall during the day or two before ovulation, while during the luteal phase the oestrogen levels remain relatively stable but at a higher level than that at the start of the cycle. In contrast, progesterone levels are negligible during the follicular phase but, after ovulation, rise to a peak during the luteal phase (Moghissi, Syner & Evans, 1972). Therefore, it would be predicted from the hypothesis of oestrogen increasing muscle strength, that a rise in MVF would be seen during the follicular phase of the cycle followed by a fall near the time of ovulation. Moreover, if the action of oestrogen was not opposed by that of progesterone, MVF would remain higher during the luteal phase than at the start of the cycle. This paper reports the results of experiments carried out to test these predictions. We compared highly trained athletes, during their training season, with non-training subjects for two reasons: (1) the highly physically active subjects may have developed oligomenorrhoea or amenorrhoea giving anovulatory cycles with little change in cyclical hormones or force; and (2) physical activity itself may saturate any force effect caused by changes in the levels of sex hormones, which would result in no cyclical changes in force.

Decreases in muscle strength around the time of menstruation were first reported more than 50 years ago (Dawson, 1935). However, since then the presence of changes in muscle strength during the menstrual cycle has been the subject of controversy and the previous work, which is reviewed in the Discussion, was not specifically aimed at the detection of the pattern of change in force predicted above. Preliminary reports of our work have appeared (Phillips, Gopinathan, Meehan, Bruce & Woledge, 1993*a*; Phillips, Rutherford, Birch, Bruce & Woledge, 1995).

## METHODS

### Subjects

We studied women aged between 17 and 39 years who were menstruating regularly. The subjects belonged to three groups as follows: (1) 'trained' ($n = 10$) and (2) 'untrained' ($n = 12$) who were both not using oral contraception; and (3) those who trained and were using oral contraceptive preparations ('OCU'; $n = 5$). The subjects in the trained and OCU groups were members of two rowing clubs and trained six times a week during the duration of the study (6 months). Rowers were studied because they were a convenient source of highly motivated athletes, who used adductor pollicis during training and who attended regular training sessions. Measurements of muscle strength for these groups were made at the training sessions, before training, usually three times a week. The subjects in the untrained group were not engaged in any regular athletic training; they attended the laboratory for measurements of force during one to three cycles (mean, 8 measurements per subject). None of the trained subjects were amenorrhoeic but their cycle lengths were more variable than in the untrained group (Table 1). An additional control group of six men aged 23–35 years, not in regular athletic training, was also studied over 1–2 months (mean, 5 measurements per subject). Further details about the subjects are given in Table 1.

### Muscle force measurement

We studied adductor pollicis MVF because subjects can maximally activate this muscle (Merton, 1954; Phillips, Bruce, Newton & Woledge, 1992), the task is simple and reproducible and no learning is necessary, which reduces the possibility of effects due to changes in psychological status. Muscle force during maximum voluntary contractions of AP muscle was measured by the method previously reported (Phillips *et al.* 1993*b*). Briefly, a transducer was held between the proximal phalanx of the thumb and the metacarpal of the index finger with the thumb in the plane of the palm of the hand. The fingers and interphalangeal joint of the thumb were kept maximally extended. Six to nine maximal contractions (adduction of the thumb) of 1–2 s duration each were recorded and the mean of the best three to five contractions was used as the measurement of muscle strength for the session. All results for muscle force are expressed relative to the mean value for that subject over all experimental sessions ('relative force'). This is the simplest way to study the proportional changes in force that were expected to occur in each subject over time. We chose this approach, rather than normalizing MVF to muscle CSA, to avoid adding extra variance from the CSA measurements between subjects.

### Detection of ovulation

**Basal body temperature.** The basal body temperature was measured orally using digital thermometers. Subjects were asked to take their temperature each morning before rising, but generally did not provide complete data sets.

**Hormone measurements.** For fourteen cycles in subjects from the trained group, urinary excretion of luteinizing hormone (LH) was assessed daily using commercial test kits (Bionike A/Q one-step LH ovulation test; Gamidor Ltd, Oxford, UK), near to the expected time of ovulation, starting 17 days prior to the expected date of menstruation. Venous blood samples were taken from nine subjects in the trained group. For each subject two to three samples were taken 2–7 days apart around the expected date of ovulation and analysed for 17-$\beta$ oestradiol. The aim was to take samples during the mid-cycle oestrogen peak and trough.

### Muscle CSA measurement

The CSA of AP was measured anthropometrically using callipers. This method has been described previously (Bruce, Newton & Woledge, 1989) and involves measuring the thickness of the hand in the plane that bisects the AP muscle, by the difference in output from two linear potentiometers which move over the skin, the distance moved being measured by a third potentiometer. The resultant muscle CSA measurement correlates well with that from CAT and NMR images through the plane of the hand. CSA was measured on each subject one to four times over the course of the study, on each occasion CSA was the mean of three to four measurements.

Subjects gave their informed consent. Ethical permission for the experiments was obtained from the University College London and University College Hospital Joint Ethical Committee.

## RESULTS

### Is there an increase in MVF during the follicular phase of the cycle?

Such an effect would be predicted if oestrogen causes an increase in muscle strength. This prediction is easy to test experimentally since the cycles are synchronized simply by the day on which menstruation starts. The results are shown in Fig. 1. In both the trained and untrained groups there were clear increases in MVF of about 10% over this period. The results for each group were similar, suggesting that the level of customary physical activity does not influence this effect, though much larger absolute forces were exerted by subjects in the trained group (see Table 1). The statistical significance of the upward trend in force is best assessed from regression analyses of the relative force (force is expressed as a proportion of the mean force for that subject) *versus* cycle day. For the trained group, the slope of this regression line was $0{\cdot}62 \pm 0{\cdot}24\%\ \text{day}^{-1}$ ($P = 0{\cdot}0112$, $n = 112$) and for the untrained group, the slope was $1{\cdot}05 \pm 0{\cdot}51\%\ \text{day}^{-1}$ ($P = 0{\cdot}049$, $n = 30$) (shown in Fig. 1*A*). In contrast, those using oral contraception (OCU) showed no significant change in force during the first 2 weeks of their cycle in which they were taking the oral contraceptive pill, following their withdrawal bleed (Fig. 1*B*). These results are clear support for the hypothesis that oestrogen increases muscle strength.

### Is there a drop in MVF at about the time of ovulation?

If oestrogen acts on muscle force sufficiently quickly, the drop in oestrogen occurring after the LH peak should be accompanied by a reversal of the increase in muscle force over the follicular phase. This effect is harder to detect than the rise during the follicular phase because ovulation will not occur at a consistent time after menstruation. Thus simply averaging data synchronized by cycle day may partly obscure any effect. We have tried three methods to overcome this problem. (a) The day of ovulation was detected by the LH peak in fourteen cycles from eight subjects in the trained group. The LH peak occurred on day $15{\cdot}0 \pm 0{\cdot}64$ (range, 11–19 days). A regression analysis of the individual force measurement for the days around this peak showed a decline but this was not significant (slope ± S.E.M., $-5{\cdot}13 \pm 3{\cdot}13\%\ \text{day}^{-1}$, $P = 0{\cdot}135$). (b) Ovulation was predicted by detecting the change in basal body temperature. Although this is known to be less accurate, it is the simplest method of predicting ovulation prospectively. We averaged all our temperature records and compared our data with that of Moghissi *et al.* (1972), which is aligned by the day that the LH peak occurred. The mean temperature records for both the trained and untrained groups agreed very well with those of Moghissi *et al.* (1972), if it was assumed that in each group the LH peak occurs on day 16 of the cycle. This is in agreement with the direct observations of the timing of the LH peak ($15 \pm 0{\cdot}64$ days). Therefore, we combined the force results from those cycles in which the LH peak was measured with those from both trained and untrained groups, where LH was not measured,

**Table 1. Comparison of subject groups**

| Group | $n$ | MVF (N) | CSA (mm²) | MVF/CSA (N mm⁻²) | Cycle length (days) | Age (years) | Height (m) | Weight (kg) | BMI (kg m⁻²) |
|---|---|---|---|---|---|---|---|---|---|
| Trained | 10 | 106·98 ± 6·58 | 568·9 ± 23·2 | 0·189 ± 0·010 | 28·5 ± 6·83§ | 26·1 ± 1·85 | 1·69 ± 0·03 | 63·32 ± 2·13 | 22·09 ± 0·56 |
| Untrained | 12 | 56·75 ± 2·15 | 360·9 ± 25·4† | 0·171 ± 0·011† | 28·2 ± 2·40‡ | 24·42 ± 1·36 | 1·64 ± 0·02 | 55·06 ± 2·08 | 20·47 ± 0·53 |
| OCU | 5 | 119·87 ± 9·03 | 608·5 ± 17·0* | 0·193 ± 0·016* | — | 21·2 ± 0·49 | 1·68 ± 0·03 | 67·51 ± 3·46 | 23·79 ± 0·43 |
| Men | 6 | 83·50 ± 4·68 | 459·2 ± 35·8 | 0·179 ± 0·016 | — | 30·00 ± 1·97 | 1·76 ± 0·06 | 65·40 ± 2·97 | 21·24 ± 0·77 |

BMI, body mass index. Data are means ± S.E.M. except for cycle length (means ± S.D., $n = 42$ for the trained group and $n = 16$ for the untrained group). * $n = 4$, † $n = 8$, ‡ $n = 16$, § $n = 42$.

on the assumption that the LH peak was on day 16. A regression analysis of the fifty individual observations from these combined data from the day before to 2 days after the LH peak gave a slope of $-3{\cdot}07\%\ \text{day}^{-1}$ (S.E.M. of the slope, 1·35%; $P < 0{\cdot}028$; Fig. 2*A*). (c) For each subject in the untrained group, interpolation was used to obtain an estimate of muscle force for each day of each of the cycles studied, i.e. where a value (or values) were missing for a day (or days) a calculated line was drawn between the actual data points and interpolated values read off from this line for the day of the missing value. Since the cycles were relatively uniform in length in this group (Table 1) we simply examined the means of the interpolated force measurements for each day of the cycle (Fig. 2*B*). This showed a decline by 7% in MVF between days 11 and 13 of the cycle. This was likely to underestimate the true size of the effect due to the asynchrony of ovulation. Therefore, we also calculated the results on the following basis. The day of the cycle between the 12th and 18th day at which force was lowest was assumed to be the day of ovulation and the interpolated force values were then averaged, with the results shown in Fig. 2*C*. This method was liable to exaggerate the size of the drop and so, as a control, the same method of analysis was applied to the results for men, giving the values shown in the dashed line in Fig. 2*C*. The size of the drop in force at ovulation in the untrained group

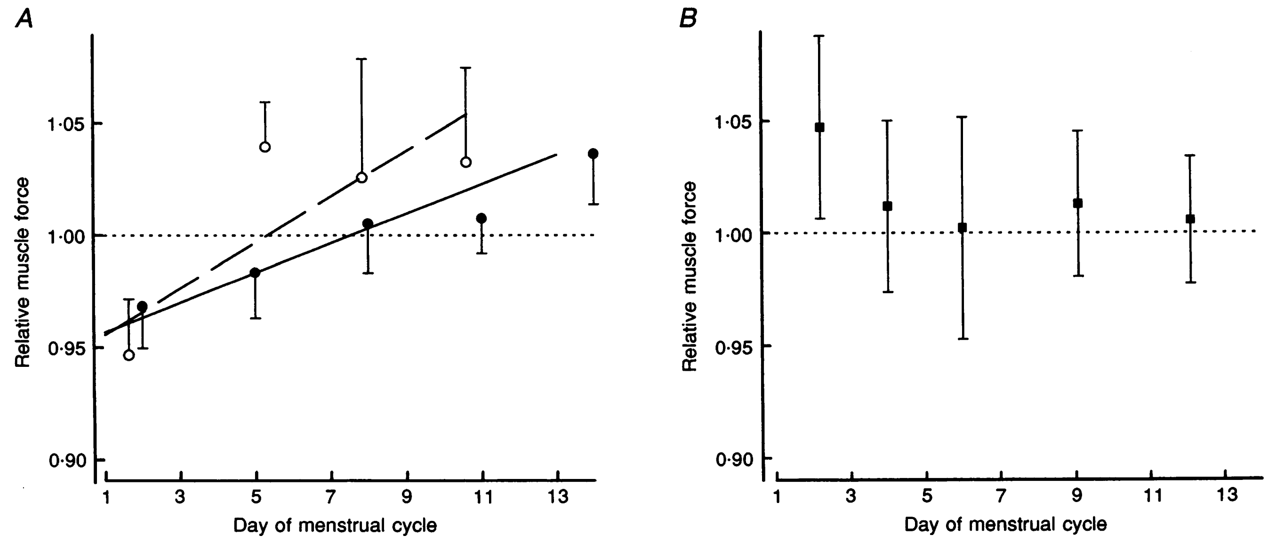


**Figure 1. The relation between relative muscle force and day in the first 2 weeks of the menstrual cycle (*A*) or of taking the oral contraceptive pill (*B*)**

Muscle force is expressed relative to the mean value for that subject over all measurements. *A*, the follicular phase of the menstrual cycle for the trained (●) and untrained (○) groups. Day 1 is the first day of menses. The lines are the regression lines for the individual data points in the respective groups. *B*, data for the OCU group. Day 1 is the first day of dosing with the oral contraceptive pill. Each symbol represents the mean ± S.E.M. of the results from 3 days.

was 11·3 %, of which the artefactual dip, estimated from the results for the men, was 3·7 %. This, therefore, gave an estimate of 7·6 % for the drop in force on ovulation.

All these methods agreed in the evidence they presented for the expected fall of force during the few days after ovulation, i.e. a fall of about 7 %, which was comparable to the rise during the follicular phase. However, no very clear picture emerged as to the exact timing of this fall, which may or may not coincide with the fall in the oestrogen level known to occur at about this time in the cycle (Moghissi *et al.* 1972).

## Does the force during the luteal phase return to that at the start of the cycle or remain higher?

The answer to this question was obtained by averaging the results for the luteal phase and comparing this mean with the mean results obtained during the first few days of the

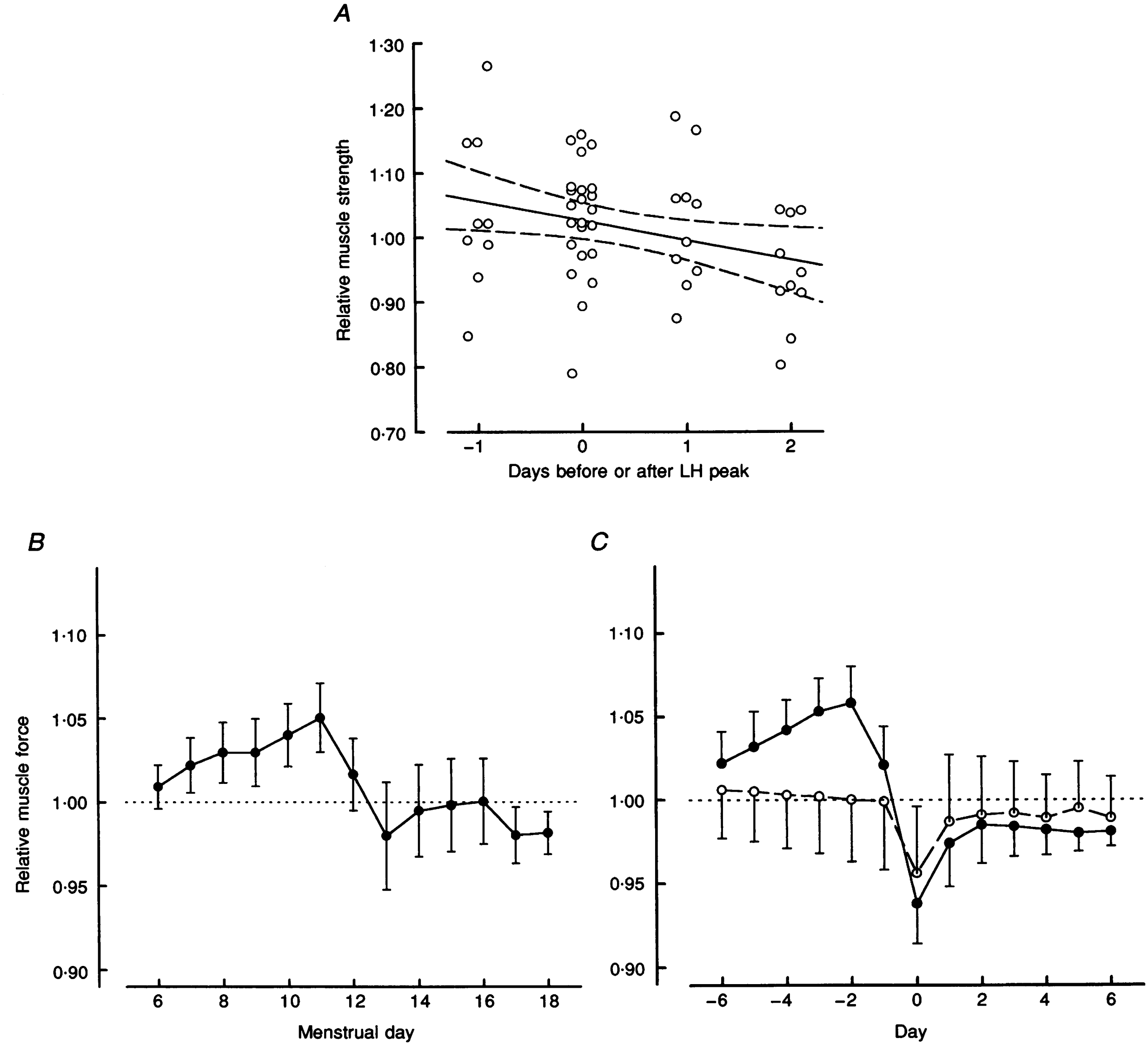


**Figure 2. The mid-cycle fall in relative muscle force**

Muscle force is expressed relative to the mean value for that subject over all measurements. *A*, relative muscle force over 4 days around mid-cycle for 14 cycles where LH was measured and for 38 cycles in which ovulation was predicted from averaged temperature records from subjects in both the trained and untrained groups, assuming LH peak is on day 16 as seen when synchronized to data of Moghissi *et al.* (1972). Individual observations from these combined data are shown, where 0 is the LH peak, with the regression line (continuous line) and 95 % confidence limits (dashed lines) for the mean relation. Individual data points have been shifted in $x$ to avoid overlap in the plot. *B*, relative muscle force for the untrained group (interpolated force measurements) aligned to first day of menses. *C*, relative muscle force (interpolated data) for men (○) and women (●). Day zero is the point of lowest force for each sex; for women this was assumed to be the day of ovulation (see text) and forces are plotted ±6 days either side of this day. Each symbol is the mean ± S.E.M.

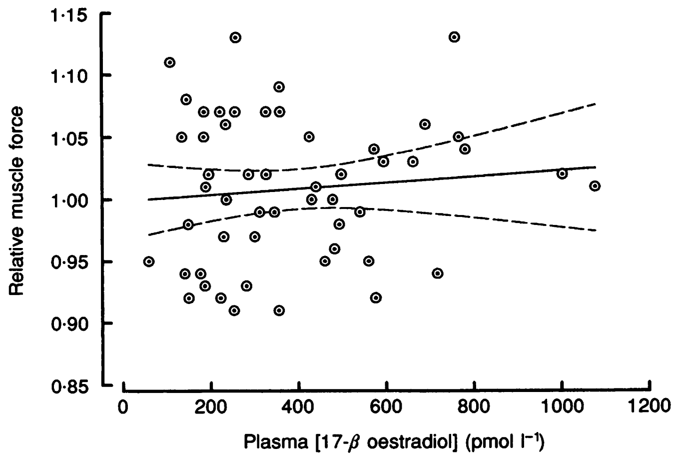


**Figure 3. The relation between relative muscle force and 17-β oestradiol concentration**

Muscle force is expressed relative to the mean value for that subject over all measurements. The symbols are individual observations from subjects in the trained group, with the regression line (continuous line) and 95% confidence intervals (dashed lines).

cycle. For the trained group, we used the data for the cycles in which ovulation was detected, and averaged all data for days beyond the third days after the LH peak. The mean force was greater by $5{\cdot}5 \pm 2{\cdot}7\%$ ($P = 0{\cdot}022$) than the force during the first 3 days of the cycle. However, in the untrained group, the corresponding figure was $2{\cdot}1 \pm 1{\cdot}1\%$ ($P = 0{\cdot}175$).

### Is there a correlation between oestrogen levels and MVF near the time of ovulation?

The simplest explanation for the fall of force near the time of ovulation would be that force responds immediately to changes in the oestrogen level. If this were so there would be a correlation between the oestrogen levels and the forces measured on the same occasion. The relation between oestrogen level and force measured on the same occasion that blood was taken is shown in Fig. 3. There was a wide variation in the oestrogen levels detected but no correlation with the force relating to the time around ovulation was apparent in this set of data.

### What is the overall pattern of change of muscle strength during the menstrual cycle?

Since the above results showed similar changes in both the trained and untrained group, we combined all of our data for these groups (404 measurements) into a single picture of the cyclic changes which occur. To take account of the variable cycle lengths, we expressed time as a proportion of cycle length for this purpose. The result, shown in Fig. 4, illustrates clearly that the cycle starts with a rise in muscle force during the first 40% of the cycle, which is approximately the duration of the follicular phase (Moghissi *et al.* 1972). The force then falls again by the end of the cycle but the pattern of this fall is not particularly clear; this lack of a clear pattern will be at least in part because of the individual variations in the duration of the follicular phases. There is a general resemblance between this pattern of force change and the pattern of change in oestrogen excretion described by Moghissi *et al.* (1972). There is no evidence that the rising levels of progesterone in the luteal phase of the cycle cause the force to fall more rapidly than the oestrogen level.

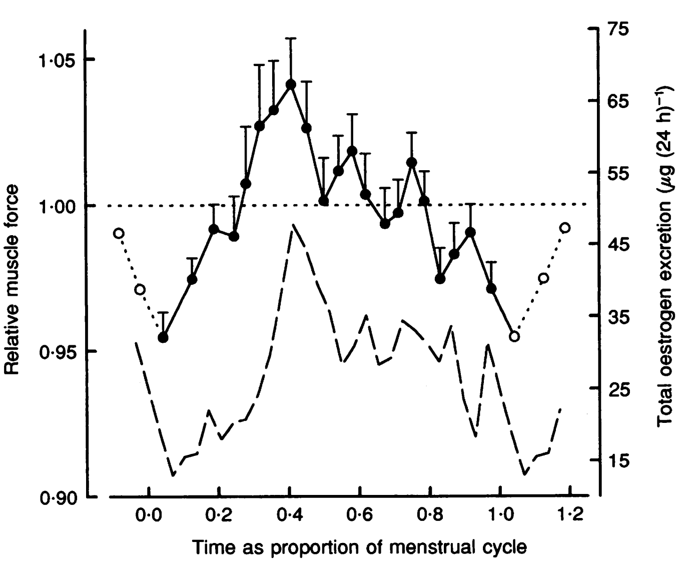


**Figure 4. Combined data from trained and untrained subjects to show the changes in relative muscle force over the whole menstrual cycle**

Muscle force is expressed relative to the mean value for that subject over all measurements. Time is expressed as a proportion of the cycle length, where 0 represents day 1 of the menstrual cycle, for that individual cycle. Each time point represents approximately 20 observations out of a total of 404. The data have been smoothed by averaging each point, weighted by the number of observations, with those on either side weighted by half the number of observations. The error bars show the standard errors of these weighted means. The open symbols show the data wrapped around. The dashed line shows the change in oestrogen excretion over the menstrual cycle taken from Moghissi *et al.* (1972).

## DISCUSSION

Our results showed a clear rise in the MVF of AP muscle during the follicular phase of the menstrual cycle and suggested a rapid fall at about the time of ovulation, thus confirming our preliminary reports and suggesting that oestrogen does exert a positive inotropic effect on skeletal muscle. Our results were also consistent with the 11% increase in isometric force of the quadriceps muscle group between the first and fourteenth days of the menstrual cycle, which has recently been similarly reported by Sarwar, Beltran Niclos & Rutherford (1995), who also found an increase in maximal hand grip. Quadriceps twitch interpolation showed that all the women could fully activate their quadriceps muscle on each occasion that they were tested (Sarwar *et al.* 1995), which demonstrates that the changes in voluntary force were modulated peripherally and not centrally. That there is a rise in muscle strength during the first half of the menstrual cycle followed by a sharp though temporary fall, seems to have been accepted in the earlier years of this century (Dawson, 1935) but more recent reports are contradictory. Davies, Elford & Jamieson (1991) found the opposite result, their subjects having a stronger hand grip during the first 4 days of their cycle, compared with either 12–14 or 19–21 days. Wirth & Lohman (1982), who made only two measurements per cycle, found grip to be significantly greater during the mid-follicular (days 6–10) than the mid-luteal phase (days 8–24), which is consistent with the results of Sarwar *et al.* (1995) and with ours (in our data the mean force for days 6–10 is higher, though not significantly, than on days 18–24). In several other studies, reviewed by Lebrun (1993), no detectable cyclical difference in hand grip in young women was found. However, it is easy to miss the changes in force because the changes are rather small and also there is a dip following the peak force around mid-cycle. We found muscle CSA to vary greatly between individuals and therefore compared the relative force changes during a cycle for each subject to avoid the large variance in force due to the different CSA of each subject. This enables small cyclical changes in force to be detected, which could be missed if means of absolute force for subjects, with very different muscle sizes, are compared at different points in the menstrual cycle.

The work we report here is the only study which has followed the detailed time course of changes in muscle strength during the menstrual cycle, particularly around the time of ovulation. We also believe that ours is the first study in which the effects on muscle force around the time of ovulation have been synchronized using LH values. A previous study using temperature measurements to detect ovulation was one of those in which no difference in maximal hand grip during the cycle was reported (Petrovsky, Ledonne, Rinehart & Lind, 1976), but only three subjects were tested and mean maximal grip measurements throughout pre-ovulatory and luteal phases were compared, a method of analysis likely to obscure changes such as Sarwar *et al.* (1995) and we have found. Thus it is not surprising that there have been no previous reports of the rapid drop in force around the time of ovulation, at or near the time when oestrogen levels fall also. Although we have demonstrated this predicted drop in force, and shown the general similarity of the cyclic force changes to those in oestradiol excretion, there is no evidence of a correlation between the plasma oestrogen levels and the force measured on the same occasion. It seems possible that this is because the action of oestrogen on the muscle is not immediate, but takes some hours or days, so that a phase lag between the oestrogen and muscle force changes is apparent when relatively rapid changes are occurring. Evidence in favour of this is provided by a recent study in which a significant negative correlation between hand grip and 17-$\beta$ oestradiol concentration during the menstrual cycle has been reported (Bassey, Coates, Culpen, Littlewood, Owen & Wilson, 1995). A negative correlation could arise if the response to oestrogen was delayed so that force continued to rise while oestrogen levels had began to fall. Therefore, we conclude that oestrogen does have a strengthening action, directly or indirectly, on skeletal muscle. We suggest that this effect, because of its probable delayed onset, is likely to be mediated by the classical steroid receptor for oestrogen which has been described in animal (Dahlberg, 1982; Saartok, 1984; Meyer & Rapp, 1985) and human muscle (Smith, Heimer, Norgren & Ulmsten, 1990), rather than the membrane receptor postulated by Sarwar *et al.* (1995), which would be expected to show a more rapid onset of action.


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