

Menstrual Cycle Phase Modulates Central but Not Peripheral Neuromuscular Fatigue in Trained Eumenorrheic Women

Sirine Hamdi

University of Sfax

Wael Daab

Wael.daab@ukb.ac.ae

University of Kalba

Firas Zghal

CIAMS, Université Paris-Saclay

Siwar Riahi

University of Sfax

Ines Ben Hssan

University of Sfax

Mohamed Amine Bouzid

University of Sfax

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Abstract

Ovarian-hormone fluctuations across the menstrual cycle may influence neuromuscular function, yet their effect on the central and peripheral contributions to fatigue remains unclear. We examined whether menstrual-cycle phase modulates exercise-induced neuromuscular fatigue in trained eumenorrheic women. Thirteen participants completed, in a randomised counterbalanced order, three sessions timed to the early follicular (EFP), late follicular (LFP) and mid-luteal (MLP) phases, verified by menstrual diaries, urinary ovulation testing and serum oestradiol and progesterone. In each session they performed a sustained isometric knee-extensor contraction at 50% of maximal voluntary contraction (MVC) to task failure; MVC, voluntary activation (VA), potentiated twitch amplitude ($Q_{tw,pot}$), surface electromyography and M-wave amplitude were assessed before and immediately after the task and analysed with linear mixed-effects models. Baseline neuromuscular variables did not differ between phases. Exercise reduced MVC, VA and $Q_{tw,pot}$ in every phase. The relative loss of MVC and VA depended on phase, whereas the ~45% decline in $Q_{tw,pot}$, M-wave amplitude and time to task failure did not. MVC loss was greatest in the MLP and did not differ between the follicular phases after correction, whereas VA loss differed between all three phases, being greatest in the MLP and smallest in the LFP. Because peripheral contractile fatigue was comparable across phases, these findings indicate that menstrual-cycle phase modulates the central, rather than the peripheral, component of neuromuscular fatigue. This pattern is consistent with, though not proof of, an influence of the high-progesterone mid-luteal environment on voluntary neural drive.

Trial registration: the Pan African Clinical Trial Registry (PACTR202607859511123) Registered 17 July 2026. Retrospectively registered.

Introduction

In women of reproductive age, physiological regulation is shaped by cyclic fluctuations in ovarian hormones, particularly oestrogen and progesterone, across the menstrual cycle (MC)^{1,2}. These endocrine variations have been proposed to influence several components of athletic performance, including muscular strength, endurance and exercise capacity^{3,4}. Circulating oestrogen and progesterone are both low during the early follicular phase (EFP); oestrogen then rises to peak before ovulation in the late follicular phase (LFP), while progesterone remains low; and both hormones are elevated during the mid-luteal phase (MLP)⁵.

The influence of the MC on exercise performance may be mediated in part by the action of ovarian hormones on the central nervous system. Because both hormones cross the blood–brain barrier, their cyclic fluctuation may modulate neuronal excitability, motor control and voluntary muscle activation⁶. The net neural effect, however, is unlikely to reduce to a simple dichotomy in which oestrogen is uniformly excitatory and progesterone uniformly inhibitory: the actions of these steroids are receptor-, region- and metabolite-specific, and in an intact motor system the aggregate effect reflects the balance

of these processes^{7,8}. This complexity notwithstanding, in vitro and animal evidence of direct effects of sex steroids on neuronal function provides a plausible substrate through which MC phase could alter central drive.

Despite these mechanistic considerations, the influence of MC phase on neuromuscular performance remains debated. Several studies report no variation in maximal strength across the cycle⁹, consistent with the apparent stability of muscle contractile and tendon mechanical properties despite hormonal fluctuation^{2,10,11}. Others describe phase-dependent variation in maximal strength and neuromuscular performance, implicating intracortical excitability and motor-unit discharge behaviour^{12,13,14}. These discrepancies likely reflect methodological heterogeneity, including differences in exercise modality, fatigue protocol, training status and the rigour of phase verification.

Neuromuscular fatigue is a multifactorial phenomenon arising from both central and peripheral mechanisms that impair force production during sustained or repeated activity¹⁵. Central fatigue reflects a reduction in voluntary neural drive, evident as decreased motor-unit recruitment and discharge rate, whereas peripheral fatigue refers to processes distal to the neuromuscular junction, including impaired sarcolemmal excitability, excitation–contraction coupling and contractile function¹⁶. Given the established action of ovarian hormones on neural excitability, it is plausible that cyclic hormonal fluctuation alters the magnitude and the central–peripheral balance of fatigue, yet studies that directly partition these contributions across the cycle remain scarce. Handgrip strength has been reported to be greater and fatigue attenuated during the follicular phase relative to the luteal and menstrual phases¹⁷, and neuromuscular fatigue appears accentuated premenstrually, with greater post-exercise force loss¹⁸. Altered motor-unit discharge behaviour has been observed across the cycle in the vastus lateralis and vastus medialis, with progesterone hypothesised to exert the greater influence on firing behaviour^{14,19}, and the mid-luteal phase has been linked to reduced force control consistent with a progesterone-mediated reduction in corticospinal excitability²⁰. Other work, however, reports no phase-related difference in fatigability²¹, underscoring the need to resolve the specific central and peripheral contributions.

Accordingly, the aim of this study was to determine whether MC phase alters the magnitude and the central–peripheral distribution of neuromuscular fatigue induced by a sustained isometric knee-extensor contraction, assessed during the EFP, LFP and MLP in trained eumenorrheic women. We hypothesised that fatigue would be attenuated during the follicular phases, particularly the late follicular phase, owing to lower progesterone and higher oestrogen concentrations, and that any phase-dependent difference would be expressed predominantly through the central rather than the peripheral component of fatigue.

Methods

Participants

Thirty female athletes volunteered to participate. Eligibility required a regular menstrual cycle of 27–31 days and no use of hormonal contraception of any form (oral contraceptives, implants, injections, intrauterine devices or transdermal patches)²², together with the absence of musculoskeletal injury, neurological disorder or any condition affecting neuromuscular performance. Following screening and a menstrual-cycle monitoring period, thirteen eumenorrheic women met all inclusion criteria, completed every session and were retained for analysis (Fig. 1). All participants provided written informed consent prior to enrolment. The study was approved by the regional research ethics committee (Comité de Protection des Personnes du Sud, N° 0102/2025), was registered in the Pan African Clinical Trial Registry (PACTR202607859511123), and was conducted in accordance with the Declaration of Helsinki.

Experimental design

Each participant attended the laboratory on four occasions: one familiarisation session followed by three experimental sessions corresponding to the EFP, LFP and MLP. The three experimental sessions were administered in a randomised, counterbalanced order to dissociate menstrual phase from session order and from any residual learning effect. During familiarisation, participants were habituated to all neuromuscular assessments and to the fatiguing protocol. Participants maintained their habitual diet and lifestyle, abstained from caffeine and alcohol in the 24 h before each session and avoided strenuous activity for at least 48 h beforehand. Perceived wellbeing (sleep, stress, fatigue and delayed-onset muscle soreness) was recorded before each session using the Hooper index to verify comparable pre-test status across visits. At each experimental visit, anthropometric measurements were obtained first, after which participants completed a standardised warm-up of progressive submaximal knee-extensor contractions. Neuromuscular assessments were performed immediately before and immediately after the fatiguing protocol. All sessions were conducted at the research laboratory of the High Institute of Sport and Physical Education, University of Sfax.

Sessions were scheduled according to expected hormonal fluctuations². The EFP (days 1–3) was characterised by low oestrogen and progesterone, the LFP (days 11–13) by elevated oestrogen and low progesterone, and the MLP (days 21–23) by elevated oestrogen and progesterone²³. To confirm cycle regularity and phase timing, participants completed a menstrual diary for at least six months before the study, recording cycle duration, menstruation dates, bleeding characteristics and symptoms²⁴. Ovulation was verified with urinary ovulation strips in the days preceding expected ovulation, and serum oestradiol and progesterone concentrations were measured to validate phase classification.

The fatigue protocol consisted of a sustained isometric knee-extensor contraction at 50% of maximal voluntary contraction (MVC) performed to task failure on an isometric dynamometer (Good Strength, Metitur, Finland). Participants were seated with the hip and knee fixed at 90° and 70°, respectively, testing the dominant leg. Real-time force was displayed on a screen, and participants maintained output within a shaded zone corresponding to 50% MVC for as long as possible. Time to task failure (T_{lim}) was

recorded in seconds and defined as voluntary cessation or the inability to maintain the target force for more than 5 s despite verbal encouragement.

Data collection and analysis

Neuromuscular assessments

Neuromuscular function was evaluated before and immediately after the fatiguing protocol and comprised MVC, voluntary activation (VA), potentiated twitch amplitude ($Q_{tw,pot}$), electromyographic activity and M-wave characteristics. Participants were seated on the dynamometer with a cuff connected to a strain gauge secured ≈ 2 cm above the lateral malleolus and were stabilised with straps across the chest, pelvis and thighs. Global fatigue was quantified as the percentage reduction in MVC ($\Delta MVC\%$) and peripheral fatigue as the percentage change in $Q_{tw,pot}$ ($\Delta Q_{tw,pot}\%$).

Femoral nerve stimulation was delivered with a constant-current stimulator (Digitimer Ltd., Hertfordshire, UK) using single 1-ms square-wave pulses (maximal output 400 V). The anode (90×50 mm) was positioned in the gluteal fold and the cathode (32 mm diameter) over the femoral nerve in the inguinal region. Stimulation intensity was increased until twitch force and M-wave amplitude plateaued, then set at 150% of the plateau to ensure supramaximal conditions²⁵. During each MVC, two stimulations were delivered: one during the force plateau (superimposed twitch) and one 3 s after the contraction ($Q_{tw,pot}$). Voluntary activation was calculated by the interpolated-twitch technique²⁶ as $VA(\%) = [1 - (\text{superimposed twitch} / Q_{tw,pot})] \times 100$, with a reduction in VA interpreted as central fatigue.

Electromyography

Surface EMG was recorded from the vastus lateralis (VL), vastus medialis (VM) and rectus femoris (RF) using bipolar Ag–AgCl electrodes (Dormo SX-50 ECG, Spain) placed according to SENIAM recommendations²⁷ with a 20-mm inter-electrode distance and a patellar reference. The skin was shaved, lightly abraded and cleansed with alcohol to reduce impedance below 5 k Ω . Signals were amplified (Octal Bio Amp ML138, ADInstruments, Australia), band-pass filtered (10–1000 Hz) and digitised at 2000 Hz (LabChart 7, ADInstruments). For each potentiated twitch, peak-to-peak M-wave amplitude (M_{max}) was determined. Knee-extensor activation was quantified as the root-mean-square (RMS) of the EMG signal normalised to M_{max} ($RMS \cdot M_{max}^{-1}$) to account for peripheral changes in sarcolemmal excitability.

Statistical analysis

Analyses were conducted in R (v 4.4.1) using the lme4²⁸, lmerTest²⁹ and emmeans³⁰ packages. Effect sizes were calculated using effectsize³¹, and figures were produced using ggplot2³². Each

neuromuscular outcome (MVC, potentiated twitch amplitude, voluntary activation, normalised EMG activity and M-wave amplitude) was analysed using a two-factor linear mixed-effects model with menstrual-cycle phase (EFP, LFP and MLP), time (pre and post) and their interaction as fixed effects. Participant-specific random effects accounted for the repeated measurements. The phase $\times$ time interaction was the primary test of whether the exercise-induced response differed among phases. When this interaction was significant, Bonferroni-adjusted pairwise comparisons were used to compare the percentage change between phases. Time to task failure and hormone concentrations were analysed using one-factor repeated-measures models with phase as the fixed effect. Model assumptions were assessed by visual inspection of residual Q–Q plots and histograms. Omnibus effects are reported as partial η^2 . Pairwise contrasts are presented as mean differences with 95% confidence intervals, Bonferroni-adjusted P values and repeated-measures standardised effect sizes (drm). Statistical significance was set at $P < 0.05$. Data are presented as mean $\pm$ SD unless otherwise stated.

Results

Anthropometric characteristics were similar across phases, with no difference in body mass, height or body mass index (all $P \geq 0.05$; Table 1). Serum hormones confirmed the expected profile of each phase: oestradiol was higher in the late follicular phase than in the early follicular and mid-luteal phases ($P = 0.04$), and progesterone was higher in the mid-luteal phase than in the follicular phases ($P < 0.01$). At baseline, no neuromuscular outcome differed across phases – MVC ($P = 0.66$), voluntary activation ($P = 0.39$), potentiated twitch amplitude ($P = 0.60$), $\text{RMS} \cdot M_{\max}^{-1}$ and M-wave amplitude (all $P > 0.05$) – indicating that resting force-generating capacity, central drive, contractile function and membrane excitability were unaffected by hormonal fluctuation (Table 2).

Table 1

Participant characteristics and phase-verification measures across menstrual-cycle phases.

Characteristic	EFP	LFP	MLP
Age (years)	25.4 ± 2.9	—	—
Body mass (kg)	57.1 ± 4.9	57.3 ± 4.8	57.2 ± 4.8
Height (m)	1.69 ± 0.04	1.69 ± 0.04	1.69 ± 0.04
BMI (kg·m ⁻²)	20.1 ± 1.5	20.2 ± 1.5	20.1 ± 1.5
Hooper index — sleep	4.9 ± 1.1	4.8 ± 1.1	4.9 ± 1.7
Hooper index — stress	2.5 ± 1.5	2.3 ± 1.5	2.7 ± 0.9
Hooper index — fatigue	3.0 ± 1.1	3.2 ± 0.5	2.9 ± 0.9
Hooper index — DOMS	1.1 ± 0.4	1.0 ± 0.8	1.2 ± 0.9
Oestradiol (pg·mL ⁻¹)	110.5 ± 20.5	215.5 ± 28.7	179.4 ± 19.2
Progesterone (ng·mL ⁻¹)	0.52 ± 0.20	0.73 ± 0.90	9.6 ± 2.9
<i>Data are mean ± SD (n = 13). Age is a single participant characteristic and is not repeated by phase. EFP, early follicular phase; LFP, late follicular phase; MLP, mid-luteal phase; BMI, body mass index; DOMS, delayed-onset muscle soreness. Hooper-index items are ordinal ratings recorded before each session.</i>			

Table 2

Neuromuscular outcomes before and immediately after the fatiguing contraction across menstrual-cycle phases.

Outcome	EFP Pre	EFP Post	LFP Pre	LFP Post	MLP Pre	MLP Post
MVC (N)	529 ± 65	364 ± 45	534 ± 86	399 ± 72	548 ± 62	341 ± 41
ΔMVC (%)	—	-30.9 ± 6.1	—	-25.2 ± 5.4	—	-37.6 ± 6.3
$Q_{tw,pot}$ (N)	137 ± 27	73 ± 11	133 ± 25	70 ± 16	129 ± 28	70 ± 15
Δ $Q_{tw,pot}$ (%)	—	-44.7 ± 13.7	—	-47.2 ± 8.6	—	-44.9 ± 9.3
VA (%)	94.6 ± 1.9	88.0 ± 2.1	95.0 ± 1.6	91.4 ± 1.8	95.4 ± 1.3	87.1 ± 1.9
ΔVA (%)	—	-7.1 ± 0.8	—	-3.8 ± 1.0	—	-8.6 ± 1.8
$RMS \cdot M_{max}^{-1}$	0.17 ± 0.05	0.17 ± 0.05	0.17 ± 0.04	0.19 ± 0.12	0.16 ± 0.04	0.16 ± 0.04
M-wave VL (mV)	3.1 ± 1.6	3.3 ± 1.8	3.1 ± 1.5	3.1 ± 1.5	2.7 ± 1.3	3.2 ± 1.6
M-wave VM (mV)	2.8 ± 1.7	2.7 ± 1.6	3.4 ± 2.4	3.4 ± 2.0	3.4 ± 1.5	2.9 ± 1.5
M-wave RF (mV)	4.1 ± 1.3	4.7 ± 2.3	4.6 ± 2.2	5.6 ± 3.5	5.3 ± 2.5	5.9 ± 2.7
<i>Data are mean ± SD (n = 13). Pre, before exercise; Post, immediately after exercise. Phase × exercise interaction: MVC $P < 0.001$; VA $P < 0.001$; $Q_{tw,pot}$ $P = 0.72$; $RMS \cdot M_{max}^{-1}$ $P = 0.51$; all M-waves $P \geq 0.19$. Main effect of exercise: $P < 0.001$ for MVC, $Q_{tw,pot}$ and VA. MVC, maximal voluntary contraction; $Q_{tw,pot}$, potentiated twitch amplitude; VA, voluntary activation; $RMS \cdot M_{max}^{-1}$, root-mean-square EMG normalised to maximal M-wave; VL, vastus lateralis; VM, vastus medialis; RF, rectus femoris.</i>						

The fatiguing contraction reduced force in every phase, with a large main effect of exercise on MVC ($F_{1,12} = 517.9$, $P < 0.001$, $\eta^2_p = 0.98$), potentiated twitch amplitude ($F_{1,12} = 168.4$, $P < 0.001$, $\eta^2_p = 0.93$) and voluntary activation ($F_{1,12} = 773.9$, $P < 0.001$, $\eta^2_p = 0.98$). Time to task failure did not differ across phases ($F_{2,24} = 0.26$, $P = 0.77$; EFP 92.2 ± 36.3 s, LFP 91.8 ± 31.5 s, MLP 86.4 ± 28.5 s), indicating that phase-dependent differences in fatigue reflected the magnitude of neuromuscular impairment rather than endurance capacity. The magnitude of impairment depended on MC phase for the global and central indices but not for the peripheral ones.

Global fatigue (MVC). A phase × exercise interaction was observed for MVC ($F_{2,24} = 9.85$, $P < 0.001$, $\eta^2_p = 0.45$). The relative reduction in MVC was greatest in the MLP (-37.6% [-41.4, -33.8]), intermediate in the EFP (-30.9% [-34.6, -27.2]) and smallest in the LFP (-25.2% [-28.5, -22.0]). The MLP loss exceeded that of the LFP (difference 12.3% [6.3, 18.4]; $d_{rm} = 2.11$, $P = 0.002$) and the EFP (6.6% [2.3,

11.0]; $d_{rm} = 1.07$, $P = 0.018$), whereas the EFP and LFP did not differ after Bonferroni correction (5.7% [0.7, 10.7]; $d_{rm} = 0.99$, $P = 0.090$).

Central fatigue (voluntary activation and normalised EMG). A large phase $\times$ exercise interaction was observed for voluntary activation ($F_{2,24} = 55.2$, $P < 0.001$, $\eta^2_p = 0.82$). The reduction in VA was graded, being greatest in the MLP (-8.6% [$-9.7, -7.5$]), intermediate in the EFP (-7.1% [$-7.6, -6.6$]) and smallest in the LFP (-3.8% [$-4.4, -3.2$]). All pairwise contrasts remained significant after Bonferroni adjustment: the LFP differed from the EFP (3.3% [2.6, 4.0]; $d_{rm} = 3.63$, $P < 0.001$) and the MLP (4.9% [3.7, 6.0]; $d_{rm} = 3.28$, $P < 0.001$), and the MLP differed from the EFP (1.6% [0.4, 2.7]; $d_{rm} = 1.07$, $P = 0.031$). Normalised EMG activity ($\text{RMS} \cdot M_{\max}^{-1}$) showed neither an interaction ($F_{2,24} = 0.70$, $P = 0.51$) nor any main effect (both $P > 0.37$), indicating that the phase-dependent central impairment was not accompanied by a detectable change in normalised muscle activation.

Peripheral fatigue ($Q_{tw,pot}$ and M-wave). Potentiated twitch amplitude declined comparably across phases, with no phase $\times$ exercise interaction ($F_{2,24} = 0.33$, $P = 0.72$, $\eta^2_p = 0.03$) and no between-phase difference in relative change (EFP -44.7% [$-53.0, -36.5$], LFP -47.2% [$-52.4, -42.1$], MLP -44.9% [$-50.5, -39.3$]; all adjusted $P = 1.00$). M-wave amplitude was unaffected by exercise or phase in all three muscles (all interaction $P \geq 0.19$), indicating preserved sarcolemmal excitability across the cycle.

Discussion

This study examined the influence of MC phase on neuromuscular fatigue induced by a sustained isometric contraction to task failure in trained eumenorrheic women. The principal findings are threefold. First, baseline neuromuscular function was unaffected by phase. Second, the exercise-induced loss of MVC and of VA was greatest in the mid-luteal phase, whereas peripheral contractile and membrane indices were comparable across phases. Third, the phase gradient was clearest for voluntary activation, which differed between all three phases. Because the substantial peripheral fatigue (a $\sim 45\%$ fall in $Q_{tw,pot}$) was invariant across the cycle, the phase-dependent differences in overall fatigability were necessarily carried by the central component rather than the peripheral one.

At baseline, MVC, voluntary activation, potentiated twitch amplitude, normalised EMG and M-wave characteristics were unaffected by MC phase, in line with previous reports of stable resting neuromuscular performance across the cycle^{2,10,35,36}. The preserved peripheral indices indicate stable sarcolemmal excitability and contractile function before exercise, consistent with limited effects of the cycle on peripheral properties^{9,37}. Discrepant reports of greater strength near ovulation or reduced force in the luteal phase^{23,38,39} are likely attributable to methodological differences in contraction type, modality, training status and phase verification; the present design mitigated several of these through standardised timing, ovulation testing and hormonal confirmation.

The fatiguing protocol reduced MVC in all phases, and the magnitude of this reduction was greater in the MLP than in either follicular phase, while the two follicular phases did not differ after correction. This indicates that cyclic hormonal fluctuation modulates the development of fatigue rather than resting force capacity, and accords with reports of reduced fatigue resistance during the luteal phase^{9,23,40}. It should be emphasised that the statistically robust MVC contrast was between the MLP and the follicular phases; the numerically greater loss in the EFP than the LFP did not survive correction and should not be interpreted as an established follicular-phase difference.

The greater MVC loss in the MLP was accompanied by, and is most parsimoniously attributed to, greater central fatigue. VA declined after exercise in all phases but markedly more so in the MLP, and uniquely among the outcomes differed between all three phases, tracking the hormonal profile such that the high-oestrogen, low-progesterone late follicular phase showed the smallest reduction. Because VA reflects the capacity of the central nervous system to drive the motor pool maximally, these data indicate a greater impairment of voluntary drive during the luteal phase. Two caveats temper this interpretation. First, the interpolated-twitch technique quantifies the completeness of voluntary activation but cannot localise the deficit to cortical, subcortical or spinal sites; the present data therefore identify a central impairment without specifying its origin. Second, although the between-phase differences in VA loss were statistically clear and associated with large standardised effects, the absolute differences (≈ 1.6 – 4.9 percentage points) were modest, and their functional relevance for athletic performance requires cautious appraisal.

Mechanistically, the larger VA reduction in the MLP is consistent with a progesterone-related enhancement of central inhibition. Progesterone and its neuroactive metabolites potentiate GABA_A-mediated inhibition and can increase short-interval intracortical inhibition, which may diminish the maintenance of voluntary drive during fatiguing exercise^{13,36,41}, whereas the high oestrogen of the late follicular phase may attenuate central fatigue by reducing inhibitory neurotransmission and enhancing excitability⁷. These mechanisms were not measured in the present study; the association between the elevated mid-luteal progesterone and the greater central fatigue is therefore consistent with, but does not establish, a causal hormonal pathway.

The absence of any phase effect on normalised EMG ($\text{RMS} \cdot \text{M}_{\text{max}}^{-1}$) does not contradict the VA findings. Surface EMG and the interpolated twitch interrogate different facets of neuromuscular activation: $\text{RMS} \cdot \text{M}_{\text{max}}^{-1}$ reflects the net motor output reaching the sarcolemma and is sensitive to amplitude cancellation and to changes in the compound action potential, whereas the interpolated twitch indexes the central capacity to recruit and drive the motor pool maximally. The two measures can therefore diverge, and the unchanged normalised EMG is best read as an absence of a detectable phase effect on that specific index rather than as evidence against a central mechanism. Likewise, the stable M-wave amplitudes indicate preserved muscle-membrane excitability under the present conditions, rather than proof of wholly unchanged neuromuscular transmission.

Peripheral fatigue contributed substantially to the overall performance decline, as shown by the marked post-exercise reduction in potentiated twitch amplitude across all phases, most plausibly reflecting disturbances of excitation–contraction coupling. Crucially, the magnitude of this peripheral impairment was comparable across MC phases, indicating that ovarian-hormone fluctuation did not detectably modify the contractile impairment induced by sustained submaximal exercise. Candidate intracellular mechanisms — impaired sarcoplasmic-reticulum calcium handling, inorganic-phosphate accumulation and intracellular acidosis^{42,43} were not assessed here and their specific contribution remains speculative.

Finally, time to task failure did not differ between phases despite the greater central fatigue in the MLP, indicating that endurance of a sustained submaximal contraction is not determined solely by the degree of post-exercise neuromuscular impairment. Similar task durations can coexist with different end-exercise neuromuscular states because task tolerance also depends on factors — pacing, motivation, afferent feedback and perceived exertion — that were not quantified here; this dissociation is therefore described rather than mechanistically explained.

Methodological considerations. Several limitations warrant consideration. The final sample was small ($n = 13$), which constrained statistical power for the smaller contrasts (notably the EFP–LFP MVC comparison) and limited the resolution of interindividual variability; no a priori sample-size calculation was reported, so the sample should not be regarded as demonstrably sufficient. The interpolated-twitch technique validly separates central from peripheral fatigue but cannot distinguish spinal from supraspinal mechanisms; transcranial magnetic stimulation would be required to refine the cortical and corticospinal interpretation. Metabolic and biochemical markers were not assessed, precluding direct evaluation of the intracellular mechanisms of peripheral fatigue. Phase timing relied on calendar windows anchored to menstrual diaries; although reinforced by urinary ovulation testing and serum oestradiol and progesterone, this approach remains susceptible to residual misclassification. Finally, only trained eumenorrheic women not using hormonal contraception were studied, so the findings do not extend to contraceptive users or to women with irregular cycles. Set against these limitations, the study's strengths include a within-participant repeated-measures design, a randomised counterbalanced session order, a familiarisation visit and hormonal confirmation of phase.

Conclusion

Menstrual-cycle phase modulates exercise-induced neuromuscular fatigue in trained eumenorrheic women. Although baseline neuromuscular function was similar across phases, the reductions in maximal voluntary contraction and voluntary activation after exhaustive isometric exercise were greatest in the mid-luteal phase, with voluntary activation differing between all three phases and being smallest in the late follicular phase. Peripheral contractile fatigue was comparable across phases, indicating that the phase-related differences in overall fatigability were attributable to central rather than peripheral mechanisms. These findings are consistent with the possibility that the elevated-progesterone mid-luteal environment may contribute to reduced voluntary neural drive, whereas the high-oestrogen, low-

progesterone late follicular environment may attenuate this effect, although the underlying hormonal and neural mechanisms require direct investigation. The results support consideration of menstrual-cycle phase when evaluating neuromuscular fatigue in female athletes, without implying broader prescriptive recommendations beyond the exercise studied here.

Declarations

Ethics approval and consent to participate.

The study was approved by the Comité de Protection des Personnes du Sud (N° 0102/2025) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent prior to enrolment. The trial was registered in the Pan African Clinical Trial Registry (PACTR202607859511123; registered 17/07/2026).

Competing interests.

The authors declare no competing interests.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not Applicable

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Author Contribution

M.A.B., S.H. and F.Z. conceptualised the study. S.H. and W.D. developed the methodology. S.H., I.B.H., S.R. and M.A.B. performed the formal analysis. S.H. and M.A.B. conducted the investigation. S.H. curated the data. S.H., W.D., S.R. and I.B.H. prepared the original draft. S.H., W.D. and F.Z. reviewed and edited the manuscript. M.A.B. and W.D. supervised the work. M.A.B. and F.Z. administered the project.

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Data Availability

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request, subject to approval by the Comité de Protection des Personnes du Sud.

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Figures

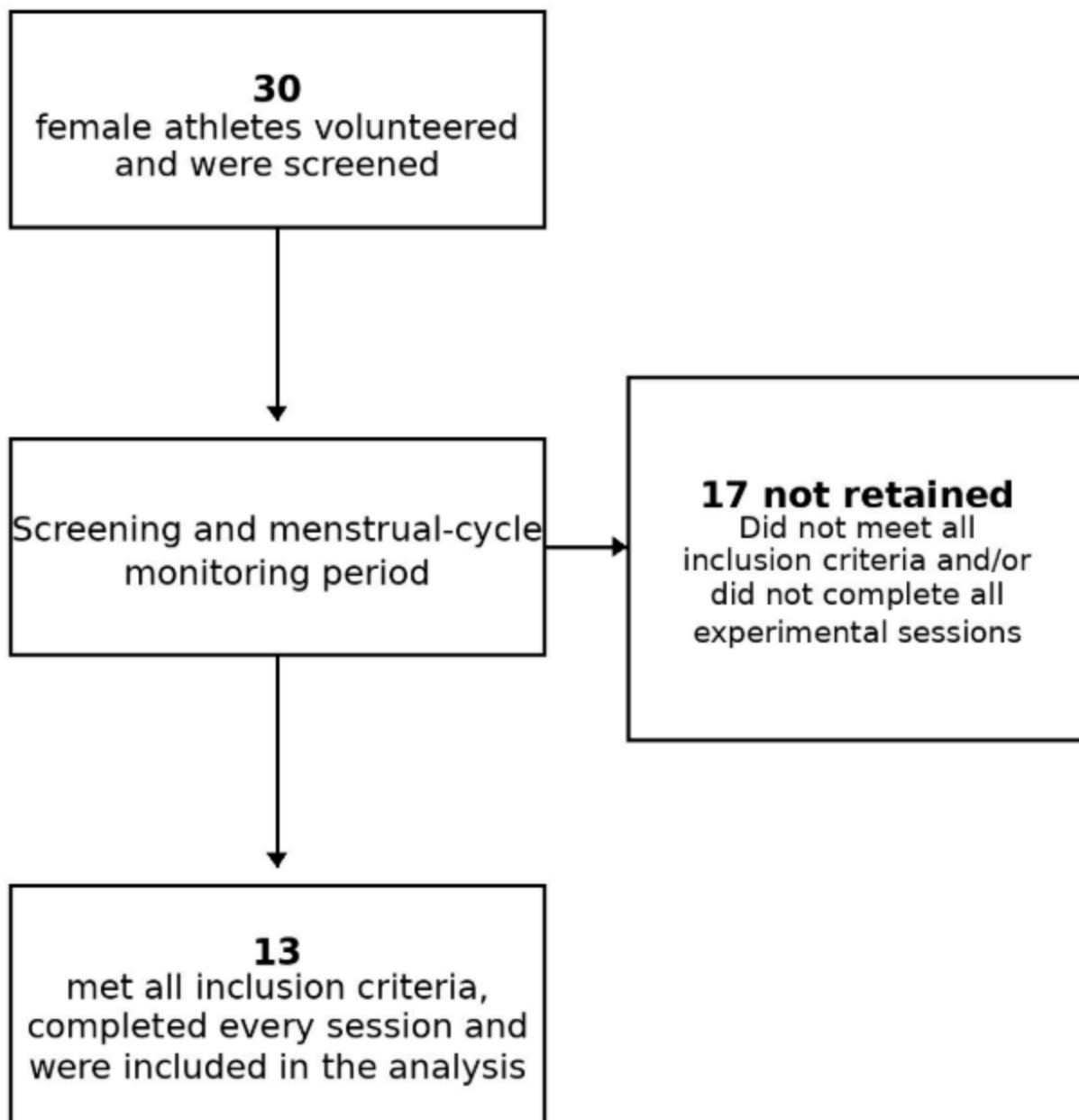


Figure 1

Flow of participants through the study.

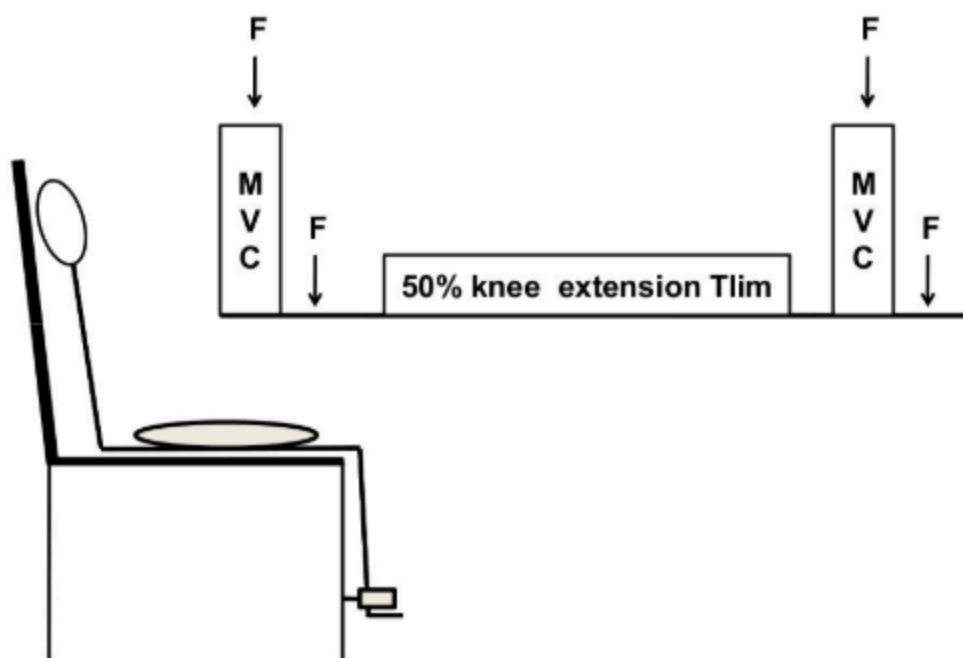


Figure 2

Schematic of the exercise protocol. Neuromuscular function was assessed before and after exercise using femoral nerve stimulations (F). MVC, maximal voluntary contraction; T_{lim}, time to task failure.

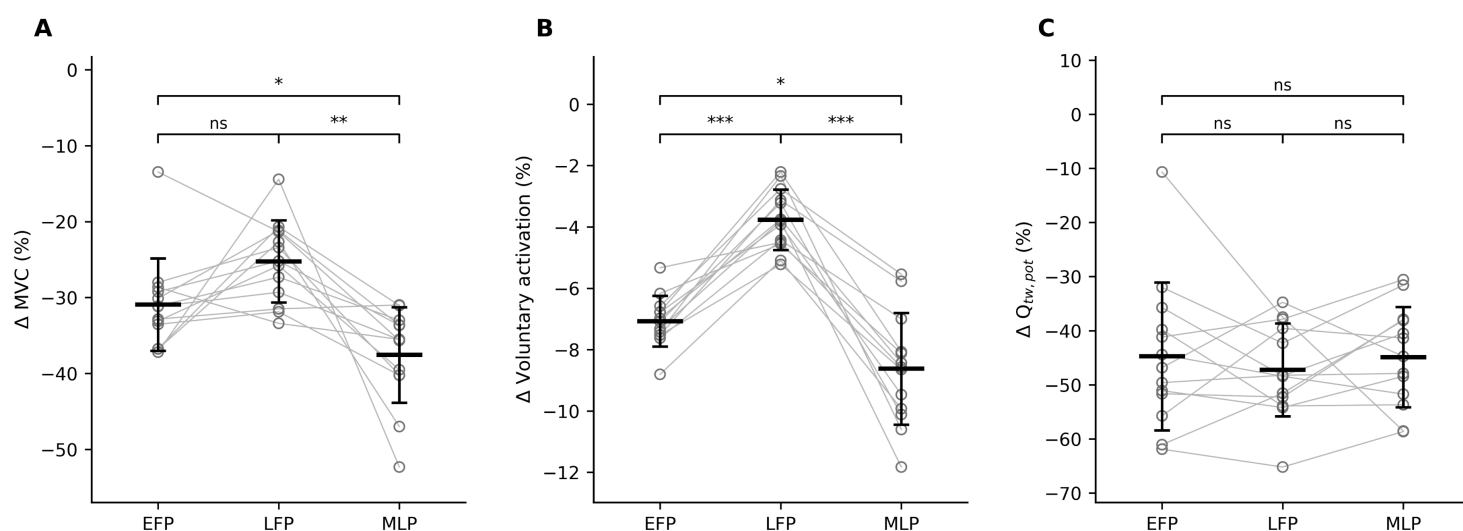


Figure 3

Exercise-induced relative change (Δ%) in (A) maximal voluntary contraction (ΔMVC%), (B) voluntary activation (ΔVA%) and (C) potentiated twitch amplitude (ΔQ_{tw,pot}%) during the early follicular (EFP), late follicular (LFP) and mid-luteal (MLP) phases (n = 13). Hollow circles are individual participants and thin grey lines connect each participant across phases; the horizontal bar and whiskers denote the mean ±

SD. Brackets show Bonferroni-adjusted pairwise comparisons of the estimated marginal means: *P < 0.05, **P < 0.01, ***P < 0.001; ns, not significant. More negative values indicate greater exercise-induced fatigue.

Supplementary Files

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