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DETERMINATION OF SENSORY PERCEPTION AND MOTOR RESPONSE THRESHOLDS IN DIFFERENT PHASES OF THE MENSTRUAL CYCLE

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ABSTRACT

Objective: To identify the variation of sensory perception and motor response in the different phases of the menstrual cycle. Method: Thirty women aged 18 to 40 years old (23.7 ± 3.60), with body mass index between 18.5 and 25kg/m² (21.15 ± 2.32) and menstrual cycle of 21-35 days, participated in this study. A pulse generator was used, with pulsed electric current frequency of 50Hz and variable phases of 20 (L20), 50 (L50), 100 (L100), 300 (L300), 500 (L500), 1000 (L1000) and 3000µs (L3000). The threshold of sensory perception (TSP) was identified as the first sensation of increased current intensity and the threshold of motor response (TMR) as the minimum muscle contraction detected. Five collections were done, at each of the following phases: phase 1- menstrual (P1), phase 2- follicular (P2), phase 3- ovulatory (P3), phase 4- luteal (P4) and phase 5- premenstrual (P5). The data analysis consisted of the Friedman test followed by the Rank test, carried out in the BioStat 4.0® software, with a significance level of 5%. Results: The TSP was lower in P5 than in the other menstrual phases, for the L20, L300, L500, L1000 and L3000 currents. For the TMR, there was difference in the L20, L50, L500 and L1000 currents between P5 and all other phases; in the L100 current, between P1 and P5; and in the L300 and L3000 currents for P1, P2 and P3 versus P5. Conclusions: The thresholds of sensory perception and motor response varied systematically through the phases of the menstrual cycle, thus influencing motor-sensory behavior.

Key words: menstrual cycle; estrogen; progesterone; electrical stimulation of transcutaneous nerves.

RESUMO

Determinação dos limiares de percepção sensorial e de resposta motora nas diferentes fases do ciclo menstrual

Objetivo: Identificar a variação de percepção sensorial e resposta motora nas diferentes fases do ciclo menstrual (CM). Método: 30 mulheres com idade entre 18 e 40 anos (23,7 ± 3,60), com índice de massa corporal entre 18,5 e 25kg/m² (21,15 ± 2,32) e CM entre 21-35 dias participaram do estudo. Utilizou-se um gerador de pulso com correntes elétricas pulsadas, freqüência de 50Hz e fases variando em 20 (B20), 50 (B50), 100 (B100), 300 (B300), 500 (B500), 1000 (B1000) e 3000µs (B3000). O limiar de percepção sensorial (LPS) foi identificado como a primeira sensação de corrente ao aumento da intensidade e o limiar de resposta motora (LRM) como a mínima contração muscular detectada. Realizaram-se cinco coletas, sendo uma em cada fase: fase 1- menstrual (F1), fase 2- proliferativa (F2), fase 3- ovulatória (F3), fase 4- lútea (F4) e fase 5- pré-menstrual (F5). A análise dos dados constou do teste de Friedman seguido do teste de Rank, realizados no programa Bioestat 4.0®, com nível de significância de 5%. Resultados: O LPS foi menor na F5 quando comparado às demais fases menstruais, para as correntes B20, B300, B500, B1000, B3000. Para o LRM houve diferença nas correntes B20, B50, B500 e B1000 entre todas as fases com a F5; na corrente B100, entre a F1 e F5; e nas correntes B300 e B3000 entre F1, F2 e F3 com a F5. Conclusões: O limiar de percepção sensorial e a resposta motora variaram sistematicamente através das fases do CM, influenciando o comportamento sensório-motor.

Palavras-chave: ciclo menstrual; estrogênio; progesterona; estimulação elétrica nervosa transcutânea.

INTRODUCTION

For many years, the female gender was considered an exclusion criterion from scientific research because of the physiological instability that results from the hormonal variation of the menstrual cycle (MC)[1,2]. However, the discovery that female sexual hormones, particularly estrogen (E_2) and progesterone (P_4), can have not only a reproductive role but also neuroactive effects of modulation on cerebral functions[3] is a watershed for women and their reproductive cycle and represents a potential source of answers to the countless questions on female specificity.

Researchers suggest that the serum levels of sexual steroids in blood plasma during the menstrual phases and their relationship with specific receptors located in various regions of the brain are capable of influencing bodily responses[4]. Such evidence is further supported when we consider the high prevalence, in reproductive-age women, of chronic and behavioral illnesses, such as fibromyalgia, rheumatoid arthritis, temporomandibular disorders, and mood disorders, besides the higher sensitivity to epidemiological and experimental tests, when compared to the male gender[5].

In literature, studies try to analyze the different physiological, physical, and behavioral responses throughout the menstrual phase. However, there is little consistency in data presentation and extensive disagreement and contradiction among the methodologies used by existing studies[6]. Among the many responses influenced by the female sex hormones are the variations in sensory perception and motor response, which are extremely relevant in the clinical area, given that the stimulation of sensitive and motor nerves influences the rehabilitation process of various illnesses.

Because transcutaneous electrical nervous stimulation is considered one of the most reliable and effective resources for neuromuscular rehabilitation, and considering the great variability of usable types of electric currents, it is valid to analyze the variations in nervous thresholds during the menstrual phases, with different parameters, in the attempt to obtain a more pleasant stimulation in some phases. Thus, this study aims to assess, through various electrotherapeutic currents, the threshold for sensory perception and motor response in different menstrual phases of eumenorrheic women, in order to provide more specific physical therapy procedures and safer, more effective interventions.

METHODS

Subjects

Forty volunteers were initially recruited by invitation, however 10 were excluded, 6 for having irregular periods, 2 for high body mass index, and 2 for abstaining from a data collection. The final sample comprised 30 Caucasian, sedentary, non-smoking women, aged 18 to 40 (23.7±3.60), body mass index (BMI) between 18.5 and 25 kg/m^2 (21.15± 2.32) and regular and constant MC between 21 and 35 days[7,8]. The women included in this study did not have a history of chronic endocrine, neurological, psychiatric, urogynecological, or upper-body musculoskeletal illness, of pregnancy or breastfeeding in the previous 6 months, or of systemic medication or hormonal use. All volunteers signed written informed consent, in accordance with National Health Council Resolution 196/96, and the study was approved by the Ethics and Research Committee (CEP) of the Institution under protocol 64/05.

All volunteers were advised not to alter their eating habits[9], not to ingest any caffeinated products – coffee, tea, chocolate[10], and alcoholic beverages[4,11] – or systemic medication[12] for 24 hours prior to the experiment.

Procedure

We used a Quark Dualpex 961® pulse generator for data collection, and we selected seven types of therapeutic currents, characterized as alternate electrical currents at a fixed frequency of 50 Hz, with symmetrical, square biphasic wave, and pulse-width varying in 20, 50, 100, 300, 500, 1000 and 3000μs.

Two new, silicon-carbon electrodes measuring 5x3 cm each were attached to the skin with 1mL of water-soluble gel and placed over the flexor muscles of the wrist and fingers of the non-dominant limb. Placement obeyed the longitudinal direction of the muscle fibers with the first electrode placed 4 cm from the elbow joint line and the second electrode placed 4 cm from the first[13], using hypoallergenic adhesive tape according to dermatome C6-8[14]. The stimulation device was calibrated before, during and after the experiment using a digital oscilloscope (Tektronix TDS 210).

Each volunteer was assessed in five different occasions, defined as menstrual phases, calculated from the first day of their period, wherein the menstrual phase corresponded to days 1 to 5 (P1); the follicular or proliferative phase, to days 6 to 11 (P2); the ovulatory

phase, to days 12 to 16 (P3); the luteal phase to days 17 to 23 (P4) and the premenstrual phase to days 24 to 28 (P5)[15]. For longer or shorter cycles within regular standards, there was proportional or individual differentiation, with addition or subtraction of extra days in the follicular phase, considered a variability period of the MC[2,3,7].

The cycle phases of each volunteer were identified using the information of at least six previous MCs, following the calendar recommended by Lamprecht and Gummer-Strawn[16], and the fixed days described by Arévalo, Sinal and Jennings[17]; and regularity was confirmed by at least six posterior MCs[18]. The estimate was determined by the mean sum of all analyzed cycles[8].

After the phases were individually determined, the experiment was always conducted on the mean day(s) of each phase, therefore each volunteer had a specific collection day, and the initial experimental phase coincided with the menstrual phase (P1) for 8 women, proliferative phase (P2) for 6, ovulatory phase (P3) for 4, luteal phase (P4) for 7 and premenstrual phase (P5) for 5 women.

Volunteers received prior training in order to familiarize themselves with the procedure and instruction regarding the ideal determination of thresholds[6,12,4,15]. All received sound information on the application of electrical stimuli and were oriented to describe the sensation of the current and the muscle contraction evoked by the stimulus under different testing conditions.

Before commencing data collection, the sequence of electrical currents to be applied was randomly selected. After that, the volunteer was instructed to describe the first sensation and any intensity increase in sensation of electrical current, identified as a sensory perception threshold[15]. Afterwards, the intensity would continue to increase so that a small but clear muscle contraction, known as motor response threshold, could be identified[14].

Intensity increase kept the same pace and the detection of the threshold stimulation was sequential and uninterrupted. Threshold values followed technical device specifications, varying from 0 to 60mA. After the two nervous thresholds were detected with the first selected electrical current, the amplitude was reduced to zero, a minute rest was given, and the same procedure was repeated with the parameters changed according to the second randomly selected current and so on until all seven types of electrical current were applied. At the end of the full sequence of currents, there was a 15-minute interval so that the procedure could be repeated two more times to obtain a mean.

Statistical analysis

The ideal sample size estimation was initially performed with the *Graphpad Statmate 2.0 (Power test*) software which indicated n= 16 volunteers with a power of 90% and significance level (alpha) of 0.05. All data were considered non-parametric according to the Shapiro-Wilk statistical test, then analyzed with the Friedman test, followed by the RANK test available in the Bioestat 4.0 software *p< 0.05.

RESULTS

The sensory perception threshold (SPT) displayed significant difference (*p< 0.05) for 50 Hz currents with 20ms (B20), 300ms (B300), 500ms (B500), 1000ms (B1000) and 3000ms (B3000) phases with higher values in the proliferative phase (P2) – (26.69-31.43, 43.00, 28.80, 18.30; 5.02-6.28, 9.30, 5.45, 2.60; 4.06-4.86, 7.60, 4.00, 2.60; 3.21-3.58, 4.60, 3.30, 2.30; 2.27-2.68, 4.00, 2.30, 1.60) and lower in the premenstrual phase (P5) – (23.67-28.01, 39.00, 23.60, 17.00; 4.14-5.25, 8.00, 4.15, 2.60; 3.27-4.03, 6.30, 3.30, 2.00; 2.49-2.85, 3.60, 2.60, 2.00; 1.77-2.06, 3.00, 2.00, 1.00) for the abovementioned currents respectively, with values expressed in higher and lower confidence interval, median and maximum and minimum deviation. There were also differences between the menstrual phase (P1) – (4.68-5.93, 10.00, 5.00, 3.00; 3.81-4.70, 4.00, 2.60, 2.85; 3.61-2.11, 2.52, 3.60, 1.00) and P5 for the B300, B500 e B3000 currents; between the ovulatory phase (P3) – (4.60-6.01, 11.00, 5.00, 2.60; 3.75-4.72, 8.30, 4.00, 2.60) and P5 for the B300 and B500 currents; and between the luteal phase (P4) – (3.74-4.55, 6.60, 4.00, 2.60) and P5 for the B500 current, always maintaining the lower values in P5 (Figure 1).

For the motor response threshold (MRT), there were differences between the menstrual phases for all currents analyzed. For currents B20, B50, B500 and B1000, P1 (52.09-56.40, 60.00, 54.30, 43.00; 28.70-33.97, 52.00, 30.30, 20.30; 7.82-9.17, 12.60, 8.15, 5.60, 6.05-7.25, 10.00, 6.45, 4.00), P2 (53.64-57.70, 60.00, 57.95, 41.60; 28.32-33.54, 50.00, 31.65, 19.00; 8.04-9.52, 14.60, 8.45, 6.30; 6.18-7.55, 11.60, 6.60, 4.60), P3 (51.34-57.21, 60.00, 59.15, 30.00; 30.02-35.84, 47.30, 33.15, 16.60; 7.76-9.47, 14.00, 8.15, 4.30; 5.75-7.29, 12.30, 6.30, 3.00) and P4 (52.38-56.76, 60.00, 55.95, 40.60; 29.35-34.30, 46.30, 30.00, 22.60; 7.64-9.34, 17.60, 8.15, 6.00; 6.00-7.41, 13.30, 6.30, 4.30) differed from P5 (48.23-53.23, 60.00, 52.30, 38.30; 25.90-29.53, 42.60, 27.15, 19.30; 6.68-7.85, 11.60, 7.15, 5.00; 5.12-5.98, 8.00, 5.60, 3.30) for the electrical currents respectively. For the B100 current, only P1 (17.55-20.57, 32.30, 17.45, 13.60) differed from

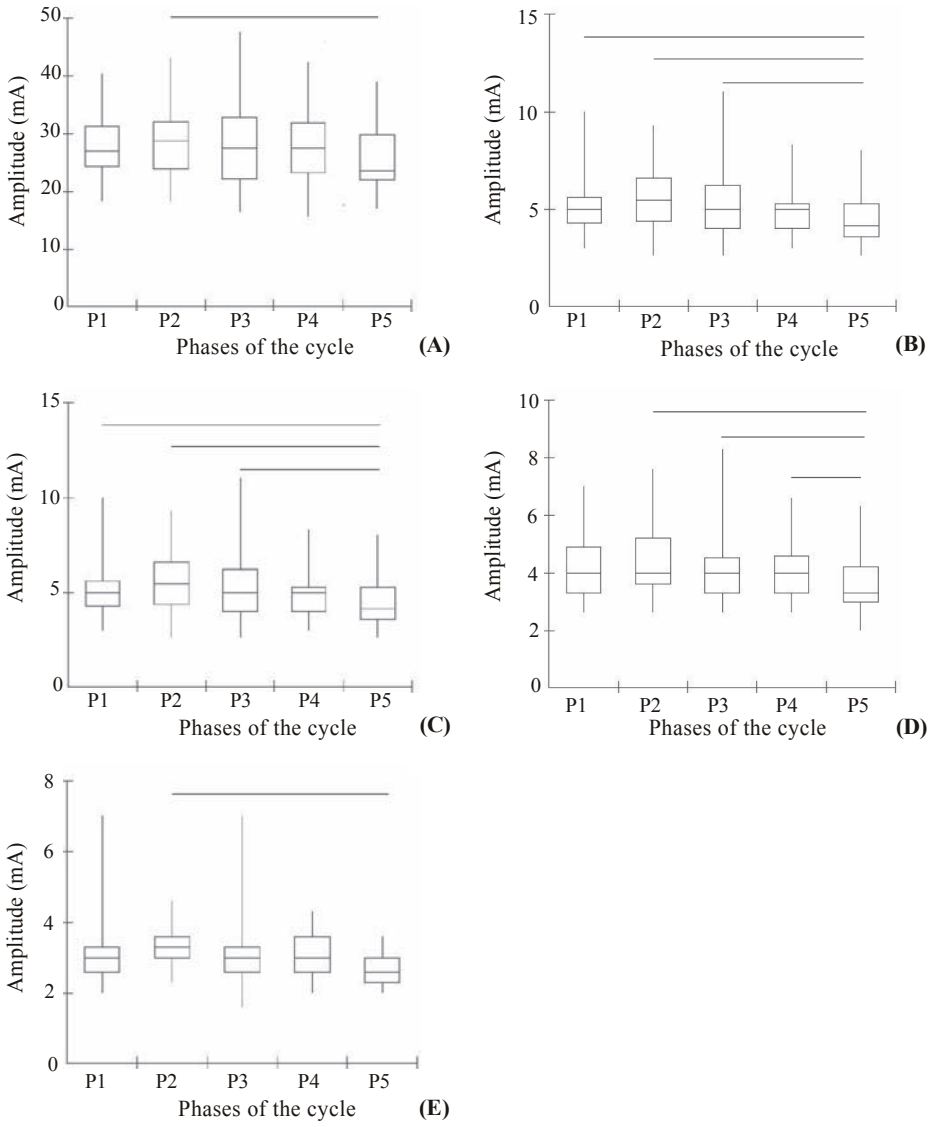

Figure 1. Sensory perception threshold (SPT) mean throughout the five phases of the menstrual cycle (MC): menstrual (P1), follicular (P2), ovulatory (P3), luteal (P4) and premenstrual (P5) for 50Hz currents and phases of 20µs (A) 300µs (B), 500µs (C), 1000µs (D) and 3000µs (E). Connective horizontal lines indicate statistical significance ($p \leq 0.05$), n=30.

P5 (16.25-19.01, 31.30, 17.00, 12.30). In the threshold of the B300 and B3000 currents, P1 (9.41-11.02, 16.30, 10.00, 7.00; 4.75-5.73, 8.30, 5.30, 3.00), P2 (9.47-11.34, 17.60, 9.80, 7.30; 5.06-6.12, 9.30, 5.30, 3.00) and P3 (9.58-11.52, 17.60, 10.30, 6.30; 4.46-5.85, 9.60, 5.00, 2.00) differed from P5 (8.52-10.47, 15.30, 8.45, 7.60; 4.75-5.23, 7.00, 4.00, 2.00), also with smaller values for P5 (Figure 2).

DISCUSSION

To obtain greater sample homogeneity and present more reliable results, we considered various factors in advance according to data explained in literature and pilot studies, factors which influence the characteristics of the menstrual cycle (MC) such as: ethnicity, age, physical activity, season, body composition and eating habits; as well as electrical stimulation processes such as: types of currents, wave types, and temperature and humidity of the surroundings.

Collected data indicated that nervous thresholds varied systematically during the MC phases, in accordance with statement by Hampson and Kimra[19] that the velocity of motor and sensory function changes with hormonal fluctuations during menstrual phases.

Lower SPTs were found in the premenstrual phase for all electrotherapeutic conditions tested. The results with significant differences were related to B20, B300, B500, B1000 and B3000 currents. Also for these currents, the highest thresholds were found in the proliferative

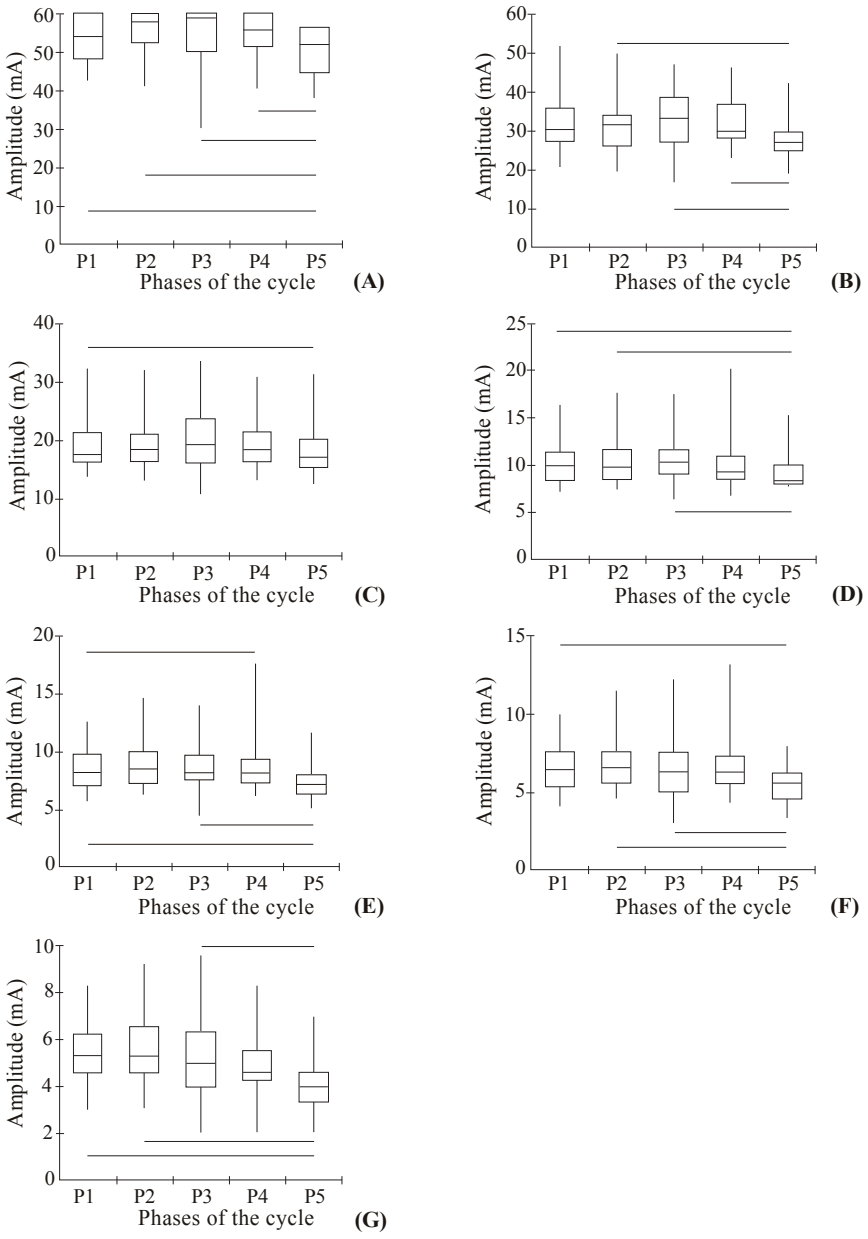

Figure 2. Motor response threshold (MRT) mean throughout the five phases of the menstrual cycle (MC): menstrual (P1), follicular (P2), ovulatory (P3), luteal (P4) and premenstrual (P5) for 50 Hz currents and phases of 20μs (A), 50μs (B), 100μs (C), 300μs (D), 500μs (E), 1000μs (F) and 3000μs (G). Connective horizontal lines indicate statistical significance ($p \leq 0.05$), n=30.

phase, demonstrating that sensibility to nervous stimuli varies and displays higher values when estrogen levels (E_2) are higher[20].

A study[21] that used transcutaneous electrical stimulation to assess variations in sensory perception with three different currents (5Hz, 250Hz and 2000 Hz) showed that there was no change in response between the proliferative phase (7th day after menstruation) and the luteal phase (21st day after menstruation). However, in subjects who had been pregnant, there was a higher threshold for myelinated fibers, which was attributed to high progesterone (P_4) and endogenous opioids during pregnancy.

Given that E_2 and P_4 are capable of influencing the endogenous opioid system (endorphins, enkephalins, beta-endorphins, met-enkephalins), contributing in an analgesic[22] fashion, it is possible that their sharp decline reduces the influences on these substances and manifests greater sensibility in the premenstrual phase[10].

It is also believed that the decline in P_4 at the end of the luteal phase and during all of the premenstrual phase increases anxiety and other common symptoms of premenstrual syndrom (PMS), negatively influencing sensory perception[23].

Another factor that may explain the high thresholds

in the proliferative phase and the low threshold in the premenstrual phase can be seen in the E_2 relationship with the limbic system. According to Edward et al.[24], high E_2 levels greatly influence the hippocampal regions and paraventricular nuclei because of the great concentration of specific receptors in the internal neural membranes. In other words, the high concentration of E_2 receptors seems to allow changes in the action of neurotransmitters, which are capable of reducing the action discharge and consequently controlling emotional and behavioral activities, while increasing common responses to the premenstrual phase (anxiety, emotional instability and irritability).

The motor response threshold displayed even more significant variation between menstrual phases, with higher values found in the proliferative and ovulatory phases and the lowest values in the premenstrual phase. There were also variations between the menstrual phase and the premenstrual phase for all currents and between the luteal phase and the premenstrual phase for B20, B50, B500 and B1000, in accordance with most literary data that assessed the effects of sexual hormones on the neuromuscular system. Studies by Woolley[25] indicate that this can be explained by the possible genomic effects of E_2 and its arousal function in cortical regions related to muscle contraction.

Inghilleri et al.[26] found that evoked motor potential is progressively increased according to parallel E_2 increase throughout the phases. The authors suggest that the interaction of E_2 with the glutamate receptors increases hippocampal excitability, both by opening sodium channels and by indirectly causing density increase in dendritic spines and specialized synapses.

E_2 level elevations in the proliferative phase and its peak in the ovulatory phase influence motor behavior through a permissive action in the arousal mechanisms of the motor cortex[27], aiding motor and sensory functions including activities which require attention and coordination[28]. Moreover, the physical performance of female athletes was found to be better during the follicular period and worse in the premenstrual phase and on the first days of menstruation[29].

The fact that there were variations between the menstrual and premenstrual phase is also due to differences in hormonal plasma conditions. The menstrual phase presents a gradual increase in E_2 as the days progress showing evidence of facilitation periods. The differences between luteal and premenstrual phases, on the other hand, can be explained by the inhibitory actions of progesterone (P_4), which aid the opening of chlorine channels and prolong the inhibitory influence of the GABAa neurotransmitter on motor cortex neurons[30].

Based on the present findings, we conclude that the hormonal conditions of the menstrual cycle influence motor and sensory functions of eumenorrheic women because they display lower sensory perception and motor response thresholds in the premenstrual phase. Therefore greater attention is recommended to the menstrual phases of reproductive-age women to find favorable conditions for the use of transcutaneous nervous electrical stimulation.

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