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ORIGINAL RESEARCH

Sex Hormone Levels and Pain Thresholds in the Luteal Phase of Healthy Women

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Objective: To explore the relationship between the level of endogenous sex hormones in the luteal phase and the pain threshold of healthy subjects, and to find the influencing factors of the change in female pain threshold.

Methods: Sixty-eight unmarried and nulliparous women, aged 22–28 years old, had regular menstruation with a cycle of 26–30 days, did not smoke, had no pain, no drug abuse, no gynecological problems, and had not participated in other clinical trials in the past 3 months. Blood was collected for analysis of sex hormone concentrations including follicle-stimulating hormone (FSH), luteinizing hormone (LH), and four different pain thresholds were measured after abdominal ultrasound confirmed that the menstrual cycle was in the luteal phase.

Results: During the luteal phase, a greater cold pain threshold was correlated with lower FSH (β=−0.743, *P*=0.012). A greater ischemic pain threshold was correlated with higher LH concentrations (β=1.397, *P*=0.011). A lower needle pain threshold was associated with higher FSH concentrations (β=0.32, *P*=0.006), which could explain 19.8% of the total variance of pain from a needle used to draw blood pain threshold.

Conclusion: The needle pain threshold, cold pain threshold, ischemic pain threshold in the luteal phase of female healthy volunteers was, respectively, correlated with the concentrations of FSH or LH. These findings suggest that when formulating pain management strategies for women, the level of sex hormone concentrations should be considered, especially during the luteal phase, which may help provide more precise pain interventions for female patients and improve their pain experience.

Keywords: follicle-stimulating hormone, luteinizing hormone, pain threshold, female healthy volunteers, luteal phase

Introduction

According to epidemiological and clinical studies, females have a higher risk of experiencing pain (eg migraine, fibromyalgia, rheumatoid arthritis or reflex sympathetic dystrophy and other painful conditions), with a significantly higher incidence than that of males.[1,2] Females may also have a higher incidence of acute and chronic postoperative pain.[3,4] Females' pain sensitivity may change at different stages of the menstrual cycle or physiological stages. For instance, studies have demonstrated females have intensified injection pain, incisional pain, and postoperative pain 12 h after surgery in the luteal phase compared to the follicular phase,[5–7] as well as aggravated postoperative pain and chronic postoperative pain during the menses.[8] Different phases of the menstrual cycle are characterized by fluctuations in sex hormone concentrations, suggesting that sex hormone profiles may be an important factor affecting pain sensitivity.[9] However, the relationship between sex hormone concentration and pain sensitivity is unclear.[10] For example, some scholars find no obvious difference in females' pain response at any stage of the menstrual cycle.[11,12] Therefore, more in-depth studies are needed to elucidate the relationship between menstrual cycle and pain sensitivity.

Prior studies mainly explored the relationship of estradiol (E2), progesterone (P), and testosterone (T) with pain, showing shortcomings of limited sex hormone types and no consideration of different stages of the menstrual cycle, resulting in inconsistent baseline data.[13] In some studies, estrogen was found to have an analgesic effect, while

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progesterone could increase pain sensitivity.[14,15] Nevertheless, these studies were performed in small samples with varied experimental designs and methods, making it difficult to compare and integrate results. Given the above contradictions and limitations, this study was carried out to evaluate the relationship between sex hormone concentrations in the luteal phase and pain thresholds in female healthy volunteers for further clarification of the relationship between sex hormones and pain sensitivity. This study measured the concentrations of six sex hormones, including E2, P, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), and testosterone (T), and adopted four pain measurements of mechanical pain, cold pain, ischemic pain, and needling pain thresholds. FSH and LH are known to modulate pain through various pathways and receptors. For example, FSH can activate the endocannabinoid-degrading enzyme fatty acid amide hydrolase, reducing cannabinoid concentrations and thereby decreasing the fatty acid amide hydrolase (FAAH), with a critical impact on Sertoli cell proliferation, and thus spermatogenesis and male reproduction.[16] A large volume of research investigating the fluctuation of pain sensitivity at different hormonal stages in animals and healthy women exists. For example, tailflick latencies are reduced in ovariectomized rats following estrogen administration.[17,18] In humans, however, the experimental results are far more inconsistent. For example, both lower and higher pain sensitivity has been reported during the luteal phase.[19–21] The inconsistent results may be attributable to the crude approach to define menstrual phases, namely depending on the number of days since the menstrual onset without confirming the hormonal concentrations. Recently, Fillingim et al[21] tested 11 healthy, naturally menstruating women at 3 points during a menstrual cycle: mid-follicular; ovulatory; and mid-to-late luteal phases. Women exhibited a phasic change in pain threshold and tolerance only to the ischemic but not noxious heat. Women showed significantly greater threshold and tolerance to ischemic pain during the mid-follicular phase compared to the other two phases. Generally, the hormone concentrations were not associated with ischemic threshold or tolerance except for progesterone with threshold only during the ovulatory phase.[22] Unfortunately, the phasing did not include a time point when estrogen was low. In addition, the study in fibromyalgia revealed a correlation of the progesterone level in the luteal phase with the degree of increase of TRPV1 level, as well as with the degree of decrease of heat pain threshold. The relationship between the degree of pain threshold, as well as TRPV1 level with FSH, LH hormones, and prolactin concentrations was not found. Also, there was no correlation between TRPV1 or heat pain threshold levels and aggression degree.[23]

Given the above contradictions and limitations, this study was carried out to evaluate the relationship between sex hormone concentrations in the luteal phase and pain thresholds in female healthy volunteers for further clarification of the relationship between sex hormones and pain sensitivity. Additionally, we assessed participants' levels of depression, anxiety, sleep quality, and pain catastrophization to explore potential psychological and emotional factors that may influence pain thresholds. These factors have been shown to affect pain perception in various populations, and their inclusion in this study helps to provide a more comprehensive understanding of the factors contributing to pain sensitivity in females.

Data and Methods

This study was approved by the Ethics Committee of Zhengzhou University People's Hospital [2021 Ethical Review No. (166)], and all healthy volunteers signed informed consent forms voluntarily. This study included 68 healthy female volunteers from January 1, 2022 to May 31, 2022. Inclusion criteria: unmarried females aged 22–28 years, with normal menstrual cycle (26–30 days), no history of pregnancy, no smoking history, no pain (eg, chronic pain, acute pain, etc), no drug abuse (including but not limited to opioids, antidepressants, anti-anxiety agents, etc), no history of gynecological diseases (eg, endometriosis, ovarian cysts, etc), and no participation in other clinical trials in the past 3 months. Exclusion criteria: females with skin abnormalities; Eczema: Characterized by red, itchy, and inflamed skin, which can increase skin sensitivity; Psoriasis: A condition that causes red, scaly patches on the skin, potentially affecting pain perception; Severe acne: Inflammation and irritation caused by severe acne could alter skin sensitivity and pain responses. By excluding participants with these skin abnormalities, we aimed to maintain the integrity of the study's findings and ensure that the relationship between sex hormone concentrations and pain thresholds is accurately assessed, pelvic ultrasound abnormalities, luteal phase defect or anovulation, any form of peripheral neuropathy (eg, diabetes neuropathy, alcoholic neuropathy, etc), mental illness or receiving psychiatric medication.

Luteal phase defects were determined through a combination of ultrasound examination and serum progesterone levels. A qualified ultrasound specialist conducted daily ultrasound examinations to monitor the development and regression of the corpus luteum. A luteal phase defect was defined as the absence of a well-formed corpus luteum or a short luteal phase (less than 10 days) as observed on ultrasound. Additionally, serum progesterone levels were measured on the 21st day of the menstrual cycle. A progesterone level below 10 ng/mL was considered indicative of a luteal phase defect, as this level is typically insufficient to maintain a normal luteal phase.[14] The luteal phase was determined based on ultrasound examination by a qualified ultrasound specialist and menstrual duration of healthy volunteers. Starting from the time of signing informed consent forms and confirming participation in the study by the participants, ultrasound examinations were conducted daily to determine the ovulation date and luteal phase. Ovulation could be confirmed when observing the presence and then disappearance of dominant follicles of 16–28 mm in diameter on abdominal ultrasound (Figure 1), with or without detectable fluid in the Douglas bag. After the confirmation of ovulation, the luteal phase can be identified considering menstrual duration (about 5–9 days after ovulation) and thickened endometrium by ultrasound (Figure 2).[11]

After the participants were confirmed to be in the luteal phase, pain threshold measurements and sex hormone concentration testing were conducted from 2:00 pm to 4:00 pm. Participants were informed of the testing instructions prior to measurement. Then, pain threshold measurements were conducted by two researchers who were blinded to the participants' menstrual cycle stages. The pain threshold measurement consisted of mechanical pain, cold pain, ischemic pain, and needling pain.

Cold pain threshold: According to the method described in published literature,[12] participants were instructed to place the non-dominant hand in ice water at 0.1~1°C from the water surface to the wrist, without touching the bottom of the container. This study recorded the time from when the participants put their hand in the water until they felt pain, which was the cold pain threshold. It was defined as "unbearable cold pain in the hand".

Ischemic pain threshold: As described previously,[13] participants were instructed to raise their right arms above the heart level for 30s, followed by the attachment of a standard Blood Pressure Cuff at the proximal end of the elbow and

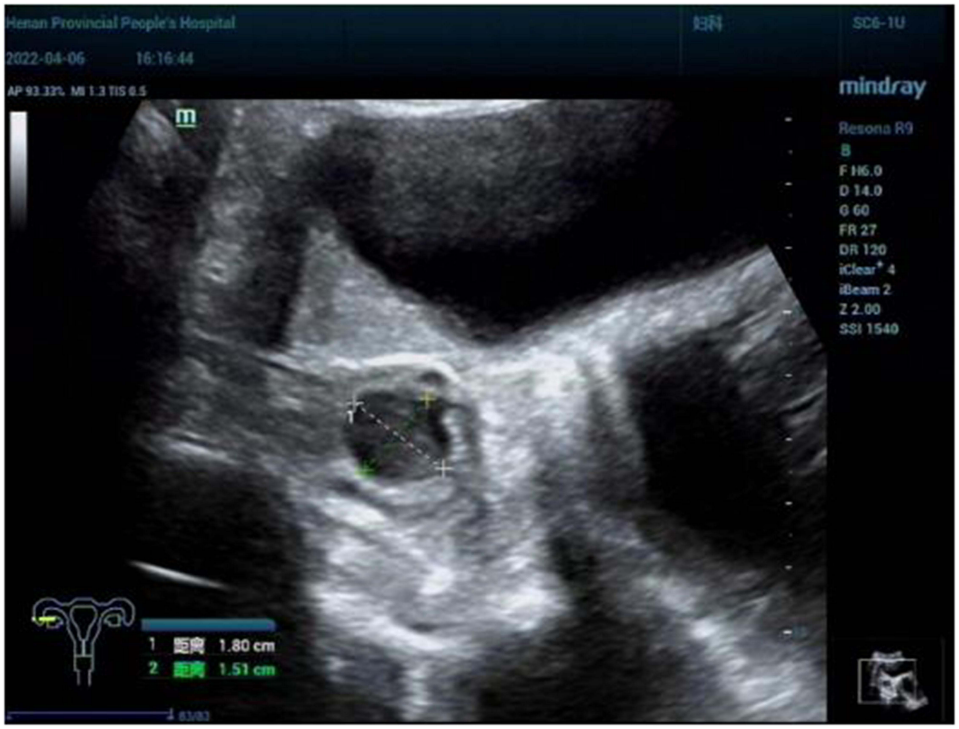

Figure 1 Ultrasonic image of the dominant follicle.

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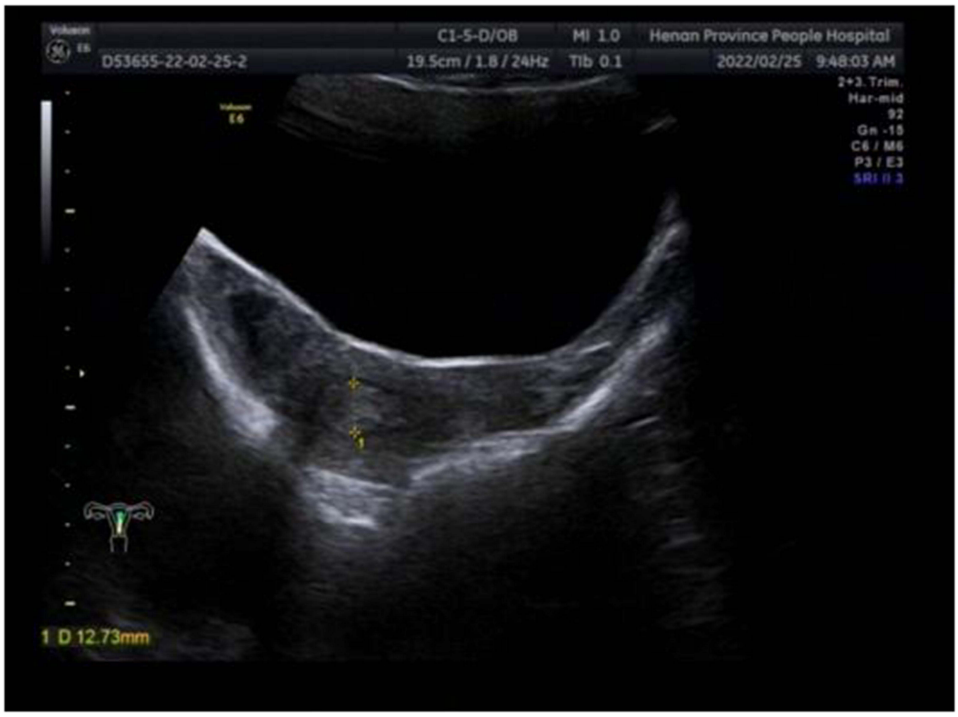

Figure 2 Ultrasonic image in the luteal phase.

inflation to 200 mmHg using a mercury sphygmomanometer (Shanghai Yuwell, registration No. 20162200750). This study recorded the time from the start of raising the pressure on the mercury sphygmomanometer to the sensation of pain, which was the ischemic pain threshold. This pain was defined as "intense ischemic pain in the arm".

Mechanical pain threshold:[13] The mechanical pain threshold was measured using a handheld PainTest FPX 25 Algometer (Wagner Instruments, USA), with pressure applied by a circular probe (1 cm in diameter) on the right ulna (8 cm from the elbow on the back of the forearm). This study recorded the pressure level at which participants felt pain for the first time. The pressure level was averaged across 3 replicate trials that were separated by 2-minute intervals. This type of pain was defined as "the feeling of discomfort or pain in the area under pressure".

Needling pain threshold test:[15,24] This measurement was conducted simultaneously with venous blood collection. Participants were subjected to blood collection from the brachial vein at the elbow by the same experienced nurse using a standard 20G blood collection needle. After that, the needle was withdrawn, and the pressure was applied to the needling site, with the participants' Numerical Rating Scale (NRS) for pain recorded.[25] This pain was defined as "the feeling of obvious discomfort or pain". The needling pain threshold test was conducted to assess the pain associated with venous blood collection, which is a common procedure in clinical settings. There is potential variance in pain perception due to factors such as the skill of the phlebotomist. We took several measures to ensure consistency and validity in our study. The same experienced phlebotomist was used for every blood draw to minimize variability related to the technique. This consistency in the procedure helps to ensure that any differences in pain thresholds are more likely due to the participants' physiological responses rather than procedural differences.

Sex hormone concentration testing: Blood samples were collected from the antecubital vein of each participant at the same time of needling pain threshold measurement. The concentrations of E2, P, FSH, LH, PRL, and T in serum were measured using UniCel Dxi 800 chemiluminescent microparticle immunoassay system (Beckman Coulter, USA). All the collected blood samples were immediately centrifuged to isolate serum, which was collected and then stored in a −80°C freezer until unified detection.

Psychological and Emotional Assessments: To better understand the potential influence of psychological and emotional factors on pain thresholds, we included assessments of depression, anxiety, sleep quality, and pain catastrophization. These assessments were conducted using validated questionnaires to ensure reliable and standardized measurements.

Depression and anxiety: Participants completed the Hospital Anxiety and Depression Scale (HAD), which is a widely used tool for assessing symptoms of anxiety and depression in clinical and research settings. The HAD consists of two subscales: the Anxiety subscale (HAD-A) and the Depression subscale (HAD-D), each containing seven items rated on a 4-point Likert scale. Higher scores on these subscales indicate higher levels of anxiety and depression, respectively.

Sleep quality: Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), a self-rated questionnaire that evaluates sleep quality and disturbances over a one-month period. The PSQI includes seven components, each scored from 0 to 3, with higher total scores indicating poorer sleep quality.

Pain catastrophizing: Pain catastrophizing was measured using the Pain Catastrophizing Scale (PCS), which assesses the tendency to magnify pain, feel helpless about pain, and excessively ruminate about pain. The PCS consists of 13 items rated on a 5-point Likert scale, with higher scores indicating greater catastrophizing tendencies.

According to the Events Per Variable rule,[26] at least 5-10 samples were required for each variable to maintain the effectiveness of the model. In this study, there were 10 variables, and the minimum sample size was 50. Normality was assessed using the Shapiro–Wilk test, which is a widely used statistical test for evaluating whether a dataset is normally distributed. Considering a dropout rate of 15%, this study recruited 68 healthy female volunteers. Statistical analyses of this study were completed using R Language 4.3.3 and SPSS 26.0. The measurement data of normal distribution was expressed as mean±standard deviation (x±s). Univariate linear regression analyses were performed first, and hormone variables that were significantly related to the outcome (ie, pain threshold measurement) were identified as independent variables for collinearity diagnostics. After confirming the existence of multi-collinearity [variance inflation factor (VIF) =5.445023], the multivariate stepwise regression-both method was used for subsequent analysis. A p-value of $P<0.05$ indicated the presence of a statistically significant correlation between the hormone measure and the pain threshold measurement.

Results

In terms of the baseline data, female volunteers had an average age of (25.9±1.81) years, BMI of (20.9±1.36) kg/m^2, menstrual cycle of (28.7±1.29) days, and age of menarche of (13.1±0.83) years. On average, the measurements were taken 6.8 days post-ovulation, with a range of 5–9 days. This timing ensured that the data collected were representative of the hormonal changes and pain sensitivity during the luteal phase. The average concentrations of estradiol, progesterone, FSH, LH, prolactin, and testosterone were 116.373pg/ml, 9.798ng/ml, 4.285IU/ml,7.267IU/ml, 15.957IU/ml, 0.568ng/ml, respectively. The variance and range of these hormone concentrations reflect the natural variability among participants. Similarly, the average pain thresholds were as follows: cold pain threshold at 7.238 seconds, ischemic pain threshold at 26.379 seconds, mechanical pain threshold at 16.706N, and needling pain threshold at 3.848 on the Numerical Rating Scale.(NRS).. These values provide a baseline understanding of the hormonal and pain profiles in the study sample (Supplementary Table 1).

Univariate linear regression analysis was conducted between four pain thresholds and sex hormones. Serum FSH concentration was negatively correlated with cold pain threshold (β=−0.743, P=0.012; Table 1). There was also a positive correlation between serum LH concentration and ischemic pain threshold (β=1.397; P=0.011; Table 2). While no correlation was observed between serum sex hormone concentrations and mechanical pain threshold ($P>0.05$; Table 3). As shown in Table 4, serum FSH concentration was positively correlated with needling pain threshold (β=0.320, P=0.006) and serum LH concentration (β=0.087, P=0.013). Furthermore, univariate regression analysis of the four pain thresholds with PSQI-L, HAD A-L, HAD D-L and pcs-L scores revealed that none of these variables had a statistically significant impact on pain thresholds ($P>0.05$). It suggested that anxiety, depression, sleep quality, and pain catastrophization scores had no significant effect on various pain thresholds in this study.

The needling pain threshold measurement was the only pain threshold measurement that was correlated with more than one reproductive hormone; therefore, multivariate regression was used only the needling pain threshold. In Table 5,

Table 1 Univariate Linear Regression Analysis Between Cold Pain Threshold and Serum Sex Hormone Concentrations

Variable	Partial Regression Coefficient	Standard Deviation	t value	Coefficient (95% Confidence Interval)	*P* value
Serum FSH concentration	−0.743	0.278	−2.678	(−0.177–1.309)	0.012
Serum LH concentration	0.154	0.088	1.757	(−0.025–0.333)	0.089
Serum PRL concentration	−0.102	0.133	−0.768	(−0.373–0.169)	0.448
Serum E2 concentration	−0.018	0.019	−0.948	(−0.057–0.021)	0.351
Serum P concentration	−1.11	0.147	−0.748	(−0.409–0.189)	0.461
Serum T concentration	1.474	6.053	0.244	(−10.870–13.819)	0.809
PSQI-L	−0.158	0.192	−0.822	(−0.549–0.234)	0.417
HAD A-L	−0.037	0.116	−0.317	(−0.272–0.197)	0.753
HAD D-L	0.003	0.163	0.016	(−0.329–0.336)	0.987
pcs-L	0.040	0.072	0.059	(−0.107–0.187)	0.580

Table 2 Univariate Linear Regression Analysis Between Ischemic Pain Threshold and Six Sex Hormones

Variable	Partial Regression Coefficient	Standard Deviation	t value	Coefficient (95% Confidence Interval)	*P* value
Serum FSH concentration	3.636	1.806	2.013	(−0.048–7.319)	0.053
Serum LH concentration	1.397	0.516	2.705	(0.345–2.450)	0.011
Serum PRL concentration	0.209	0.834	0.25	(−1.494–1.912)	0.804
Serum E2 concentration	−0.186	0.116	−1.607	(−0.423–0.052)	0.118
Serum P concentration	−1.573	0.869	−2.017	(−3.525–0.020)	0.052
Serum T concentration	−21.46	37.58	−0.571	(−98.111–55.197)	0.572
PSQI-L	−5.601	9.571	−0.585	(−24.961–13.759)	0.562
HAD A-L	2.340	5.733	0.408	(−9.333–14.014)	0.686
HAD D-L	−0.155	8.024	−0.019	(−16.472–16.161)	0.985
pcs-L	−0.786	3.548	−0.222	(−8.019–6.448)	0.826

Table 3 Univariate Linear Regression Analysis Between Mechanical Pain Threshold and Six Sex Hormones

Variable	Partial Regression Coefficient	Standard Deviation	t value	Coefficient (95% Confidence Interval)	*P* value
Serum FSH concentration	0.097	0.476	0.205	0 (−0.873–1.067)	0.839
Serum LH concentration	−0.058	0.142	−0.41	(−0.347–0.231)	0.685
Serum PRL concentration	0.137	0.206	0.667	(−0.282–0.557)	0.511
Serum E2 concentration	−0.038	0.029	−1.323	(−0.098–0.021)	0.195
Serum P concentration	−0.322	0.222	−1.454	(−0.774–0.130)	0.156
Serum T concentration	2.567	9.352	0.275	(−16.506–24.640)	0.786
PSQI-L	−0.237	0.332	−0.714	(−0.913–0.439)	0.479
HAD A-L	0.057	0.199	0.285	(−0.347–0.462)	0.778
HAD D-L	−0.040	0.278	−0.145	(−0.606–0.526)	0.885
pcs-L	0.052	0.123	0.421	(−0.200–0.304)	0.676

serum FSH concentration entered the regression equation ($P<0.05$), which could explain 19.8% of the total variance in the needling pain threshold. The results of this study provide several novel insights into the relationship between sex hormone concentrations and pain thresholds in the luteal phase of female healthy volunteers. Specifically, the findings demonstrate that the needling pain threshold is positively correlated with FSH concentrations, while the cold pain

Table 4 Univariate Linear Regression Analysis Between Needling Pain Threshold and Serum Sex Hormone Concentrations

Variable	Partial Regression Coefficient	Standard Deviation	t value	Coefficient (95% Confidence Interval)	*P* value
Serum FSH concentration	0.320	0.107	2.98	0.101–0.539	0.006
Serum LH concentration	0.087	0.033	2.634	0.020–0.154	0.013
Serum PRL concentration	0.058	0.051	−1.379	−0.176–0.034	0.178
Serum E2 concentration	0.009	0.007	1.167	−0.007–0.240	0.252
Serum P concentration	−0.060	0.058	−1.039	−0.178–0.058	0.307
Serum T concentration	2.871	2.338	1.228	−1.898–7.639	0.229
PSQI-L	0.394	0.308	1.278	0.208–0.232	1.020
HAD A-L	−0.121	0.186	−0.650	0.498–0.519	0.257
HAD D-L	−0.018	0.263	−0.068	0.552–0.946	0.516
pcs-L	−0.004	0.117	−0.035	0.242–0.972	0.234

Table 5 Multiple Linear Regression Analysis of Factors Affecting Needling Pain Threshold

Variable	Partial Regression Coefficient	Standard Deviation	t value	Coefficient (95% Confidence Interval)	*P* value
Serum FSH concentration	0.320	0.107	2.98	0.101–0.539	0.006

Notes: R^2=0.223, adjusted R^2=0.198, F=8.879, *P*=0.006.

threshold is negatively correlated with FSH concentrations. Additionally, the ischemic pain threshold is positively correlated with LH concentrations.

Discussion

This study intended to explore the relationship between different types of pain thresholds and sex hormones in young female volunteers during the luteal phase of the menstrual cycle. The luteal phase was selected for investigation, as previous studies have found that individuals in the luteal phase were more sensitive to various experimental pain measurements.[7–15,27–31] The results may facilitate the identification of factors influencing higher pain sensitivity during the luteal phase. Moreover, isolating a single phase of the menstrual cycle for study reduces the potential influence of other factors that can fluctuate during the menstrual cycle in addition to hormones, such as mental and psychological factors and sleep.[32,33] It may eventually benefit the clarification of specific types of sex hormones related to pain.

The pain threshold models used in the study have been shown to be critical in quantifying the sensitivity.[34] Moreover, there are distinct interactions of menstrual cycle, location, tissue depth and gender on pain thresholds. Therefore, it is advisable to study pain thresholds using multiple pain models.[35] Needling pain model shares similar mechanism to that of incisional pain, which may be mediated by Adelta fibers, while cold pain and ischemic muscle pain are considered the most clinically relevant types of pain.[7,10] Mechanical pain testing is a key component of quantitative sensory testing in the laboratory, which may be useful for identifying individuals at high risk of chronic pain.[6] While mechanical pain is not directly linked to specific clinical conditions like cold or ischemic pain, it plays a crucial role in identifying individuals at high risk for developing chronic pain. Mechanical pain thresholds are often used in quantitative sensory testing (QST) to assess the sensitivity of the somatosensory system. Lower mechanical pain thresholds can indicate heightened pain sensitivity, which is a known risk factor for the development of chronic pain conditions such as fibromyalgia and chronic neuropathic pain. Therefore, mechanical pain testing is an important tool in clinical settings for early detection of individuals who may be more susceptible to chronic pain, allowing for early intervention and management strategies. Collectively, the proposed pain tests are of great significance clinically. In this study, higher FSH concentrations were

associated with a lower needling pain threshold, as indicated by higher pain ratings on the NRS. This suggests that elevated concentrations of FSH may increase pain sensitivity during needle insertion. These results were consistent with the conclusion in a clinical study that plasma FSH level was associated with needling pain and hyperalgesia in patients with rheumatoid arthritis.[30] As for the underlying mechanism, FSH can activate the endo-cannabinoid-degrading enzyme fatty acid amide hydrolase, reducing cannabinoid concentrations by up to 7 times, leading to a reduction in the less pain sensing of cannabinoid 1 receptor located on nociceptive primary sensory neurons expressing TRPV1.[31]

Greater LH concentrations were associated with a higher ischemic pain threshold. In general, LH concentrations change remarkably during pregnancy, postpartum, and menopausal periods.[36] Critically, the described special periods in females are closely related to changes in pain sensation. At present, there are few studies on the pain mechanisms involving these sex hormones, which may provide potential reference for exploring pain mechanisms of females during pregnancy, postpartum, and menopause in the future. In prior research, estrogen was considered the main hormone associated with pain regulation.[37] In this study, however, four types of pain thresholds in the luteal phase showed no association with estrogen concentrations. It was consistent with the finding that changes in estrogen concentrations exceeding 100 times in the human body did not significantly alter pain sensitivity in clinical or experimental settings.[7]

This study still has several limitations. Firstly, this study primarily focused on the relationship between sex hormone concentrations and pain thresholds, providing valuable insights into the hormonal modulation of pain sensitivity during the luteal phase. However, there are several limitations that should be acknowledged. While we did collect data on participants' emotions, diet, exercise condition, these factors were not included in the main analyses. Secondly, there was a limited scope of healthy volunteers enrolled in our studies, without including individuals with severe changes in sex hormones, such as females during puberty, pregnancy, and menopause. FSH was positively associated with needling pain thresholds and negatively associated with cold pain thresholds, while LH was positively associated with both needling and ischemic pain thresholds. These exploratory results lay the foundation for further exploration of mechanisms underlying the high incidence of female painful conditions and formulation of corresponding solutions. According to the results of univariate regression analysis, needling pain threshold was subjected to multivariate regression analysis merely considering that all the other three pain thresholds had no significant association in the univariate analysis. Future studies can be performed by comprehensively analyzing more variables (lifestyle factors like diet, exercise, and sleep quality) based on larger sample size.

Conclusion

This study primarily explored the relationship between sex hormone concentrations and PSQI-L, HAD A-L, HAD D-L and pcs-L scores and pain thresholds in healthy female volunteers during the luteal phase. The findings revealed that higher follicle-stimulating hormone (FSH) concentrations were associated with a lower needling pain threshold, indicating higher pain sensitivity. Conversely, higher FSH concentrations were associated with a lower cold pain threshold, suggesting higher sensitivity to cold pain. Additionally, higher LH concentrations were linked to a higher ischemic pain threshold, indicating reduced sensitivity to ischemic pain. These results align well with the study's objective of investigating the hormonal modulation of pain sensitivity during the luteal phase. The conclusion that FSH and LH have distinct effects on different types of pain thresholds is supported by the significant correlations observed in the study. This highlights the complex interplay between hormonal concentrations and pain perception, emphasizing the importance of considering hormonal factors in understanding pain sensitivity in females.

Data Sharing Statement

All data generated or analyzed during this study are included in this article.

Ethics Approval and Consent to Participate

The present study was conducted in accordance with the Declaration of Helsinki. This study has been approved by the Ethics Committee of Henan Provincial People's Hospital, People's Hospital of Zhengzhou University. Written informed consent was obtained from all participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

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