Research Paper: The Effects of Estrogen and Progesterone Hormones on Active Hip Joint Position Sense in Healthy Women in Different Phases of a Menstrual Cycle

Maliheh Mosavi Ghomi[1], Mehrdad Shariati[1], Mokhtar Mokhtari[1*], Fatemeh Ramezani Nowrozani[1]

1. Department of Biology, Department of Biology, Faculty of Sciences, Kazerun Branch, Islamic Azad University, Kazerun, Iran.

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ABSTRACT

Introduction: The proprioceptive system is a sensory system based on an individual's knowledge of his or her body. This knowledge is transmitted to the brain through inputs received from joints, muscles, tendons, and ligaments. As a result, these inputs inadvertently inform the brain of the state of the body's muscles. Numerous factors can affect this system. This study aimed to investigate the effect of estrogen and progesterone hormones on understanding and recognizing the proprioceptive sense of hip joint in healthy women during the menstrual cycle.

Materials and Methods: In this quasi-experimental study, 15 healthy women participated voluntarily. They had regular menstrual cycles without any history of disease and drug use. The concentration of estrogen and progesterone during a cycle in the follicular (4-6 days), ovulation, and luteal phases were evaluated to detect their effects on the sense of perception and cognition of the proprioceptive joint in the two movements of abduction and flexion by the target angle reconstruction method (30°).

Results: The errors of active joint position sense were reduced in abduction and flexion during ovular and luteal phases compared to the follicular phase. However, in the flexion direction of hip movement, there was a significant difference in absolute error during hormonal changes in the menstrual cycle (P=0.000).

Conclusion: The results showed that due to more involvement of motor control of hip muscles joint by motor neuron activity (increase release of estrogen hormone), all errors reduced in ovular and luteal phases compared to the follicular phase. The flexion movement is more disturbed, and due to more flexibility in this direction, absolute errors are significantly reduced. This reduction of errors in ovular and luteal phases compared to the regular stage of hormone release (follicular phase) may cause some rigidity in the hip joint and an increase of trauma in external mechanical forces. This study's findings showed that the lowest proprioception sensation is in the follicular phase. Decreasing the concentration of sex hormones in this phase is likely to reduce the sense of recognition of the joint, thus increasing the likelihood of injury in this phase. Findings from this study showed that the lowest proprioceptic sensation is in the follicular phase. The results of this study showed that the least sense is Prvpryvsptyk in Fazfvlykvlar.

Keywords: Proprioceptive sense, Estrogen hormone, Hip joint

*** Corresponding Author:**
Mokhtar Mokhtari, PhD.
Address: *Department of Biology, Kazerun Branch, Islamic Azad University, Kazerun, Iran.*
Tel: *+98 (917) 181963*
E-mail: *m.mokhtari246@yahoo.com*

1. Introduction

The nervous system and the endocrine glands both control the activities of the human body. The endocrine system is mainly engaged in controlling the body's metabolic activities. However, the nervous system controls muscle contraction, visceral organs, and the secretion of some endocrine glands [1, 2].

The proprioceptive sensory system is a system that subconsciously sends information about the state of the body from the subject's joints, ligaments, and muscles. Accordingly, the brain understands when and how muscles are in rest and stretch position [2].

Controlling the movement and position of a continuous flow of information depends on the surrounding events. Motor responses are generally subject to three levels of motor control as follows: the spinal cord for simple reflexes, the lower cerebral cortex for more complex responses, and the cerebral cortex for the most complex responses. Moreover, the cerebellum, basal ganglia, and hippocampus are the underlying motor areas. Although the underlying areas do not directly control the activity of motor neurons, their presence is necessary for modulating and regulating motor commands issued by motor centers. Thus, proprioceptive sensory information is coded and processed in each of these centers. The highest level of regulation is in the somatosensory cortex, which processes deep sensory information to create a conscious awareness from the sense of position and joint motion. It is believed that proprioceptive sensory information is stored in the cerebellum, basal ganglia, hippocampus, and somatosensory cortex to be used in subsequent motor commands. Different factors can affect the deep sensations of the joints, consisting of gender, age, anatomical and structural orientation, genetic factors, neuromuscular and hormonal factors [3-6].

Since 1991, the word "steroids" has been classified as being able to control nerve function. Subsequently, the regulatory function of progesterone, estradiol, and androgens of the central nervous system has been stated in several studies. Studies indicate that steroid hormones easily cross the blood-brain barrier and act on brain receptors, such as the hypothalamus, hippocampus, cerebellum, basal ganglia (putamen), raphe nucleus, and cerebral cortex through the binding mechanism of ligand-phosphorylation receptor in the brain [7].

On the other hand, the presence of estrogen and progesterone receptors on the Anterior Cruciate Ligament (ACL) of women and identifying the relationship between the neuromuscular system and the level of their sex hormones, differences in the sense of position at different times of a menstrual cycle and the amount of mon the other hand there are estrogen receptors and Prvzhstrrvn ACL on women and identify the relationship between the nervous system and the level of sex hormones -Zlany them a different sense of the situation at different times of the menstrual cycle and the changing hormones has been observed that the maximum error sense. Menopause occurs when the amount of female sex hormones is at a minimum. Studies have also shown that women are more prone to ligament damage than men [8-10].

New findings indicate that the density of steroid receptors is very high in hypothalamic and hippocampal neurons. Researchers have indicated that estradiol can increase stimulation by glutamate receptors and inhibit gamma-aminobutyric acid (GABA). In addition, estradiol regulates the function of NMDA (N-methyl-D-aspartate) receptors in the hippocampus [11, 12].

Current studies show that ovarian steroids have protective functions on the central nervous system (CNS) in addition to their hormonal role in reproductive activities [13, 14]. There are several areas in the CNS that have estrogen and progesterone receptors, including the hypothalamus, hippocampus, limbic system, and cerebral cortex. Conducted investigations have indicated that steroid hormones protect and divide neurons in these areas of the brain. Furthermore, the findings indicate the role of progesterone along with a combination of estrogen called β-17 estradiol affects the regulation of cognitive and behavioral functions. The protective effects of estrogen and progesterone against altercations in amyloid-beta glutamate, seizure behaviors, and oxidative stress have been approved [15, 16].

This study aimed to investigate the effects of female sex hormones during different phases of the menstrual cycle on the proprioception sensation of the hip joint.

2. Materials and Methods

This research is a quasi-experimental study, and the sampling was done by the available sampling method. The study samples were 15 healthy women in the age range of 21 to 45 years. The study procedure was performed in a closed room with proper ventilation, temperature, light, and sound control. The study imaging was done with a Canon LXUS960-5 digital camera. The camera was mounted on a tripod perpendicular to the hip movement plane 80 cm from the standing position and 80 cm from the ground so that the lens was completely aligned with the hip joint. The digital images were sent to a computer, and the data were identified and processed through the software.

Several criteria and conditions have been set for the inclusion of individuals. They include no cardiovascular diseases, no diabetes, no thyroid disease, no polycystic ovary syndrome, not being under diet or treatment, no addiction to any drugs, smoking, alcohol, and caffeine, natural menstrual cycles, no medication, even contraception, no neuromuscular disorders, no history of fractures or abnormalities in the joints of both knees, lumbar spine and neck, pain and limitations in the joints of the limbs, with a normal posture. Three days before sampling, the subjects were controlled for abstinence from medication, smoking, caffeine, and physical activity in addition to daily life activities and non-sexual intercourse, as well as for adequate sleep and consumption of an isocaloric diet.

The participants first filled out a consent form and another form to collect study information, including demographic information. Then the majority of individuals were identified and given the necessary training on what to do. The test was conducted in three sessions of 10 to 15 minutes each.

Blood samples

Having a 7-day menstrual cycle, the participants had bloodletting in three cycles, namely the beginning of the cycle is 3-4 (follicular time), 12-14 days (ovulation time), and 21-24 days (luteal time) to measure the concentration of estrogen and progesterone hormones. These days were considered indicators of the peak of the presence of sex hormones.

Blood samples taken by the examiner were transferred to the laboratory after at least 4 minutes (to form a clot). All blood samples were analyzed in the laboratory by the ELISA method using the Elisa reader SLT model, which is based on colorimetric methods. The diagnostic kits of the hormones estrogen, progesterone, and prolactin from the kit company were ELISA Diameters.

Active joint position sense test

The target angle reconstruction test was conducted in the standing position. Hip angles were calculated using skin markers, digital imaging, and 558 Analyzer Motion software. Before starting, the test validity was obtained, and the amount of camera error was measured. Moreover, the validity and repeatability of recording detailed angles were checked by the software.

For goniometry, 4 markers consisting of 2×2 cm squares were used. They were connected to the apex of the large trochanter of the femur, the external condyle of the femur, and the protrusion of the right anterior superior iliac spine and left pelvis to control pelvic deviation [17].

A. Hip abduction movement

To examine the movement of the hip abduction movement, the person was asked to stand up and place her left hand (provided the right foot is dominant) on a table that was set next to her at the same level as the length of the limb. The subject was then asked to transfer the hip to the abduction position by controlling the examiner and the 30° goniometer. Moreover, the subject was asked to hold for 5 seconds to learn its status. In this position, a camera image was recorded and encoded as a reference image. After recording the reference image, the subject was asked to return to the original state.

Then the subject's eye was closed with a blindfold. She was asked to reconstruct the reference angle after 5 seconds and announced to reach the desired angle with a laser light message. At this time, the joint position was photographed and coded as a repetition. Then, the subject returned to the original position. This operation was repeated three times and photographed all three times.

Error variable (VE) is the root mean square of the difference between the reconstructed joint angle and the set angle minus the square of the constant error: VE=√= [Σ (B-A)2 / K-(CE)2]. According to the formula, B is the values of the placement of the joint marker on the x and y coordinate in the spatial reconstruction of the joint. A is the placement values of the marker in the selected conventional domain. K is the number of times the test is conducted, and CE is a constant error.

Thus, 4 repetitions of the detailed reconstruction with the reference range were calculated and compared by the software. Besides, the error values were calculated as shown in Figure 1 (absolute error, constant error, variable error of sense of position).

Absolute Error (AE) is the mean absolute value of the difference between the reconstructed joint angle and the specified angle: AE=Σ [B-A]/K. According to the formula, B is the value of the placement of the joint marker

Figure 1. Imaging steps of four repetitions in the abduction of the hip joint to reconstruct and determine the sense and understanding of the hip position (the record 1 was a reference image)

on the x and y coordinate axis, besides it is the spatial reconstruction of the joint. A is the placement value of the marker in the selected conventional domain. K is the number of times the test is conducted.

Error Constant (CE) is the mean difference between the reconstructed joint angles and set angle: CE=Σ (B-A)/K. According to the formula, B is the values of the placement of the joint marker on the x and y coordinate axis. Also, it is the spatial reconstruction of the joint. A is the placement values of the marker in the selected conventional domain, and K is the number of times the test was conducted.

B. Hip flexion movement

For the flexion of the hip joint movement, the subject was asked to move the hip at an angle of 30° with the help of an examiner and a goniometer and then to maintain its position for 5 s to learn the move.

The image was photographed and coded as the reference image. Then, the subject was asked to return to the original position. Next, the subject's eyes were closed with a blindfold. After 5 s, the subject reconstructed the reference angle without controlling the examiner and announced as soon as reaching the angle with an optical laser. The reconstructed angle was photographed with the announcement of the subject and coded as repetition 1. Then, the subject was placed in the starting position. This reconstruction was repeated 3 more times (Figure 2). Thus, 4 repetitions of the reconstruction with the reference domain were calculated and compared by the software (absolute error, constant error, variable error) (Figure 3).

Statistical analysis

The obtained data were analyzed by SPSS v. 21. Moreover, the normal distribution of variables was evaluated by the Smirnov-Kolmogorov test. Descriptive statistics calculations comprised determining the mean and standard deviation. A comparison test was performed with repeated measurements between three stages of the menstrual cycle. Also, hormone changes and the values of absolute, constant, and variable errors were evaluated.

Figure 2. Imaging steps of four repetitions in bending or flexion of the hip joint to reconstruct and determine the sense and understanding of the hip position (the record 1 was a reference image)

Table 1. Comparing between the phases of the menstrual cycle on the reconstructed state in constant, absolute, and variable errors of perception of the state of hip abduction (n=15)

Research Variables	Phases/Mean±SD			F	Sig.	Effect size
	Follicular	Ovulation	Luteal			
Constant error	7.38±6.03	7.60±6.58	6.75±7.02	0.099	0.906	0.015
Absolute error	7.53±5.87	7.66±6.68	7.29±6.42	0.023	0.978	0.003
Variable error	12.07±9.84	13.30±11.63	12.28±10.87	0.71	0.932	0.011

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3. Results

The subjects had a mean age of 34.46 years, a mean height of 161.3 cm, and a body mass index of 25.4 kg/m2. There is no significant difference in demographic data. Research variables were measured in three states, namely follicular (before the cycle or pre), ovulation (during the cycle or Dur), and luteal (after the cycle or post). The Kolmogorov-Smirnov test (KS) showed that all the variables of errors, i.e., constant, absolute, and variable, had a normal distribution, so they were compared by repeated measurements in three stages of the menstrual cycle.

There was no significant difference in the measured angles of the reference hip abduction domain (3 repetitions) in the comparison between subjects in the three stages of the menstrual cycle (P=0.699). Moreover, this showed the accuracy of the test and the level of the test.

Comparing individuals in the three phases of the menstrual cycle, no significant difference was observed between constant error, absolute error, and variable error of proprioceptive perception and cognition to assess joint perception in thigh abduction (Table 1).

Concerning hip flexion movement, no significant differences (P=0.914) were observed in the reference angles between individuals in the phase of menstrual cycles. This matter shows the degree of accuracy of the test and the level of the test.

According to Table 2, no sense of hip position was observed in flexion mode at different phases of the menstrual cycle between constant and variable error angles. However, this error was significant in absolute error (P<0.05).

Comparing between individuals in the three phases of the menstrual cycle, a significant difference was observed in absolute error with a significant level of P=0.000.

Following the observation of a significant difference in the follow-up tests, the absolute error showed that the largest error was in reconstructing flexion motion in the follicular phase (Table 3 and 4).

Using paired t-test, post hoc tests showed the highest difference and significance between follicular stage with ovulation and follicular with luteal phase.

4. Discussion

In the ovulation and luteal phase, the concentrations of hormones are high, especially estrogen, which increases from the end of the follicular phase. High estrogen level

Table 2. The comparison between the phase of the menstrual cycle on the reconstructed state in constant, absolute, and variable errors of proprioception of hip flexion (n=15)

Research Variables	Phases/Mean±SD			F	Sig.	Effect size
	Follicular	Ovulation	Luteal			
Constant error	13.44±16.26	4.46±7.13	4.39±9.00	2.96	0.063	0.257
Absolute error	14.118±5.19	5.75±3.72	7.89±5.91	11.44	0.000	3.219
Variable error	23.48±28.01	12.27±9.61	83.42±269.52	0.9	0.414	0.163

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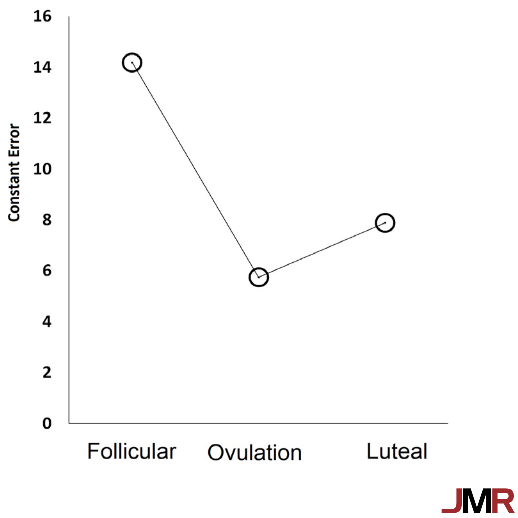

Figure 3. Absolute error changes in hip flexion movement

is likely to affect the areas of the brain related to proprioceptive perception and cognition, which in turn reduces the error in angle reconstruction (Figure 4).

The current study results indicate that female sex hormones do not affect the hip joint in the abduction state during the menstrual cycle. Since the angle determined for the subjects was significantly different between the reference angle and 4 repetitions in the constant, absolute, and variable error.

This evidence supports the high power of muscles around the hip joint (pelvic muscles and gluteus maximus and medius) since the hip joint has a high degree of freedom and very mobile in moving away and opening. They have excellent control over the hip joint in many daily movements. Therefore, hormonal changes during the menstrual cycle do not affect this joint in moving away and opening.

In hip flexion, hormonal changes in the menstrual cycle sense of cognition and sense perception of proprioception affected the follicular phase only in absolute error. This error, which is a physical error, shows the difference between the actual values of the error apart from its relation to its direction.

Findings of the current study showed that individuals in the ovulation and luteal phases had the least error in reaching the set angle, and it may be directly related to an increase in the level of estrogen.

No study has been carried out on the effect of this hormone on proprioception sensations. However, some suggestions regarding the proprioception errors can be made due to the high level of the hormone estrogen based on previous studies on the effect of this hormone on the hippocampus.

Moazedi et al. (2010) showed that high estrogen concentrations in the hippocampus interfered with its action. It has a significant role in the transfer of acetylcholine to brain synapses, according to their statements [18].

Therefore, it can be predicted that high estrogen concentration has increased acetylcholine-dependent synaptic transitions. Moreover, this increase in synaptic transitions has reduced the error in the ovulation and luteal phases compared to the follicular phase (phase of normal conditions of women considering physiological and psychological).

In other words, in the two phases after the follicular phase, hormonal changes cause variations in the release of synaptic mediators in the brain and the mechanisms of using motor and sensory units. Furthermore, the degree of joint freedom decreases that leads to a reduction in error in joint perception. It limits the joint movement system to several movement control factors and increases the risk of injury. While in the follicular phase (normal phase) in which there is more error meaning that the control system is floating with a greater degree of freedom and the joint ability to control and keep down the shocks caused by external forces. In addition, the damage in this phase will be much lower. Estrogen receptors are widely present in the brain and reproductive organs [19, 20].

In addition, it affects the classical effects of estrogen receptors through neuronal excitability due to its effects on synaptic structure and its function [21, 22]. This mechanism, possibly in estradiol, can increase stimulation by glutamate receptors and inhibit GABA. Estradiol acts on

Table 3. Hip flexion, the absolute position sense error

Multivariate Tests[b]						Sig.	Partial Eta-Squared
Effect		Value	F	Hypothesis df	Error df		
Abs. ERROR	Hotelling's Trace	0.649	4.216[a]	2.000	13.000	0.039	0.393

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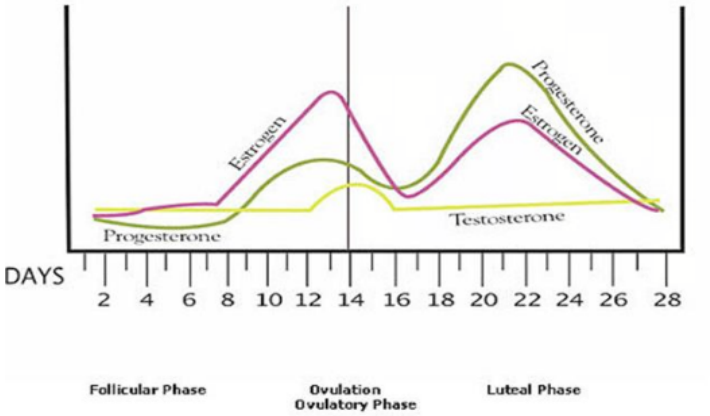

Figure 4. Relative changes in estrogen concentration in the three phases of the menstrual cycle

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the nerve cells of the limbic system, cerebral cortex, and other areas and plays a role in developing nervous activity [23, 24].

Moreover, two types of glutamate receptors have a direct and indirect effect on the N-methyl-D-aspartate (NMDA) receptors by increasing the dendritic density in the hippocampus. Furthermore, studies have supported its role in regulating estradiol related to NMDA receptor function [25, 26].

Electrophysiological studies have shown that estradiol increases synaptic transmission and density of Coudal Anterior Hipocampus (CA1) dendritic spines in the hippocampus and flexibility to attenuate NMDA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor activity, leading to nerve stimulation [27].

Cimarosti et al. (2006) indicated that estrogen affects glutamate receptors and glutamate transporters, thereby inhibiting the stimulatory activity of glutamate in the brain [28]. Therefore, according to the studies, it can be predicted that the activity of glutamate receptors decreases in the ovulation and luteal phases due to the high concentration of estrogen or affects proprioceptive sensory due to the increase in the number of glutamate receptors in the hippocampus. Hence, it reduces the error in the proprioceptive sensory in the hip joint [28].

GABA is the most important neurotransmitter in the brain. The density of GABA receptors is very high in different brain areas, especially in the hippocampus [29]. Previous studies have shown that GABA receptors are affected by sex hormones so that estrogen hormones increase GABA inhibitory activity [30, 31].

Therefore, based on the conducted studies, it can be expected that high concentrations of estrogen increase the inhibitory activity of GABA in the hippocampus in the ovulation phase. Besides, it can be one reason for reducing error in proprioceptive sensations in the ovulation and luteal phases. Furthermore, in the studies that have been carried out on ACL injuries [32], it was found that the rate of ACL injuries in females is much higher than in males. Also, they observed the most injuries in female athletes on days 9, 14, and 28 [32]:

The days when a person experiences the highest concentration of estrogen during one's menstrual cycle. Along with reducing errors on these days, this finding can raise a kind of contradiction. It can be suggested that error reduction is a type of increase in the degree of freedom in

Table 4. Hip flexion follow-up testing, absolute error position sense

(I) Abs. ERROR	(J) Abs. ERROR	a			95% Confidence Interval for Differencea	
		Mean Difference (I-J)	Std. Error	Sig.	Lower Bound	Upper Bound
1	2	6.905	3.853	0.095	-1.358	15.169
	3	5.697	4.582	0.234	-4.130	15.525
2	3	-1.208	1.149	0.311	-15.169	1.358

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the central control system over the joints; moreover, the amount of flexibility is reduced in doing exercises or sports competitions. Besides, the joint is very constant and does not interact with external forces and loses the ability to absorb incoming forces, and suffers damage. Therefore, the reduction of joint error cannot always be considered a positive point. Furthermore, this reduction in error coincides with an increase in estrogen concentration in the late follicular phase (day 9) and in the ovulation phase (day 14) and luteal phase (day 28) that cause alterations in motion control and joint rigidity and injury in athletes.

Nevertheless, the exact mechanism of estrogen effects on proprioception is still unknown. Moreover, the effects of alterations in estrogen concentrations during the menstrual cycle in women need further study. Although the present study did not investigate brain structures affected by high concentrations of sex hormones, this project paves the way for future studies to determine the exact mechanism of the effects of estrogen and progesterone in determining the effective mechanisms in proprioception changes related to different concentrations of these steroid hormones.

5. Conclusion

The findings of this study show that the lowest proprioception sensation occurs in the follicular phase. Decreasing the concentration of sex hormones in this phase is likely to reduce the sense of cognition of the joint. Therefore, the risk of a hip injury in the follicular phase is higher than in the ovulation and luteal phase. Findings from this study showed that the lowest proprioceptive sensation is in the follicular phase. The results of this study showed that the least sense is Prvpryvsptyk in Fazfvlykvlar.

Ethical Considerations

Compliance with ethical guidelines

This project was approved by the Islamic Azad University. All ethical principles were observed in this study (Code: IR.IAU.REC.1399.004).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Häggström M. Reference ranges forestradiol, progesterone, luteinizing hormone and follicle-stimulating hormone during the menstrual cycle. WikiJournal of Medicine. 2014; 1(1):1-5. [DOI:10.15347/wjm/2014.001]

[2] Valero-Cuevas FJ. Predictive modulation of muscle coordination pattern magnitude scales fi ngertip force magnitude over the voluntary range . Journal of Neurophysiology. 2000; 83(3):1469-79. [DOI:10.1152/jn.2000.83.3.1469] [PMID]

[3] Laible C, Sherman OH. Risk factors and prevention strategies of non-contact anterior cruciate ligament injuries. Bulletin of the Hospital for Joint Diseases. 2014; 72(1):70-5. [PMID]

[4] Beynnon BD, Shultz SJ. Anatomic alignment, menstrual cycle phase, and the risk of anterior cruciate ligament injury. Journal of Athletic Training. 2008; 43(5):541-2. [DOI:10.4085/1062-6050-43.5.541] [PMID] [PMCID]

[5] LaBella CR, Hennrikus W, Hewett TE. Council on sports medicine and fitness, and section on orthopaedics. Anterior cruciate ligament injuries: Diagnosis, treatment, and prevention. Pediatrics. 2014; 133(5):e1437-50. [DOI:10.1542/peds.2014-0623] [PMID]

[6] Shultz SJ, Schmitz RJ, Benjaminse A, Chaudhari AM, Collins M, Padua DA. ACL research retreat VI: An update on ACL injury risk and prevention . Journal of Athletic Training. 2012; 47(5):591-603. [DOI:10.4085/1062-6050-47.5.13] [PMID] [PMCID]

[7] Arevalo MA, Azcoitia I, Garcia-Segura LM. The neuroprotective actions of oestradiol and oestrogenreceptors. Nature Reviews Neuroscience. 2015; 16(1):17-29. [DOI:10.1038/nrn3856] [PMID]

[8] Frontera WR, Micheli LJ, Herring SA, Silver JK, Young TP. Clinical sports medicine, medical management and rehabilitation. Pennsylvania: Saunders; 2006. https://books.google.nl/books?id=w6FSamw-7_AC&printsec=frontcover&dq

[9] Fouladi R, Nasseri N, Rajabi R, Geranmayeh M. [Joint position sense of the knee in healthy female athletes across the menstrual cycle (Persian)]. Koomesh. 2010; 12(1):31-8. http://koomeshjournal.semums.ac.ir/article-1-957-fa.html

[10] Aydoğ ST, Hasçelik Z, Demirel HA, Tetik O, Aydoğ E, Doral MN. The effects of menstrual cycle on the knee jointposition sense: Preliminary study. Knee Surg Sports TroumatolArthrosc. 2005; 13(8):649-53. [DOI:10.1007/s00167-004-0604-7] [PMID]

[11] Witkowska HE, Carlquist M, Engstrom O. Characterization of bacterially expressed rat estrogen receptor β ligand binding domain by mass spectrometry: Structural comparison with estrogen receptor α. steroids. 1997; 62(8-9):621-31. [DOI:10.1016/S0039-128X(97)00047-0]

[12] Kuiper GG, Lemmen JG, Carlsson B, Corton JC, Safe SH, van der Saag PT, et al. Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta. Endocrinology. 1998; 139(10):4252-63. [DOI:10.1210/endo.139.10.6216] [PMID]

[13] Gibbs RB. Long-term treatment with estrogen andprogesterone enhances acquisition of a spatial memorytask by ovariectomized aged rats. Neurobiology of Aging. 2000; 21(1):107-16. [DOI:10.1016/S0197-4580(00)00103-2]

[14] Gaignard P, Savouroux S, Liere P, Pianos A, Thérond P, Schumacher M, et al. Effect of sex differences on brain mitochondrial function and its suppression by ovariectomy and in aged mice. Endocrinology. 2015; 156(8):2893-904. [DOI:10.1210/en.2014-1913] [PMID]

[15] Brinton RD, Thompson RF, Foy MR, Baudry M, Wang J, Finch CE, et al. Progesterone receptors: Form and function in brain. Frontiers in Neuroendocrinology. 2008; 29(2):313-39. [DOI:10.1016/j.yfrne.2008.02.001] [PMID] [PMCID]

[16] Lammerding L, Slowik A, Johann S, Beyer C, Zendedel A. Poststroke inflammasome expression and regulation in the peri-infarct area by gonadal steroids after transient focal ischemia in the rat brain. Neuroendocrinology. 2016; 103(5):460-75. [DOI:10.1159/000439435] [PMID]

[17] Aliabadi S, Khanmohammadi R, Olyaei Gh , Ghotbi N, Talebian S, Naser Moghadasi A. Comparison of the position sense of the knee joint in patients with multiple sclerosis and healthy controls. Journal of Modern Rehabilitation. 2019; 13(1):59-64. [DOI:10.32598/JMR.13.1.59]

[18] Moazedi AA, Moosavi M, Chinipardaz R. [The effectof estrogen on passive avoidence memory in an experimental model of Alzheimer's disease in male rats (Persian)]. Physiology and Pharmacology. 2011; 14(4):416-25. http://ppj.phypha.ir/article-1-656-en.pdf

[19] Trabert B, Wentzensen N, Yang HP, Sherman ME, Hollenbeck AR, Park Y, et al. Is estrogen plus progestin menopausal hormone therapy safe with respect to endometrial cancer risk? International Journal of Cancer. 2013; 132(2):417-26. [DOI:10.1002/ijc.27623] [PMID] [PMCID]

[20] Chen P, Wang H, Duan Z, Zou JX, Chen H, He W, et al. Estrogen-related receptor alpha confers methotrexate resistance via attenuation of reactive oxygen species production and P53 mediated apoptosis in osteosarcoma cells. BioMed Research International. 2014; 2014:616025. [DOI:10.1155/2014/616025] [PMID] [PMCID]

[21] Lakaye B, Foidart A, Grisar T, Balthazart J. Partial cloning and distribution of estrogen receptor beta in the avian brain. Neuroreport. 1998; 9(12):2743-8. [DOI:10.1097/00001756-199808240-00011] [PMID]

[22] Brzozowski AM, Pike AC, Dauter Z, Hubbard RE, Bonn T, Engström O, et al. Molecular basis of agonism and antagonism in the oestrogen receptor. Nature. 1997; 389(6652):753-9. [DOI:10.1038/39645] [PMID]

[23] Gibson CL, Gray LJ, Bath PM, Murphy SP. Progesterone for the treatment of experimental brain injury: A systematic review. Brain. 2008; 131(Pt 2):318-28. [DOI:10.1093/brain/awm183] [PMID]

[24] Liang Z, Valla J, Sefidvash-Hockley S, Rogers J, Li R. Effects of estrogen treatment on glutamate uptake in cultured humanastrocytes derived from cortex of Alzheimer's disease patients. Journal of Neurochemistry. 2002; 80(5):807-14. [DOI:10.1046/j.0022-3042.2002.00779.x] [PMID]

[25] Jobling S, Reynolds T, White R, Parker MG, Sumpter JP. A variety of environmentally persistentchemicals, including some phtalate plasticizers, are weakly estrogenic. Environ Health Perspectives. 1995; 103(6):582-7. [DOI:10.1289/ehp.95103582] [PMID] [PMCID]

[26] Herman C, Adlercreutz T, Goldin BR, Gorbach SL, Höckerstedt KA, Watanabe S, et al. Soybean phytoestrogen intake and cancer risk. Journal of Nutrition. 1995; 125(3):757-70. https://academic.oup.com/jn/article-abstract/125/suppl_3/757S/4774197

[27] Frye CA. The neurosteroid 3α,5α-THP has antiseizure and possible neuroprotective effects in an animal model of epilepsy. Brain Research. 1995; 696(1-2):113-20. [DOI:10.1016/0006-8993(95)00793-P]

[28] Cimarosti H, O'Shea RD, Jones NM, Horn AP, Simão F, Zamin LL, et al. The effects of estradiol on estrogen receptor and glutamate transporter expression in organotypic hippocampal cultures exposed to oxygen--glucose deprivation. Neurochemical Research. 2006; 31(4):483-90. [DOI:10.1007/s11064-006-9043-9] [PMID]

[29] Pivard B, Baudoux G, Durant F. Electronic properties of $GABA_B$ agonists and antagonists. European Journal of Medicinal Chemistry. 1994; 29(7-8):513-17. [DOI:10.1016/0223-5234(94)90143-0]

[30] Labombarda F, Ghoumari AM, Liere P, De NicolaAF, Schumacher M, Guennoun R. Neuroprotectionby steroids after neurotrauma in organotypic spinal cord cultures: A key role for progesterone receptorsand steroidal modulators of GABA(A) receptors. Neuropharmacology. 2013; 71:46-55. [DOI:10.1016/j.neuropharm.2013.03.010] [PMID]

[31] Backstrom T, Haage D, Lofgren M, JohanssonIM, Stromberg J, Nyberg S, et al. Paradoxical effects of GABA-A modulators may explain sex steroid induced negative mood symptoms in some persons. Neuroscience. 2011; 191:46-54. [DOI:10.1016/j.neuroscience.2011.03.061] [PMID]

[32] Joseph AM, Collins CL, Henke NM, Yard EE, Fields SK, Comstock RD. A multisport epidemiologic comparison of anterior cruciate ligament injuries in high school athletics. Journal of Athletic Training. 2013; 48(6):810-7. [DOI:10.4085/1062-6050-48.6.03] [PMID] [PMCID]

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