The Journal of International Advanced Otology

J Int Adv Otol 2023; 19(6): 517-522 • DOI: 10.5152/iao.2023.221027

Original Article

Comparison of Functional Vestibulo–Ocular Reflex in Follicular and Luteal Phase in Young Girls

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Cite this article as: Cengiz DU, Çolak SC, Ünver Koca H. Comparison of functional vestibulo–ocular reflex in follicular and luteal phase in young girls. *J Int Adv Otol.* 2023;19(6):517-522.

BACKGROUND: The aim of this study is to compare the possible functional involvement of the vestibulo–ocular reflex in the follicular and luteal phases.

METHODS: The research was carried out at a university located in eastern Turkey. The study included 37 healthy female volunteering students aged 18-25 years. The functional head impulse test was applied twice in the follicular phase and in the luteal phase, and the results in both phases were compared.

RESULTS: In the functional head impulse test, statistically significant differences were obtained between the follicular phase and the luteal phase at the stimulus to the lateral semicircular canal direction total and 6000°/s^2 acceleration percentage of correct answers values, the posterior semicircular canal direction stimulations at 3000°/s^2 and 5000°/s^2 acceleration percentage of correct answers values, and the anterior semicircular canal direction stimulations at 5000°/s^2 acceleration percentage of correct answers values.

CONCLUSION: In the luteal phase, which corresponds to the period before menstruation, the vestibulo–ocular reflex is functionally negatively affected.

KEYWORDS: Menstruation, follicular phase, luteal phase, vestibulo–ocular reflex, f-HIT

INTRODUCTION

Menstruation is a physiological event that takes place in women regularly every month from puberty to menopause, affecting the whole body, primarily the reproductive system.[1] These changes, which occur regularly every month for the realization of reproduction in women, form the menstrual cycle, which lasts for an average of 28 days. During the menstrual cycle, an ovum matures and becomes ready for fertilization. At the same time, the uterine endometrium is prepared for implantation. When fertilization does not occur, the layer prepared in the endometrium is shed, and menstruation occurs.[2] The execution of this process takes place by the hormones secreted from the hypothalamus and pituitary. Estrogen and progesterone hormones are secreted from the ovaries, which are under the control of gonadotropic hormones secreted from the anterior lobe of the pituitary.[3]

The menstrual cycle consists of two phases, the follicular phase and the luteal phase.[4] The follicular phase, which is the first phase of the menstrual cycle, constitutes part of the 28-day menstrual cycle until the 14th day. The prolongation of this phase causes the prolongation of the menstrual cycle. The follicular phase is under the influence of follicle-stimulating hormone (FSH). Toward the end of menstruation, the follicles begin to mature under the influence of FSH and they secrete estrogen. One of the follicles formed by the effect of hormones on each other grows larger and is called the Graafian follicle. The evacuation of the maturing follicle from the ovaries is called ovulation and it takes place around the 12th-14th day when the estrogen level is the highest. The phase that lasts 13-15 days after ovulation is called the luteal phase. In the luteal phase, the group of cells called the corpus luteum secretes more progesterone hormone. The secreted progesterone hormone has an effect on the pituitary gland. If fertilization has not occurred, estrogen and progesterone secretion decreases as a result of the effect of hormones on each other, causing the corpus luteum to degenerate and a new menstruation begins.[2]

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Received: December 19, 2022 • **Accepted:** July 15, 2023 • **Publication Date:** November 30, 2023
Available online at www.advancedotology.org

As a result of varying hormonal activities, the menstrual cycle has physical and psychological effects, such as pain, restlessness, irritability, depression, headache, nausea, dizziness, and imbalance, which vary from person to person. Especially 4-10 days before menstruation, estrogen, progesterone, and aldosterone levels rise and dizziness or imbalance can be seen due to these changes.[5] Progesterone is secreted by the adrenal glands of the central nervous system and increases in the luteal phase.[6] Labyrinth edema caused by high progesterone in the luteal phase creates fluid and pressure changes in the inner ear, causing symptoms such as imbalance, ear fullness, and tinnitus.[7] However, labyrinth edema should not be considered as the only cause of dizziness.[8] Progesterone can cause hyperventilation and can cause dizziness and imbalance due to its effects on the brain. The increased amount of cerebrospinal fluid in and around the brain during the premenstrual period can cause increased intracranial pressure. This pressure is transmitted to the inner ear via the cochlear aqueduct and can also cause balance and hearing symptoms.[9] These symptoms disappear with the onset of menstrual bleeding.[8] Vestibulo–ocular reflex (VOR) is one of the basic reflexes that plays a role in maintaining balance by keeping the visual field stable during head movements. Due to its connection with the vestibular nerve and vestibular nuclei, the VOR is affected in balance disorders.[10] There is no study in the literature regarding the effect of the menstrual cycle on the VOR. This is the first study functionally evaluating the VOR during menstruation. In our study, it was aimed to determine in which period the vestibular system is affected by functionally comparing the VOR according to the follicular and luteal phases.

MATERIAL AND METHODS

Study Design

In this study, a descriptive cross-sectional design was used to obtain information about the possible functional effects of the VOR in the follicular and luteal phases.

Individuals

The functional head impulse test (f-HIT) was applied to 37 healthy female students twice, in the follicular phase and in the luteal phase, and the results from both phases were compared. The population of the research is 18-25 years old volunteering female students studying at the university. Inclusion criteria were as follows: having not used any hormonal contraceptives in the previous 6 months and having no communication disability, cognitive problem, diagnosed balance problem, and diagnosed hearing loss. The sample of the study was determined by power analysis. According to the calculation made using the G*power 3.1 program, the sample size was determined as a minimum of 31 individuals, with an effect size of 0.30, a margin of error of 0.05, a confidence level of 0.95, and a population representation of 0.95.[11] The study was completed with 37 people who accepted to participate in the study, signed the Informed Consent Form and met the inclusion criteria.

MAIN POINTS

- The menstrual cycle is effective on vestibular function.
- Functional VOR differences were observed between menstrual cycle phases.
- In f-HIT, %CA was obtained higher in the follicular phase than in the luteal phase.

Data Collection

A Personal Data Form and the f-HIT were administered to the individuals participating in the study by the researcher.

The Personal Data Form

A form containing information about age and menstruation period was filled by the researchers.

Functional Head Impulse Test

Beon Solution f-HIT (Zero Branco, Italy) system was used in the research. The participant was positioned 1.5 m away from the computer screen. The test was explained after placing a headband with a gyroscope. The participant was given a mini keyboard and asked to choose the direction of the C-shaped optotype, which flashed at 80 ms on the computer screen and shrunk according to the answers given. Static visual acuity was determined by the minimum optotype size that the participant could read. The determined optotype size was increased by 0.6 LogMAR and the testing phase was started. The patient was asked to select the direction of the optotype, which flashed rapidly on the computer screen during the movement, using the keyboard by making head movements with stimulating effect in different acceleration ranges in the direction of the semicircular canal (SCC). As a result of the test, the percentage of correct answers (%CA) was evaluated.

Statistical Analysis

Data analysis was carried out with the Statistical Program for the Social Sciences version 25.0 (IBM SPSS Corp.; Armonk, NY, USA) program. The Kolmogorov–Smirnov test was used to check whether the data included in the study fit the normal distribution.[12] The significance level (P) for comparison tests was taken as .05. Since the variables did not have a normal distribution ($P > .05$), the analysis was continued with non-parametric test methods. For comparisons in dependent pairs, since the assumption of normality was not provided, the Wilcoxon sign test was used.

Ethical Principles of Research

The research was carried out at a university located in eastern Turkey. Approval was obtained from the İnönü University Institute of Health Sciences Non-Interventional Clinical Research Ethics Committee (Decision number: 2022/3320, Date: March 29, 2022) and from all individuals participating in the study.

RESULTS

The data including the age and menstrual period characteristics of the participants are shown in Table 1.

In the f-HIT test applied to the individuals included in the study, the comparison of the %CA values between the phases as a result of stimulations at different acceleration intervals in the lateral SCC direction is shown in Table 2.

While there was no statistically significant difference between the phases regarding %CA values at 4000 and 5000°/s^2 accelerations in the lateral SCC plane ($P > .05$), a statistically significant difference

Table 1. Age and Menstruation Period Characteristics

Variable	Mean ± SD	*M* (Minimum–Maximum)
Age	20.62 ± 1.04	(18-23)
Age of menarche	13.11 ± 1.20	(11-16)
Menstruation cycle (days)	28.65 ± 2.25	(21-32)
Menstruation length (days)	5.86 ± 1.18	(3-8)

M, median.

Table 2. Comparison of Mean Lateral Semicircular Canal Percentage Correct Answers by Phases

Variable	Follicular Phase	Luteal Phase	*P*
	Mean ± SD *M* (Minimum–Maximum)	Mean ± SD *M* (Minimum–Maximum)	
4000°/s² %CA	94.57 ± 11.66 100 (50-100)	90.53 ± 15.98 100 (50-100)	.090
5000°/s² %CA	89.96 ± 14.02 100 (50-100)	85.35 ± 19.50 100 (10-100)	.090
6000°/s² %CA	86.22 ± 17.19 100 (50-100)	80.16 ± 21.78 80 (25-100)	.034*
Total %CA	90.61 ± 8.71 92.9 (64.7-100)	85.83 ± 12.90 87.1 (41.7-100)	.023*

M,median; *P*, Wilcoxon sign test significance value.
**P* < .05; there is a statistically significant difference between the groups.

was found in the 6000°/s² acceleration and total %CA values ($P < .05$, Table 2).

As a result of the stimulations made in the lateral SCC, the measurement values in the luteal phase were lower than those in the follicular phase (Figure 1).

In the f-HIT test applied to the individuals included in the study, the comparison of the %CA values between the phases as a result of stimulations at different acceleration intervals in the posterior SCC is shown in Table 3.

While there was no statistically significant difference between 4000 and 6000°/s² acceleration and total %CA values in the posterior SCC plane between phases ($P > .05$), a statistically significant difference was found in 3000 and 5000°/s² acceleration %CA values ($P < .05$) (Table 3).

As a result of the stimulation made toward the posterior SCC, the measurement values in the luteal phase were lower than the measurement values in the follicular phase (Figure 2).

In the f-HIT test applied, the comparison of the %CA values between the phases as a result of stimulations at different acceleration intervals in the anterior SCC direction is shown in Table 4.

While there was no statistically significant difference between phases regarding 3000, 4000, 6000°/s² acceleration and total %CA values in the anterior SCC plane ($P > .05$, Table 3), a statistically significant difference was found at the 5000°/s² acceleration %CA value ($P < .05$, Table 3).

As a result of the stimulation made toward the anterior SCC direction, the measurement values in the luteal phase were lower than those in the follicular phase, except for the 6000°/s² acceleration value (Figure 3).

DISCUSSION

As a result of hormonal activities that vary during the menstrual period, the menstrual cycle has physical and psychological effects. One of these effects is dizziness.[5] In the study, the functional comparison of the VOR according to the follicular and luteal phases was made and it was evaluated in which period the vestibular system may be affected. Participants included in the study were examined in terms of age at menarche, menstrual cycle time, and menstruation length. The menarche age of the individuals was observed as

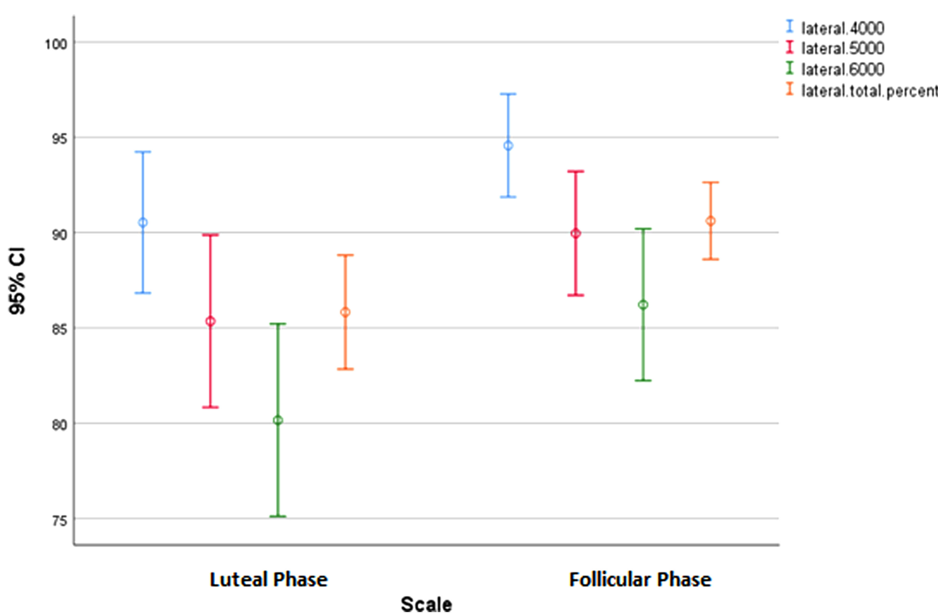

Figure 1. Mean Standard Deviation Graph of Mean Lateral Semicircular Canal Percentage Correct Answer Values by Phases.

Table 3. Comparison of Mean Posterior Semicircular Canal Percentage Correct Answer by Phases

Variable	Follicular Phase	Luteal Phase	*P*
	Mean ± SD *M* (Minimum–Maximum)	Mean ± SD *M* (Minimum–Maximum)	
3000°/s² %CA	94.15 ± 10.96 100 (67-100)	88.97 ± 19.61 100 (33-100)	.022*
4000°/s² %CA	89.74 ± 14.61 100 (50-100)	88.54 ± 18.00 100 (17-100)	.935
5000°/s² %CA	89.99 ± 14.44 100 (50-100)	83.41 ± 20.11 97.5 (33-100)	.022*
6000°/s² %CA	85.14 ± 16.53 100 (50-100)	80.82 ± 24.91 100 (33-100)	.099
Total %CA	89.47 ± 8.65 91.13 (70.2-100)	85.83 ± 12.90 87.1 (41.7-100)	.126

M; median; *P*, Wilcoxon sign test significance value.
**P* < .05; there is a statistically significant difference between the groups.

13.11 ± 1.20 years. This value is similar to the results of studies on the age of menarche in the literature.[13,14] The menstruation cycle time of individuals was 28.65 ± 2.25 days, while the length of menstruation was 5.86 ± 1.18 days. These values are similar to the menstruation cycle times[15,16] and menstruation lengths in studies in the literature.[17] This shows that the menstrual cycles of the participants included in our study were not irregular.

The individuals included in the study were evaluated in terms of the functionality of the VOR, one of the most important reflexes of the vestibular system. Disturbances in the vestibular system can affect the VOR through neural connections. In other words, the VOR gives us important information about the functionality of the vestibular system. The f-HIT device is a new test battery developed to evaluate the functional performance of the VOR.[18] The individuals in the study were evaluated in terms of the %CA of the stimulations at different accelerations in the lateral, posterior, and anterior SCC planes between the follicular and luteal phases. Statistically significant differences were obtained in 6000°/s² acceleration and total %CA values in the lateral SCC plane, 3000°/s² and 5000°/s² acceleration %CA values in the posterior SCC plane, and 5000°/s² acceleration %CA values in the anterior SCC plane. When the mean %CA and SD graphs for the lateral, posterior, and anterior canals were examined, the measurement values in the luteal phase were lower than those in the follicular phase, albeit not significant in all values. The reason for this outcome is thought to be the increase in estrogen, progesterone, and aldosterone hormones in the premenstrual period, which coincides with the luteal phase.[2] The increase in these hormones causes the body to retain water and salt, causing a change in the homeostasis of ear fluids and affecting inner ear functions.[19] It is also thought that estrogen and progesterone directly affect the visual–vestibular interaction areas in the central system.[20,21] It was reported that estrogen and progesterone levels in the premenstrual period affect optokinetic function by modulating both gamma-aminobutyric acid and glutamate receptor function in the cerebellum.[22] It was also reported that progesterone affects the transmission mechanism of vestibular nuclei related to vestibulo-ocular and vestibulo-spinal reflexes as well as optokinetic function.[23]

Emekçi and Erbek (2021) examined the relationship between age and %CA via f-HIT in 18-35 years old healthy individuals. The mean %CA values of the lateral SCC (88.66 ±12.07), anterior SCC (88.76 ± 11.37), and posterior SCC (90.54 ±12.19) they reported were higher than the present values from the premenstrual period, which is the luteal phase in the present study, support the idea that the vestibular system may be affected during this period.[24] In addition, in another study investigating the effects of menstruation on the vestibular system, it was stated that 16% of individuals in the premenstrual period had spontaneous nystagmus, 24% had positional nystagmus, and 36% had abnormal caloric responses, and these findings improved in the week after menstruation. The fact that the %CAs in the luteal phase, which corresponds to the premenstrual period in our study, were lower than the follicular phase, which corresponds to the postmenstrual period, is similar to the improvement of the postmenstrual findings in this study. In addition, it was determined that 7 of the

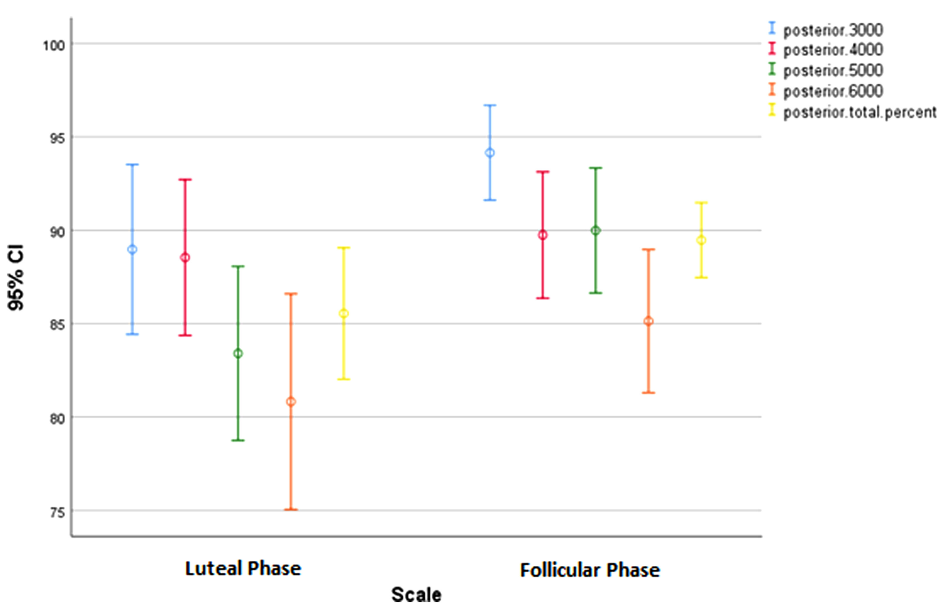

Figure 2. Mean Standard Deviation Graph of Mean Posterior Semicircular Canal Percentage Correct Answer Values by Phases.

Table 4. Comparison of Mean Anterior Semicircular Canal Percentage Correct Answer by Phases

Variable	Follicular Phase	Luteal Phase	*P*
	Mean ± SD *M* (Minimum–Maximum)	Mean ± SD *M* (Minimum–Maximum)	
3000°/s^2 %CA	95.84 ± 10.68 100 (50-100)	93.39 ± 13.94 100 (33-100)	.257
4000°/s^2 %CA	92.49 ± 12.76 100 (40-100)	90.99 ± 14.62 100 (33-100)	.424
5000°/s^2 %CA	92.35 ± 12.82 100 (50-100)	86.95 ± 15.28 100 (50-100)	.028*
6000°/s^2 %CA	86.04 ± 17.30 100 (33-100)	88.46 ± 19.62 100 (33-100)	.497
Total %CA	91.73 ± 7.99 92.9 (68.75-100)	89.87 ± 10.05 92.9 (64.3-100)	.237

M, median; *P*, Wilcoxon sign test significance value.*$P < .05$; there is a statistically significant difference between the groups.

cases with abnormal caloric response had a peripheral problem and 2 had a central problem. In this study, it was pointed out that vestibular disorders occurring in the premenstrual period are not only caused by labyrinth edema but also brain edema may cause these disorders.[8]

Symptoms reminiscent of Meniere's disease such as dizziness, nausea, and pressure in the ear can be experienced in the premenstrual period.[7,24] The cause of Meniere's disease is endolymphatic hydrops. Different hypotheses have been present regarding the cause of hydrops. One of these hypotheses is about hormonal changes. These hormonal changes affect the severity and frequency of Meniere's attacks by causing pressure changes in the endolymph and perilymph.[25] Kirazlı (2021) evaluated patients with unilateral vestibular insufficiency, including Meniere patients, with f-HIT, and found in the patient group that lateral SCC (65.88 ± 31.04), anterior SCC (74.8 ± 23.9), and posterior SCC (72.57 ± 24.67) total %CA values in the direction of the affected ear were lower compared to those of the control group.[26] It is known that ovarian hormones have edema-forming properties. High progesterone in the luteal phase can cause changes in electrolyte fluid levels, causing symptoms similar to Meniere's disease such as a feeling of fullness in the ears, imbalance, and tinnitus.[7] In other studies in the literature, it is stated that hormones may play a role in vestibular disorders such as Meniere's disease.[27] The %CA values in the luteal phase in our study were better than the %CA values reported in Kirazlı's study. In the literature, it is reported that even if hormonal changes show symptoms similar to Meniere's disease, sometimes audiology tests will be within physiological limits.[28] However, the fact that some %CA values in the luteal phase in our study was lower than those in the follicular phase draws attention to the fact that the VOR may have been affected due to hormonal changes. Although it is thought that this effect stems from labyrinth edema, which results from water and salt retention caused by hormones, it is stated in some studies that premenstrual symptoms may also be caused by edema in the brain. However, in both cases, with the onset of menstrual bleeding, hormone levels decrease and complaints improve.[8]

Studies in the literature report that dizziness and imbalance complaints can be seen with the effect of hormones in the premenstrual period and vestibular involvement may occur.[22] The findings of our study support the literature and it is seen that the VOR is functionally affected in the luteal phase, which corresponds to the premenstrual period.

Functional comparison of the VOR according to the follicular and luteal phases was made and it was examined in which period the vestibular system could be affected. Functional examination of the VOR only at 3000-6000°/s^2 acceleration values in the f-HIT test used in our study is one of the limitations of our study. In future studies, the effects of menstrual cycle phases should be examined by evaluating the VOR in more detail with test batteries (video head impulse, caloric, and head shake test) that evaluate the VOR at different frequencies. In addition, since the menstrual cycle is affected by many factors, re-testing in the next menstrual cycle phases will increase the reliability.

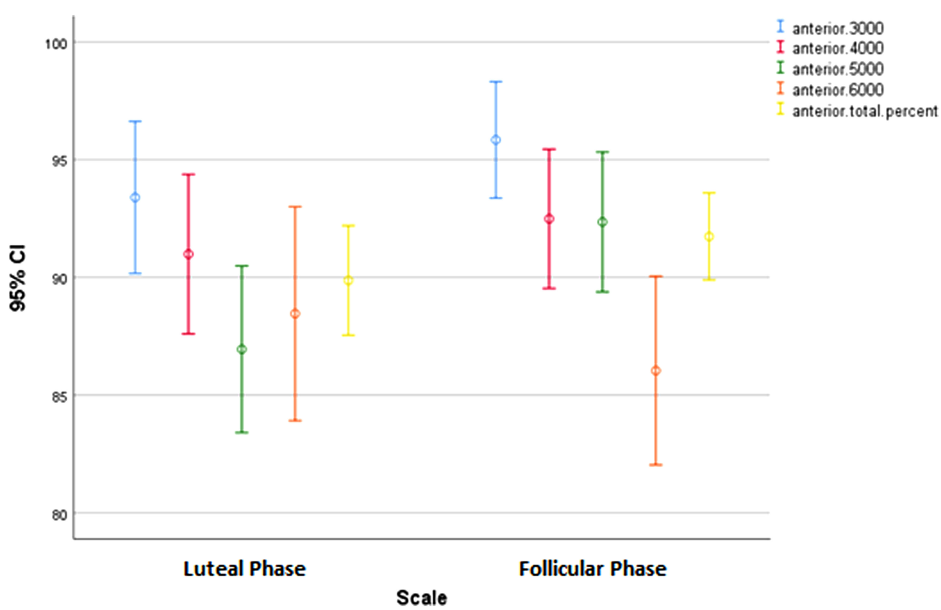

Figure 3. Mean Standard Deviation Graph of Mean Anterior Semicircular Canal Percentage Correct Answer Values by Phases.

It was determined that the VOR in the luteal phase is functionally negatively affected by the physiological effect of hormones in the menstrual cycle. More objective test batteries are needed to determine whether the peripheral or central part of the vestibular system is responsible for this negative impact of the VOR in the luteal phase. It should be noted that there may be balance problems along with many problems that occur in the menstrual cycle in young girls. When considering this physiological process, detailed evaluations should be made in terms of the balance system. In future studies, in order to explain the effects of the menstrual cycle on the vestibular system in more detail, it is recommended to evaluate it in combination with different vestibular test batteries according to phases and these studies should be supported by subjective measurements.

Ethics Committee Approval: This study was approved by the Ethics Committee of İnönü University Institute of Health Sciences Non-Invasive Clinical Research (Decision number: 2022/3320, Date: March 29, 2022).

Informed Consent: Informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – D.U.C., H.Ü.K.; Design – D.U.C., H.Ü.K.; Supervision – D.U.C., H.Ü.K.; Resources – D.U.C., S.C.Ç.; Materials – D.U.C., S.C.Ç.; Data Collection and/or Processing – D.U.C., S.C.Ç.; Analysis and/or Interpretation – D.U.C., S.C.Ç.; Literature Search – D.U.C., S.C.Ç., H.Ü.K; Writing – D.U.C., S.C.Ç., H.Ü.K.; Critical Review – D.U.C., H.Ü.K.

Acknowledgments: We would like to thank our patients who participated in our study for their contribution to the studies.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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