Original Article

Effect of different phases of menstrual cycle on brainstem auditory evoked response

Meenal Batta, Shashi Kant Dhir[1], Avnish Kumar[2], KD Singh[2]

Departments of Physiology and [1]Pediatrics, Guru Gobind Singh Medical College, Faridkot, [2]Department of Physiology, Government Medical College, Patiala, Punjab, India

Abstract

Introduction: The change in the hormonal levels during the three phases of menstrual cycle, namely, menstrual phase (hormonal withdrawal), proliferative phase (estrogen peak), and secretory phase (progesterone peak), influences the conduction velocities in the central auditory pathways. Variable findings of brainstem auditory evoked response (BAER) have been reported during different phases of menstrual cycle by different researchers. **Aim:** To study the effect of different phases of menstrual cycle on BAER. **Methodology:** A prospective observational study on 80 audiometrically normal, healthy, eumenorrheic female students in age group of 18–24 years was done at a medical college of northern India. BAER was recorded across the three phases of the menstrual cycle, i.e., menstrual phase (day 1–3), proliferative phase (day 10–12), and secretory phase (day 20–22). Recordings of peak latencies, interpeak latencies, and amplitude of waves of BAER were taken and statistically analyzed. **Results:** In this study, significant decrease in the latencies of wave III, wave V, and interpeak latency I–III and a trend of decrease in latencies of wave I and interpeak latency I–V (which was statistically insignificant) were observed in proliferative (estrogen peak) phase as compared to menstrual and secretory phase. However, there was no statistically significant difference found in the amplitude of waves of BAER during all the three phases of menstrual cycle. **Conclusion:** The hormonal changes during different phases of menstrual cycle do seem to influence BAER.

Key words: Brainstem auditory evoked response, estrogen, phases of menstrual cycle

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Introduction

Hormones bring about physiological changes during menstrual cycle. The proliferative phase of endometrium is initiated and controlled by estrogen. The secretory phase is controlled by progesterone.[1] Auditory pathways have been known to get influenced by the changing hormonal levels across menstrual cycle. The exact role of various hormones is still not known. Different investigators have reported different findings of brainstem auditory evoked response (BAER) including prolongation, no change, and even decrease in the latencies during the proliferative phase of the menstrual cycle.[2-8] BAER has been used by researchers to study the influence of hormones on auditory pathways. BAER is the potential recorded from the ear and vertex in response to a brief auditory stimulation to assess the conduction through the auditory pathway up to midbrain. In an effort to see the effects of three phases of the menstrual cycle on the conduction in auditory pathways, we planned to record BAER across them.

Address for correspondence: Dr. Meenal Batta,
Department of Physiology, Guru Gobind Singh Medical College, Faridkot, Punjab, India.
E-mail: meenalbatta@gmail.com

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Methodology

This prospective observational study was conducted on eighty females in age group of 18–24 years at a medical college in northern India. The subjects for the study were audiometrically normal, healthy eumenorrheic medical and nursing students of the same medical college.

Exclusion criteria

Subjects with abnormal hearing, otological diseases, family history of deafness and/or phenotypical markers (such as low set ears, ear tags, facial dysmorphism, and ear deformity) suggesting ear involvement were excluded from the study. The subjects having menstrual disorders, oral contraceptive pills intake in last 6 months, and anovulatory cycles were also excluded from the study. Those subjects who refused to give consent or did not participate till the end were also excluded from the study.

Experimental design

All the participants were provided with detailed written and verbal information about the test. Ethical committee clearance was taken for the study. Informed consent was taken from all enrolled subjects. Confidentiality and privacy of the subjects was maintained.

Each subject underwent detailed physical examination. A complete ENT checkup of the subjects along with pure tone audiometry was done to assess hearing of subjects before doing BAER. Thorough menstrual history including nature, days of menstrual flow, regularity, and total duration of cycle was taken from each subject. The selected subjects were given a chart and a thermometer and were asked to record the morning basal temperature before rising from bed daily, starting from the 1st day to last day of the cycle, to document ovulation and to exclude the females with anovulatory cycles.[9]

On each subject, BAER was performed at three separate occasions of the menstrual cycle, in the menstrual phase (day 1–3), proliferative phase (day 10–12), and secretory phase (day 20–22). The study was carried out at same time of the day to avoid diurnal variation.

The correct procedure of the test was explained to all subjects. The subjects were asked to come with their hair washed and without any oil applied to improve the accuracy of the results. The information of the participants was collected in accordance with the predesigned pro forma. For the test, RMS EMG EP MARK II™ instrument (Recorders and Medicare Systems, Chandigarh, India) was used in an electrically and acoustically shielded air-conditioned room. The recordings were taken by placing electrodes on the scalp: the reference electrode at the vertex, ground electrode on the forehead, and active electrodes at the left and right ear lobe. The impedance of skin to electrode was kept below 5 kΩ. The 2000 click stimuli having intensity of 60 dB above the normal hearing threshold were given to each ear independently using headphones at the rate of 11.1/s and for a duration of 0.1 ms. Latencies in waveforms were displayed on the monitor after filtration (at 100 and 3000 Hz), amplification, and averaging of the waves in the first 10 ms.[10] The sweep speed was set at 1 ms/division and the sensitivity of 0.5 μV/division was adjusted. The peak latencies of the waves I, II, III, IV, and V, the interpeak latencies of I–V, I–III, and III–V, the amplitudes of waves I (I–Ia) and V (V–Va), and the absolute amplitude were recorded. Both ears of each subject were taken as independent reading because of anatomical difference. Contralateral ear was masked while taking recording from each ear. We took average of the mean value of latencies of both ears as there was insignificant difference between the latencies of both ears similar to Mann *et al.*[11]

The findings were statistically analyzed using ANOVA. $P < 0.05$ was considered statistically significant and <0.01 was considered highly significant.

Results

In the present study, 88 students fulfilled the inclusion criteria. Of these, eight students were excluded because of various reasons and remaining eighty students were analyzed for the results [Figure 1]. The baseline variables of the subjects are shown in Table 1. The mean peak latencies of wave I–V, mean amplitude I–Ia, V–Va, and mean absolute amplitude of BAER in three phases of menstrual cycle are shown in Table 2 and Figure 2. The mean interpeak latencies I–III, I–V, and III–V are shown in Table 3 and Figure 2.

The difference of peak latencies of waves III and V and interpeak latency I–III was found to be statistically significant across the three phases. There was no statistically significant difference found in the amplitude of BAER during all the three phases of menstrual cycle.

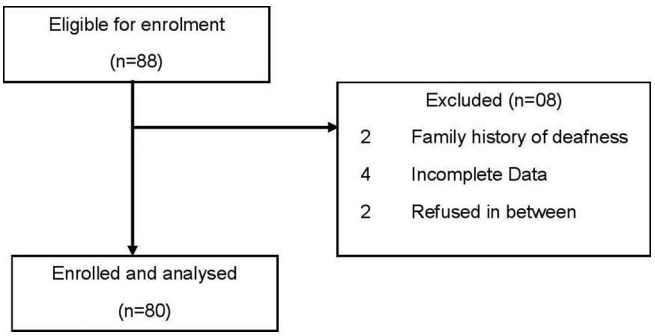

Figure 1: The study flow

Table 1: Baseline variables (*n*=80)

Parameter	Mean±SD
Age (years)	18.82±1.10
Height (cm)	158.54±5.84
Weight (kg)	51.9±6.87
Body mass index (kg/m^2)	20.68±2.81
Body surface area (m^2)	1.51±0.10

SD: Standard deviation

Table 2: Latencies and amplitude of various waves of brainstem auditory evoked response across three phases of menstrual cycle

Parameters of BAER	Mean±SD			*P*	Significance
	Menstrual phase	Proliferative phase	Secretory phase		
Wave I (ms)	1.57±0.17	1.51±0.08	1.58±0.18	0.06	NS
Wave II (ms)	2.73±0.18	2.72±0.19	2.76±0.21	0.56	NS
Wave III (ms)	3.59±0.14	3.46±0.06	3.60±0.18	0.00	HS
Wave IV (ms)	4.87±0.20	4.91±0.17	4.93±0.19	0.22	NS
Wave V (ms)	5.54±0.25	5.38±0.14	5.51±0.26	0.001	HS
Amplitude I-Ia (μV)	1.02±0.78	0.89±0.84	0.99±0.59	0.65	NS
Amplitude V-Va (μV)	1.19±0.69	1.10±0.71	1.06±0.42	0.51	NS
Absolute amplitude (μV)	1.1±0.57	1.15±0.69	1.21±0.59	0.67	NS

P<0.01=HS; *P*<0.05=S; *P*>0.05=NS. NS: Not significant; HS: Highly significant; S: Significant; BAER: Brainstem auditory evoked response; SD: Standard deviation

Table 3: Interpeak latencies of brainstem auditory evoked response across three phases of menstrual cycle

Parameters of BAER	Mean±SD			*P*	Significance
	Menstrual phase	Proliferative phase	Secretory phase		
IPL I-III (ms)	1.93±0.23	1.87±0.17	1.97±0.20	0.04	S
IPL I-V (ms)	3.88±0.28	3.79±0.25	3.90±0.31	0.09	NS
IPL III-V (ms)	1.95±0.27	1.93±0.16	1.94±0.36	0.89	NS

P<0.01=HS; *P*<0.05=S; *P*>0.05=NS. NS: Not significant. BAER: Brainstem auditory evoked response; SD: Standard deviation; IPL: Interpeak latencies

On doing post hoc analysis, a significant decrease in the peak latencies of waves III and V and a trend of decrease in peak latency of wave I, though statistically insignificant, was found during proliferative (estrogen peak) phase as compared to menstrual and secretory phase. Also, in the proliferative phase, significant decrease in interpeak latencies I–III and a trend of decrease in interpeak latency I–V, though not significant, were seen as compared to other phases.

Discussion

In the present study, statistically significant decrease in the latencies of wave III, wave V and interpeak latency I–III was observed in proliferative phase as compared to menstrual and secretory phase. Also, a trend of decrease in latencies of wave I and interpeak latency I–V (which was not statistically different) was seen in proliferative phase as compared to other two phases.

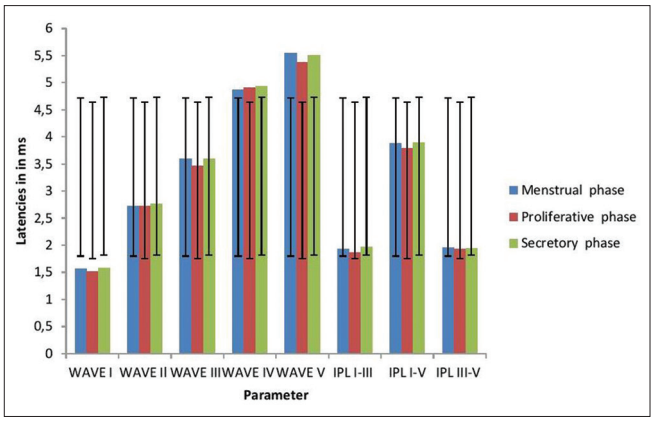

Figure 2: Comparison of parameters of brainstem auditory evoked response in different phases of menstrual cycle

The precise role of hormones on auditory transmission is still under research and previous studies report wide variation in the results ranging from decreased latencies to no change to increased latencies of BAER in all phases. Some researchers did not find any effect of hormones on latencies and interpeak latencies.[2,3,12]

Similar to our study, increased conduction in the auditory pathways in the proliferative phase (estrogen peak) has been reported earlier.[4,7,8,13] Shorter values for wave I and interpeak latency I–V were found during follicular phase in earlier studies.[7,8] Also, longer latencies have been seen in estrogen deficient females.[4] Increased conduction in neural pathways due to effect of estrogen has also been reported in another previous study.[13]

Contrary to our results, delayed conduction in the auditory pathway has also been shown in other studies during the proliferative phase.[5,11,14-17] Prolonged latency of wave III and V and interpeak latency I–V in estrogen peak phase were observed in some studies.[5,14] In another study, increased latency of wave V and interpeak latency III–V were seen in late follicular phase.[15] An increase in the peak latencies in the estrogen peak mid cycle with statistically insignificant change in interpeak latencies was also reported in few studies.[11,17] Little data are available about interpeak latency I–III and this was significantly decreased in our study during the estrogen peak phase and could be attributed to its effect. There was no statistically significant difference found in the amplitude of BAER during all the three phases of menstrual cycle. Very little data are available regarding the variation in the amplitude during different phases of menstrual cycle.

The decrease in the latencies and interpeak latencies in proliferative phase in our study could be attributed to estrogen effect, indicating increased conduction in auditory pathways. This may be due to effect of estrogen leading to increased

sensitivity of the central nervous system to catecholamines. This leads to change in the opening frequency of voltage-related L-type calcium channels and augments the effect of glutamate as well as inhibition of the formation of gamma-amino butyric acid by the inhibition of glutamate decarboxylase enzyme, thus increasing the conduction through the neural pathways.[18]

The variation in the findings in earlier studies may be due to different sample size, different classification of menstrual cycle phases as well as different time of doing BAER during a particular phase, and separate parameters studied by different investigators.

Limitations

The sample taken in our study was not representative of the general population. Long latency auditory evoked potentials (LLAEPs) were not studied and their inclusion would have made the observations more elaborative. We used basal body temperature method as an indicator of ovulation. This method is not most accurate and is prone to get influenced by variables such as psychological state of mind, lack of sleep, and physical activity.

Future prospects

Research with stratification of various phases of menstrual cycle can help in better evaluation of the significance of changes in BAER. Further studies with large sample size are required from general population to explore the possible biomechanisms underlying the findings of this study. The effect of the menstrual phases on BAER on higher pathways should also be studied using LLAEPs.

Conclusion

This study shows the fact that hormonal changes during different phases of menstrual cycle do affect the auditory conduction pathways. Estrogen increases transmission in the auditory pathways and it might be responsible for the shorter latency values of BAER during the proliferative phase.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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