



TO IDENTIFY THE SINGLE BEST PREDICTOR OF HORMONE SENSITIVE CHANGES IN BERA DURING MENSTRUAL CYCLE

Physiology

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ABSTRACT

INTRODUCTION: Numerous studies have been carried out in the last few decades studying the effect of female hormones on the Brainstem Auditory Evoked Responses (BERA). This study was undertaken to identify the single best predictor of hormone sensitive changes during menstrual cycle of the various parameters of BERA.

MATERIAL METHODS: 50 females (students and staff) at Government Medical College Amritsar underwent BERA testing thrice in one menstrual cycle; day 1-3 i.e Menstrual Phase, day 11-14 i.e Estrogen peak Mid cycle and day 17-22 i.e progesterone peak Luteal phase.

RESULTS: Eleven parameters were recorded by BERA. A significant to highly significant increase in latencies seen in phase 2. Similar trends seen in inter-peak latency I-III, I-V and III-V. No significant change in amplitude of Wave I or V while significant decrease in amplitude ratio is seen in phase 2. On comparing the phase 2 and 3 the only significant change seen is a decrease in latency of all waves.

CONCLUSION: The absolute latency of the waves is thus the single most sensitive indicator of hormone induced changes in BERA during menstrual cycle.

KEYWORDS

BERA, menstrual cycle, latency, sensitive.

INTRODUCTION

The progress in technology and its application in physiology has made feasible the recording of even minute biological action or signs arising from the human brain. These signals are related to an event i.e a stimulus and are thus time locked to it. These stimuli can be a visual, a auditory stimulus or a mental event etc. Auditory evoked potentials (AEPs) are a subset of Event Related Potentials as described above. It reflects the electrical activity which passes along the auditory nerve pathway. The AEPs are divided into 3 sections based on the latency of waves those recorded early i.e. within 0-5 ms of application of the stimulus are called auditory brainstem response. Various literature unanimously agree about the origin of the waves as shown in Table 1

Table 1 Waves of BERA with their site of generation

Wave	Site of generation
Wave I	Cochlear Nerve
Wave II	Cochlear Nucleus
Wave III	Superior Olivary Complex
Wave IV	Lateral Lemniscus
Wave V	Inferior Colliculus

Also from these can be calculated the inter peak latencies, amplitudes and amplitude ratio of the waves.

A large quantity of research has examined the relation between menstrual cycle and BERA, however there are no conclusive studies that clearly identify the direction of the link which joins these two variables. This study differs from earlier studies in that it focuses on the finding the single best predictor of hormone sensitive changes of all the parameters of BERA.

MATERIAL AND METHODS

This study was done Department of Physiology, Government Medical College, Amritsar, India, over a one year period, after obtaining a clearance from the institutional "Ethics Committee". An informed consent was obtained from subjects. 50 females were randomly selected from students (medical and paramedical) and staff at Government Medical College Amritsar. They underwent BERA testing thrice in one menstrual cycle. Three recordings were done on day 1-3 i.e Menstrual Phase, day 11-14 i.e Estrogen peak Mid cycle and day 17-22 i.e progesterone peak Luteal phase in the same menstrual cycle. All participants had regular menstrual cycles of 28-30 days and they had not taken any hormonal pills during the past 6 months. Only those subjects who had a Body Mass Index (BMI) which

was within the normal range (18.5-24.99 kg/m²) were included in the study. Tuning fork tests were carried out to rule out any conduction defect. A retrospective calculation of the approximate day of ovulation was done from the day of onset of the next menstrual cycle.

The recordings were obtained by using the RMS EMG EP MARK II version: 7.5.7 2Ch (PC-based) machine. The standard protocol of carrying out the BERA recording was followed. All precautions pertaining to subject preparation, resistance offered while recording, application of filters etc were duly taken care of. The waves in the first 10 ms of the latency were considered for ABR. The peak latencies of the waves, I, II, III, IV and V, the inter peak latencies of I-V, I-III and III-V, the amplitudes of waves I and V and the amplitude ratio (V/I) were recorded.

A paired data t-test was used to compare each phase of the menstrual cycle. All the recorded values were reported as mean $\pm$ SD. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

Eleven parameters were recorded by performing brain stem auditory evoked potentials. In each subject the BAEP recordings were obtained three times in a menstrual cycle i.e. once in each phase of menstrual cycle. Out of the enrolled subjects the recordings could not be completed 4 times in 5 subjects. They were replaced by an equal number of new subjects. Each value was expressed as mean $\pm$ SD (in ms or v); hence smaller values indicate more rapid neural transmission. The results obtained were examined and analysed to find out which parameter was most sensitive in responding to the fluctuating hormone level.

It was seen as shown in Table 2 that a significant to highly significant increase in latencies is seen in phase 2. Almost similar trends are followed by inter-peak latency I-III, I-V and III-V. No significant change in amplitude of either Wave I or V while significant decrease in amplitude ratio is seen in phase 2. On comparing the phase 2 and 3 as seen in table 3 the only significant change seen is a decrease in latency of all waves.

Table-2 Comparison Of Latencies, Inter-peak Intervals, Amplitudes And Amplitude Ratio Of Different Waves Between Phase 2 (proliferative) And Phase 1 (menstrual)

	Phase 1 (Mean $\pm$ SD)	Phase 2 (Mean $\pm$ SD)	't' value	'p' value	Significance
Latency(ms) Mean SD					
International Journal of Scientific Research					
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I	1.540.17	1.600.18	-2.112	0.04	S
II	2.570.31	2.900.14	-7.092	<0.001	HS
III	3.500.15	3.600.17	-3.059	0.004	S
IV	4.650.19	4.780.18	-3.494	0.001	S
V	5.520.23	5.620.22	-2.439	0.018	S
Inter-peak Latency(ms) Mean SD					
I-III	1.960.25	2.000.23	-0.916	0.364	NS
I-V	3.970.27	4.020.28	-0.944	0.35	NS
III-V	2.020.25	2.020.28	-0.108	0.914	NS
Amplitudes (v) Mean SD					
I	0.630.24	0.570.13	1.733	0.089	NS
V	0.510.20	0.450.14	1.718	0.092	NS
Amplitude ratio (V/I)					
AR	1.150.93	0.850.36	2.413	0.020	S

HS=highly significant ($p<0.001$); S=Significant ($p<0.05$); NS=Not significant ($p>0.05$)

Table-3 Comparison Of Latencies, Inter-peak Intervals, Amplitudes And Amplitude Ratio Of Different Waves Between Phase 3 (secretory) And Phase 2 (proliferative)

	Phase 2 (Mean±SD)	Phase 3 (Mean±SD)	't' value	'p' value	Significance
Latency(ms) Mean SD					
I	1.600.18	1.550.20	2.112	0.04	S
II	2.900.14	2.610.20	8.232	<0.001	HS
III	3.600.17	3.530.17	2.293	0.026	S
IV	4.780.18	4.690.15	3.186	0.003	S
V	5.620.22	5.520.25	2.237	0.03	S
Inter-peak Latency(ms) Mean SD					
I-III	2.000.23	1.980.19	0.517	0.608	NS
I-V	4.020.28	3.970.31	0.882	0.382	NS
III-V	2.020.28	2.000.28	0.44	0.662	NS
Amplitudes (v) Mean SD					
I	0.570.13	0.630.25	-1.96	0.056	NS
V	0.450.14	0.420.19	1.044	0.301	NS
Amplitude ratio (V/I)					
AR	0.850.36	0.770.31	1.356	0.181	NS

HS=highly significant ($p<0.001$); S=Significant ($p<0.05$); NS=Not significant ($p>0.05$)

DISCUSSION

The hormones secreted by ovary have been found to affect the sensory conduction. A decrease in threshold during menstruation means that lowest level of sex hormones is associated with better hearing.^{3,4} A decrease in estrogen⁵ could directly change neurotransmitter levels at the synapse and thus influence conduction time.⁶ Estrogen could modify the secretion of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) resulting in delayed synaptic conduction time.⁷ Estrogen might influence acetylcholine synthesis, which is present in the auditory system too.⁸

Table 2 shows comparison of absolute latencies, inter-peak latencies, amplitudes and amplitude ratio of different Waves of BAEP between phase 2 (proliferative) and 1 (menstrual) subjects. The absolute latencies of Waves I to V and amplitude ratio (V/I) shows a statistically significant change (increase) in phase 2 subjects compared to phase 1. On the other hand the inter-peak latencies (IPL) of Waves I-III, I-V & I-V and absolute values of amplitudes of Waves I & V do not show a statistically significant variation in phase 2 subjects compared to phase 1. Our these findings tally with the findings of^{4,9} but are in disagreement with others.¹⁰ These variations could be attributed to the effect of estrogenic hormones during proliferative phase (phase 2) on the conduction velocities of auditory impulses along the auditory pathways. The insignificant change in the inter-peak latencies I-III, I-V & III-V could be due to prolongation of absolute latencies of Waves I, III & V.

Table 3 shows the comparison of absolute latencies I-V, inter-peak latencies I-III, I-V & III-V, amplitudes and amplitude ratio V/I of BAEP waves between phase 3 (secretory phase) and 2 (proliferative). The data revealed highly significant ($p<0.001$) to significant ($p<0.05$) variations (decrease) in the absolute latencies of Waves I to V in phase 3 (secretory) subject compared to proliferative phase (phase 2). The data further shows statistically insignificant ($p>0.05$) variation of IPL

I-III, I-V & III-V, absolute value of amplitude of I & V and amplitude ratio V/I in phase 3 subjects compared to phase 2. The changes found in our study showing a highly significant to significant decrease in absolute latencies could be due to higher levels of progesterational hormones in secretory phase (phase 3) compared to proliferative levels (phase 2). The significant decrease in the conduction velocities of auditory impulses along the auditory pathways could be due to antagonistic effect of progesterone to estrogen in phase 3 of the menstrual cycle compared to phase 2 where there is an increase in the blood levels of estrogen only. However statistically, insignificant variations ($p>0.05$) in IPL I-III, I-V and III-V can be explained due to overall prolongation of absolute latencies of waves I, III & V.

CONCLUSION

Though Amplitude ratio would have been a good indicator as well but in this scenario the hormone sensitivity in modulating the wave latencies is best seen. The absolute latency of the waves is thus the single most sensitive indicator of hormone induced changes in BERA during menstrual cycle.

LIMITATIONS

The precise effects of the fluctuating hormone levels can be assessed by a blood level estimation of hormones rather than assumptions made by calendar timing. Also a higher number of subjects if recruited would give a better idea of the trends of association and show significant results.

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