RESEARCH ARTICLE

BRAIN STEM AUDITORY EVOKED RESPONSE DURING DIFFERRENT PHASES OF MENSTRUAL CYCLE

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ABSTRACT
Background: Due to the existing controversy on the effect of female sex hormones on the cerebral electrophysiology and the absence of conclusive study in south India about the sex hormonal influence on brain stem auditory evoked responses during different phases of menstrual cycle, this study was chosen.
Aims & Objective: The aim of the study was to evaluate the correlation of auditory brain stem response (ABR) with different phases of menstrual cycle in young healthy women in our area.
Materials and Methods: ABR recording was done in 35 healthy regular menstruating females of 20-40 years of age with normal BMI during 4 different phases of menstrual cycle. Peak latencies of waves I-V and inter peak latencies of I-III, I-V, III-V for four phases of menstrual cycle were compared.
Results: Data showed statistically significant increase in peak latencies in wave IV in phase 2 compared to all other phases. Other waves showed a trend of increase in peak latencies in the phase 2 when compared to all other phases. Inter peak latencies did not show any significant variations between different phases of menstrual cycle.
Conclusion: The results favour that female sex hormones do affect the central auditory pathway in menstrual cycle.
Key Words: Auditory Brain Stem Response; Menstrual Cycle; Central Auditory Pathway

Introduction

Auditory brain stem response (ABR) is a non-invasive method of recording electrical activity of the brain stem in response to sound stimulus. The brain stem activity is picked up by the electrodes placed on the scalp. According to Jewett and Williston in 1971 the waves recorded were labelled with Roman numerals I, II, III, IV and V. All the 5 waves are positive deflections that occur in first 10 milliseconds after the onset of auditory stimulus.[1]

The auditory structures that generate the auditory brain stem responses are[2],

- Wave I - generated by peripheral portion of 8th cranial nerve
- Wave II - from central portion of 8th cranial nerve
- Wave III - from cochlear nucleus
- Wave IV - from superior olivary nucleus / lateral lemniscus
- Wave V - from lateral lemniscus / inferior colliculus

While interpreting we mainly look at,

- Amplitude which represents the number of neurons firing
- Latency, Inter peak latency which indicates the speed of transmission

ABR is used to screen newborn's hearing ability, auditory threshold estimation, to determine the type and degree of hearing loss. It is also used in intra operative monitoring and to identify the lesions in the auditory nerve and the brain stem. The effects of female sex hormones on electrical activity of the brain can also be assessed by ABR.[3]

The female sex hormones estrogen and progesterone quantitatively changes during menarche, menstrual cycle, pregnancy and menopause. These changes not only have physical and emotional impact on them, but also affect the cerebral electrophysiology to a marked extent.[4]

Electro encephalogram (EEG) had shown variation during various phases of menstrual cycle with increase in α wave frequency at the time of ovulation.[5,6] Gonadal hormones are also known to have an effect on sexual differentiation of the brain. These hormones not only modify the taste, olfactory and auditory thresholds but also the threshold for light touch and two-point discrimination.[7,8] Various other techniques like visually evoked potential (VEP), somatosensory evoked potential (SSEP) also had shown variations during different phases of menstrual cycle.[9]

Non-communicable diseases like diabetes, hypertension and mal nutrition can also influence ABR by their effect on myelination of the nerves.[10,11] ABR also changes with variation in the mental efficacy of the individual. Reports have shown that intelligent persons produce long ABR latencies which might be due to their associated increased head circumference.[12]

Previous studies done on Auditory evoked responses showed changes during different phases of menstrual cycle.[3,9,10] Study done by Howard P et all in 1992 showed no changes in ABR during different phases of menstrual cycle in normal menstruating female but ABR showed changes in moderate and severe premenstrual syndrome subjects during their late luteal phase compared to the normal females.[13] Though number of studies was done in North India about the effects of gonadal hormones on ABR only few were in South. Hence this study was under taken to assess the auditory brain stem response during different phases of menstrual cycle.

Materials and Methods

After getting the institutional ethical committee clearance, this study was done in the department of physiology, Sri Venkateshwaraa Medical College Hospital and Research Centre, Pondicherry. 35 female subjects of 20-40 years of age with regular menstrual cycle (28-30 days) at least for the past 6 months with 1-5 days flow and ideal BMI (18.5-24.99 kg/m2) were selected.[9]

Females on hormonal pills, hearing loss, ear discharge and endocrinal disorders were excluded. Care was taken to see that the person did not suffer from cold during the time of recording. After getting informed consent, detailed medical, menstrual and drug history were taken. Complete ENT examination along with Rinne's test, Weber's test and Absolute bone conduction test were carried out to rule out ear pathology. ABR recordings were done using Physiopac PP4, Medicaid Chandigarh in our department. All recordings were done from 10 am-12 pm in a quite air conditioned room.[14]

The subjects were asked to lie down on semi-reclined bed, made to relax completely in order to minimize the artefacts. Ornaments like earrings, hair clips were removed as it may alter the readings. Ground electrode was placed around the wrist. After cleaning the site with spirit (to prevent contact impedance) active electrode was placed on the respective mastoid of the ear through which the click stimuli has to be given. Reference electrode was kept in the vertex using cup electrode and the electrode paste. All the electrodes were plugged to the junction box. Contact impedance was constantly monitored using impedance meter to keep electrode impedance below 5 k ohms. The electrical activity of the brain stem was picked up by the electrodes when the click stimuli were given. The filtered, amplified, averaged values were displayed on the screen. The machine is provided with inbuilt artefact rejection facility.[14]

For recording ABR 2000 click stimuli were given at 60 dB intensity. The rare type stimuli were generated by passing 0.1ms square pulses through head phones. Monaural stimulation was used at the rate of 10 pulses per second and the contra lateral ear was masked with white noise with intensity less than that of the click stimuli. The responses in the first 10 ms were averaged. Filtration was done between 5Htz to 3000Htz.[14] Four recordings were done during menstrual phase (1-3 days) and mid cycle (11-14 days), mid luteal (17-22 days) premenstrual (25-27 days) phases. Peak latencies of the waves I to V and inter peak latencies I-V, I-III, III-V were analysed.[15]

Both ears of each woman were taken as independent samples since anatomically both auditory pathways are different. Average of both the ear latencies was taken as the differences between the latencies were negligible.[15]

Statistical analysis done after presenting the data as means (SD). Multivariate ANOVA and post Hoc Dunnett test done by using Graph pad prism 5 version. P value less than 0.05 is considered to be statistically significant.

Results

Table 1 showed that all the 5 wave latencies showed trend of increase in the mid cycle compared to mid luteal phase. Wave IV showed statistically significant increase 4.7 (0.18) in the mid cycle compared to all other phases.

The peak latencies of the waves I to V again showed a trend of increase in premenstrual compared to mid luteal phase but there was no significant difference.

Table 2 didn't show any significant difference between different phases of menstrual cycle. Amplitude of ABR waves showed high degree of variations in the same individual hence not taken in to consideration.[14]

Table-1: Peak Latencies of ABR during different phases of menstrual cycle

Wave	Peak Latency in ms, Mean (SD)				P value
	Menstrual	Midcycle	Midluteal	Premenstrual	
Wave I	1.34 (0.18)	1.38 (0.1)	1.31 (0.1)	1.36 (0.19)	> 0.05
Wave II	2.48 (0.23)	2.54 (0.2)	2.42 (0.2)	2.48 (0.22)	> 0.05
Wave III	3.46 (0.23)	3.51 (0.2)	3.43 (0.2)	3.47 (0.23)	> 0.05
Wave IV	4.54 (0.24)	4.7 (0.18)	4.51 (0.2)	4.53 (0.22)	< 0.05*
Wave V	5.31 (0.21)	5.33 (0.2)	5.23 (0.1)	5.27 (0.19)	> 0.05

* Statistically significant

Table-2: Inter peak latencies of ABR during different phases of menstrual cycle

Wave	Inter Peak Latency in ms, Mean (SD)				P value
	Menstrual	Midcycle	Midluteal	Premenstrual	
Wave I-III	2.12 (0.26)	2.13 (0.28)	2.12 (0.25)	2.11 (0.30)	> 0.05
Wave I-V	3.97 (0.31)	3.94 (0.29)	3.92 (0.27)	3.91 (0.27)	> 0.05
Wave III-V	1.85 (0.35)	1.81 (0.38)	1.79 (0.30)	1.79 (0.28)	> 0.05

Discussion

Our results are concurrent with the study done by Navpreet Mann et al. in 2012 which showed that there was a significant increase in peak latencies of the waves I to V in mid cycle which has high estrogen level and significant decrease in midluteal phase where progesterone is high.[15] Thus female sex steroids estrogen and progesterone modify the speed of transmission at the brain stem by secretion of GABA in a counter regulatory fashion.[16]

Estrogen increases GABA there by delaying conduction, showed as increased peak latencies.[17] GABA decreases acetylcholine release resulting in change in excitability of the nerve cells in the hypothalamus and the hippocampus.[9] Progesterone decreases the sensitivity of the neurons to estrogen and also decreases the estrogen potentiated GABA release. Thus there is speedy conduction resulting in decreased peak latencies.

Estrogen was known to have a biphasic effect on GABA. Hypothalamic GABA was significantly increased in female monkeys at the time of estrogen surge and not during follicular and late luteal phase.[18] Similarly in females estrogen has a positive feedback mechanism on GABA in mid cycle and negative feedback on GABA release in the brain during early follicular and late luteal phase.

Wallace E et al. in 1992 showed that females with premature ovarian failure, estrogen replacement increases peak latency of wave V and combined estrogen and progesterone replacement decreases the latency. This showed that the source of latency change is central compared to peripheral auditory pathway.[19] Our study also showed statistically significant increase in peak latency in wave IV in midcycle compared to other phases.

Peak latencies of the waves I to V further increased in premenstrual phase compared to midluteal phase as shown by the table 1. This might be due to the effect of estrogen on retention of Na+, K+ and water during the premenstrual phase. Since ABR is the volume conducted electrical activity, increase in volume affect the process of axonal conduction time thereby increases the peak latencies.[20] Increased secretion of prolactin, aldosterone and ADH in the premenstrual phase can also be the reason to delay the conduction. Prostaglandins and β endorphins in the late luteal phase might also prolong the latency.[21]

Conclusion

From our study we conclude that variation in the female sex hormones estrogen and progesterone during different phases of menstrual cycle can influence the Brain stem auditory evoked potential at the central level. Further studies are required with hormonal estimation for better correlation of hormones with ABR latencies.

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