NORTHWESTERN MEDICAL JOURNAL

Northwestern Med J. 2024;4(4):238-245
DOI: 10.54307/NWMJ.2024.92

RESEARCH ARTICLE

Evaluation of auditory middle latency response during the menstrual cycle

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Cite as: Bal N, Tas Elibol N, Ayan A, Soğancı İN, Başöz Behmen M, Gedik Toker Ö. Evaluation of auditory middle latency response during the menstrual cycle. Northwestern Med J. 2024;4(4):238-245.

ABSTRACT

Aim: The hormone levels during the menstrual cycle, directly and indirectly, affect the hearing system. In our study, it was aimed to examine the effects of changing hormone levels during the menstrual cycle on auditory middle latency responses in healthy individuals with different stimuli types and the psychosomatic effects of premenstrual complaints on auditory performance.

Methods: In the study, 20 healthy women aged 18-35 years, with regular menstrual cycles and no auditory or vestibular complaints were evaluated for auditory middle latency responses with click and level-specific (LS) CE-Chirp® stimuli during the menstruation period of the follicular phase (1-5 day, menstrual phase), the ovulation phase (14-17 day) and the luteal phase (21-28 day). To evaluate the effect of premenstrual complaints on auditory performance, the participants were asked 5 questions.

Results: In the auditory middle latency assessment with click stimuli, a statistically larger Na-Pa amplitude was obtained in the menstruation phase compared to the ovulation phase in both ears. In the auditory middle latency evaluation with LS CE-Chirp® stimulus, statistically shortened Nb latencies were obtained in the right ear in the menstruation phase compared to the ovulation phase.

Conclusion: Although the clear effect of changing gonadal hormone levels on auditory evoked middle latency responses could not be determined, the findings show that neural transmission increases in the menstrual phase when the estrogen level is low. Click stimulus is more sensitive to hormonal changes, and the use of click stimulus has been recommended in the later side of lesion studies. In our study, no psychosomatic effect of complaints in the premenstrual period on auditory performance was observed.

Keywords: auditory middle latency response, menstrual cycle

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Received: 16.11.2023 **Accepted:** 17.04.2024 **Published:** 22.10.2024

INTRODUCTION

Auditory evoked middle latency responses (AMLR) are electrical potentials of the thalamocortical area measured by electrodes placed on the scalp at 10-50 ms after auditory stimulation (1). AMLR consists of Po, Pa, Pb, Pc positive and Na, Nb, Nc negative peaks (2). It is utilized in clinics to estimate behavioral hearing thresholds, localize brain lesions (thalamocortical area), diagnose auditory processing problems, and evaluate cochlear implant candidates. AMLR is also used to evaluate auditory system development with the Pb wave, which is a biomarker of auditory system maturation (3). Many factors affect AMLR, including hormonal changes (4).

Menstrual cycle refers to the 28-day periods that begin in the menarche and continue until menopause in women. These 28-day periods consist of follicular, ovulation, and luteal phases; many hormonal changes are observed during these phases. During the menstrual cycle, the main changes occur in the production of the female ovarian hormones estrogen and progesterone (5). Changing hormone levels during the menstrual cycle have been proven in studies to have direct and indirect effects on the cochlea and central auditory system (6). The presence of estrogen receptors in inner and outer hair cells, spiral ganglion, stria vascularis, and brain explains this situation (7). The precise effect of estrogen and progesterone on the auditory system is unknown. However, estrogen causes changes in cochlear blood flow and affects the auditory system and central nervous system by increasing the production of neurotransmitters such as glutamate, dopamine, and GABA (8,9). Furthermore, there is evidence that estrogen influences brain volume (10). According to another research, premenstrual symptoms that begin 7-10 days before menstruation, as well as the link between estrogen and the limbic system, cause changes in auditory function (11).

Although the effects of changing estrogen and progesterone levels on the auditory system during the menstrual cycle in the literature have been mostly examined at the brain stem and cortical levels, there are limited studies examining AMLR (12,13). Considering that gonadal hormone receptors are localized in different parts of the auditory system, it is predicted that different effects may occur in different parts of the central auditory system. Due to the limited number of studies examining the effects of changing hormone levels on AMLR during the menstrual cycle, our study aimed to investigate the effect on the thalamocortical level in different phases of the menstrual cycle in healthy individuals, to compare the sensitivity of different stimuli types to hormonal changes, and to examine the psychosomatic effect of premenstrual complaints on auditory performance (12,13).

MATERIALS AND METHODS

The clinical trial was conducted at Bezmialem Vakif University, Audiology Clinic. Permission was obtained from the Non-Interventional Ethics Committee of Bezmialem Vakif University to conduct the study (Ethics Committee No: 2022/15). It was conducted in accordance with the ethical principles stated in the Declaration of Helsinki.

Twenty healthy women between 18-35 years of age with menstrual bleeding at 21/35-day intervals were included in the study (14). The study's inclusion criteria are as follows: normal otoscopic evaluation findings, presence of bilateral Type-A tympanogram and ipsilateral and contralateral acoustic reflexes at 500-1000-2000-4000 Hz in immitancemetric evaluation, pure tone hearing thresholds of 15 dB HL or less at octave frequencies between 250-8000 Hz and being right-handed. Subjects with neurological, psychiatric, metabolic disease, dizziness, or using oral contraceptives were excluded from the study.

The acoustic immittance measurement was performed with the GSI Tymp Star Pro (Grason-Stadler, Minnesota, USA) clinical tympanometer device. Acoustic immittance tests included 226 Hz tympanometry, and thresholds for ipsilateral and contralateral acoustic reflexes at 500Hz, 1000Hz, 2000Hz, and 4000Hz.

The Madsen Astera 2 (GN Otometrics, Denmark) or the AC40 (Interacoustics, Eden Prairie, MN) clinical audiometry was used for audiometric evaluation. Pure tone audiometry was performed at frequencies of 250, 500, 1,000, 2,000, 4,000, 6,000, and 8,000 Hz via TDH39 supra-aural headphones. Bone conduction was tested at 500, 1,000, 2,000, and 4,000 Hz via a B71 bone conductor.

AMLR

An Interacoustics Eclipse EP25 (Middelfart, Denmark) was used for AMLR. AMLR was performed three times with click and LS CE-Chirp® stimuli during the menstrual period:1st the follicular phase when estrogen levels were low (1-5 days, menstrual phase), 2nd the ovulation phase when estrogen levels were high (14-17 days), and 3rd the luteal phase when progesterone hormone was dominant (21-28 days) (5). ER-3A insert earphones were placed in the outer ear canal of the participants to transmit the sounds. Click and LS CE-Chirp® were presented to the patient at 70 dB nHL, at the rate of 6.1, in alternating polarity. Absolute latencies of Na, Pa, Nb, Pb waves, Na-Pa interwave latencies, and amplitudes of wave Na-Pa were determined.

5 questions prepared by the researchers, including complaints in the premenstrual period

To assess the psychosomatic influence of premenstrual period complaints on the auditory system, participants were led to 5 questions created by the researchers, in which their premenstrual period complaints were appraised (Table 1). Participants gave yes/no answers to the first 4 questions. They rated the last question on a scale of 0 to 5.

Data analysis

Descriptive statistics of the parameters were calculated using IBM SPSS Statistics 22.0 program. The sample size was set at a minimum of 20 to provide 80% power at the 95% confidence level. Statistical significance was set at $p<0.05$. The distribution of the data was analyzed by using the Shapiro-Wilk test. The analysis of normally distributed data was done with the T- test, and the analysis of the non-normally distributed data was done with the Mann- Whitney U test.

RESULTS

In the study, AMLR was evaluated with click and LS CE-Chirp® stimuli in different phases of the menstrual cycle. Absolute latencies of Na, Pa, Nb, Pb waves, Na-Pa interwave latencies, and amplitudes of wave Na-Pa were evaluated.

The Na, Pa, Nb, Pb absolute latencies and Na-Pa interwave latencies values obtained in the right and left ears in the AMLR evaluation performed with a click stimulus in different phases are given in Table 2. In the evaluation of AMLR with a click stimulus, no significant difference between the phases was obtained in the Na, Pa, Nb, Pb wave absolute latencies and Na-Pa interwave latencies values in the right and left ears.

In Figure 1, there is an AMLR wave obtained with a click stimulus in different phases. The blue wave indicates the menstrual phase, the light gray wave indicates the ovulation phase and the orange wave indicates the luteal phase.

Table 1. 5 questions prepared by the researchers, including complaints in the premenstrual period

Are you easily irritated during your premenstrual period? (Yes/No)
Does your appetite grow during your premenstrual period? (Yes/No)
Do you have difficulty focus on in the premenstrual period? (Yes/No)
Does your desire to eat chocolate foods increase during the premenstrual period? (Yes/No)
How much does your mood change in the premenstrual period affect your life? (Score 1 to 5)

Table 2. Na, Pa, Nb, Pb wave absolute latencies and Na-Pa interwave latencies in the right and left ears in different phases in the auditory middle latency evaluation with click stimulus

Parameter And Evaluated Ear (Mean±SD)		Menstrual Phase	Ovulation Phase	Luteal Phase	p value
Na Latency (ms)	Right	15,01 ± 2,76	15,85 ± 1,97	15,71 ± 2,68	0,127
	Left	15,06 ± 2,81	15,7 ± 2,5	15 ± 2,63	0,081
Pa Latency (ms)	Right	26,28 ± 4,24	28,1 ± 5,34	26,53 ± 4,72	0,178
	Left	27,08 ± 6,46	27,58 ± 3,24	26,10 ± 4,44	0,622
Nb Latency (ms)	Right	41,26 ± 4,49	42,5 ± 7,63	40,88 ± 5,7	0,311
	Left	41,98 ± 6,77	42,74 ± 6,25	42,95 ± 6,20	0,595
Pb Latency (ms)	Right	56,36 ± 6,27	57,6 ± 6,83	55,18 ± 12,96	0,698
	Left	57,29 ± 6,61	56,65 ± 6,36	58,6 ± 7,42	0,168
Na-Pa Latency (ms)	Right	11,26 ± 3,07	12,55 ± 5,01	10,81 ± 3,81	0,786
	Left	12,01 ± 4,38	11,38 ± 3,86	11,1 ± 3,04	0,183

The Na, Pa, Nb, Pb absolute latencies and Na-Pa interwave latencies values obtained in the right and left ears in the AMLR evaluation performed with an LS CE-Chirp® stimulus in different phases are given in Table 3. Statistically shortened Nb latencies in the right ear were obtained in the menstrual phase compared to the ovulation phase in the auditory middle latency measurement recorded with LS CE-Chirp® stimuli in different phases (p=0,011) (Table 3).

The Na-Pa amplitude values obtained in the right and left ears in the AMLR evaluation performed with a click and LS CE-Chirp® stimulus in different phases are given in Figure 2. In the evaluation of AMLR with click stimulus, statistically larger Na-Pa amplitude was obtained in both ears in the menstrual phase compared to the ovulation phase (right ear p= 0,011) (left ear p= 0,002) (Figure 2).

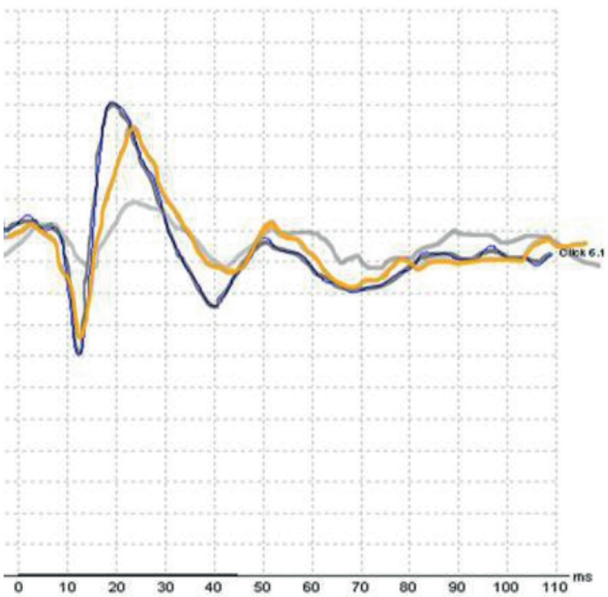

Figure 1. AMLR waves obtained with click stimulus in different phases (The blue wave; menstrual phase, the light gray wave; ovulation phase, and the orange wave; luteal phase).

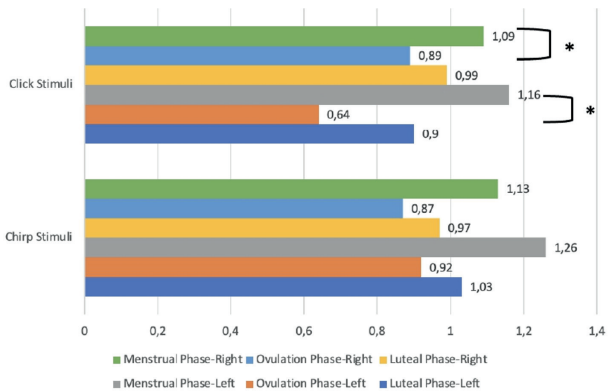

Figure 2. Na-Pa amplitude value in the right and left ears in different phases in the auditory middle latency evaluation with click and LS CE-Chirp® stimulus

*Indicates values are significant at the 0.05 level.

Table 3. Na, Pa, Nb, Pb wave absolute latencies and Na-Pa interwave latencies in the right and left ears in different phases in the auditory middle latency evaluation with LS CE-Chirp® stimulus

Parameter And Evaluated Ear (Mean±SD)		Menstrual Phase	Ovulation Phase	Luteal Phase	p value
Na Latency (ms)	Right	15,06 ± 2,31	16,3 ± 2,1	15,55 ± 2,03	0,302
	Left	15,73 ± 4,1	15,36 ± 2,85	15,25 ± 2,92	0,779
Pa Latency (ms)	Right	26,38 ± 3,54	27,61 ± 3,84	27,48 ± 3,93	0,271
	Left	26,58 ± 5	27,89 ± 3,91	27,46 ± 4,9	0,529
Nb Latency (ms)	Right	**39,78*** ± 5,98	41,46 ± 9,02	42,29 ± 7,08	**0,011***
	Left	41,75 ± 7,71	42,83 ± 6,98	42,53 ± 8,37	0,815
Pb Latency (ms)	Right	57,18 ± 8,53	58,58 ± 7,61	57,83 ± 9,26	0,619
	Left	56,13 ± 8,32	59,88 ± 9,06	57,71 ± 7,71	0,784
Na-Pa Latency (ms)	Right	11,55 ± 2,51	11,31 ± 3,53	11,91 ± 3,92	0,861
	Left	11,54 ± 3,57	12,53 ± 3,38	12,2 ± 3,72	0,618

Table 4. Answers to questions directed to participants

Questions	Yes	No
Are you easily irritated during your premenstrual period?	80%	20%
Does your appetite grow during your premenstrual period?	85%	15%
Do you have difficulty focus on in the premenstrual period?	65%	35%
Does your desire to eat chocolate foods increase during the premenstrual period?	85%	15%
How much does your mood change in the premenstrual period affect your life?	Minimum score: 2 Maximum score: 5 Mean score:3,35	

The answers to the questions directed to the participants are given in Table 4.

DISCUSSION

The study was conducted to evaluate the effects of hormonal changes during the menstrual cycle on AMLR in healthy individuals, to compare the sensitivity of stimulus types to intrinsic factors, and to examine the psychosomatic effects of premenstrual complaints on auditory performance. The AMLR test with a click and LS CE-Chirp® stimuli was performed on the participants in the menstrual phase, ovulation phase, and luteal phase. In the AMLR test performed with a click stimulus, a larger Na-Pa amplitude was obtained in both ears in the menstrual phase compared to the ovulation phase. This is explained by the decrease in estrogen levels in the menstrual phase causing an increase in neural transmission (15). In addition, Prabhu et al. (16) examined the impact of changing hormone levels in the menstrual cycle on the frequency following response (FFR). In the study, larger amplitudes and shorter latencies were obtained in the menstrual phase, and these results supported that the decrease in estrogen level, similar to our study, increases neural transmission.

In the evaluation of AMLR with LS CE-Chirp® stimulus, Nb latency was shortened in the menstrual phase compared to the ovulation phase in the right ear. We think that the shortened Nb latency obtained in the right ear during the menstrual phase may be related to the increase in the right ear advantage due to a decrease in estrogen level. In the literature, there were studies in which the auditory brainstem latency and middle and late latency are shortened during the menstrual phase (4,17). This is explained by the fact

that there is a decrease in the production of GABA, an inhibitory neurotransmitter, as a result of a decrease in estrogen levels in the menstrual phase, and an increase in neural transmission (17).

While some studies in the literature suggest that estrogen reduces neuronal transmission, other studies suggest the exact reverse (12,13). Khaliq et al. (12) examined the AMLR responses after estrogen replacement therapy in 32 postmenopausal women, statistically shortened Po, Na, and Pa latencies were obtained after estrogen replacement in the participants. Kilicdag et al. (18) also found that estrogen therapy reduces aging in postmenopausal women. In the literature, it has been observed that there is a shortening of auditory brainstem responses, improvement in dichotic listening, understanding in noise, and working memory performance in the ovulation phase when the estrogen level is high (11,19,20). This is explained by the fact that increased estrogen levels increase dopamine and glutamate production and contribute to auditory processing (20,21). Also, Tucker et al. (22) examined AMLR according to gender and found prolonged wave latencies in males and larger amplitudes in females. This condition has been associated with high estrogen levels in women.

Atcherson et al. (23) compared chirp, click, and tone burst stimuli in AMLR. Although they thought that the peak-peak amplitude values would be large in the chirp stimulus, they did not find a difference between the stimuli. In our study, the sensitivity of click and LS CE-Chirp® stimuli to hormonal changes was examined. The increase in bilateral Na-Pa amplitude obtained during the menstrual phase in the AMLR evaluation with click stimulus suggested that click stimulus is more sensitive to intrinsic factors and may be preferred in the subsequent site of lesion studies. Studies have also found that AMLR responses may influence depending on right-left handedness and that Pb latency is prolonged in left-handed individuals (24-26). This difference has been reported to be related to anatomical and functional differences in left-handed individuals (26). Considering the studies in the literature, left-handed individuals were not included in our study.

Most of the participants in the 5 questions prepared by the researchers; stated that they are prone to irritability in the premenstrual period, their appetite is increased, their desire to eat chocolate increases and they experience distraction. With the scores given, the participants showed that mood changes in the premenstrual period significantly affected their lives. Carneiro et al. (11) found that complaints such as anxiety, mood change, and irritability in the premenstrual period affect the results of the dichotic test and that the right ear advantage decreases in the luteal phase, which includes the premenstrual period. Considering that AMLR is affected by the attention state of individuals, it is thought that AMLR responses due to distraction complaints occurring in the premenstrual period may be affected and mood changes in this period may cause a psychosomatic effect on the auditory system (27). However, in our study, no significant difference was observed in wave latencies in the luteal phase, which includes the premenstrual period.

CONCLUSION

There are many studies in the literature showing that changing hormone levels during the menstrual cycle affect the auditory system. Although the clear effect of changing gonadal hormone levels on AMLR could not be determined in our study, the findings show that neural transmission increases in the menstrual phase when the estrogen level is low.

In our study, evaluation was performed with click and LS CE-Chirp® stimuli. An increase in bilateral Na-Pa amplitude was observed in the menstrual phase compared to the ovulation phase in the evaluation with click stimuli. This demonstrated the sensitivity of click stimulus to intrinsic factors and suggested that click stimulus may be preferred in the future site of lesion studies.

Additionally, we suggest that menstrual phases should be considered, especially in studies involving female participants. Although studies have shown that premenstrual period complaints have a psychosomatic effect on auditory performance, our study did not show any effect on AMLR due to premenstrual complaints.

We think that future studies using electrophysiological testing in which individuals may actively participate might produce different outcomes.

Ethical approval

This study has been approved by the Non-Interventional Ethics Committee of Bezmialem Vakif University (approval date 10/02/2022, number 2022/15). Written informed consent was obtained from the participants.

Author contribution

Concept: NB; Design: NB; Data Collection or Processing: AA, ÖGT, İNS, MBB; Analysis or Interpretation: MBB; Literature Search: NTE, NB; Writing: NB, NTE. All authors reviewed the results and approved the final version of the article.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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