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Research Article

Language Asymmetry and Hormonal Fluctuations During The Menstrual Cycle

Handan CAN[1], Constanze HAHN[2], Sebastian OCKLENBURG[2], Anna BALL[2], Onur GÜNTÜRKÜN[2]

[1]Faculty of Arts and Sciences,Uludağ University, Department of Psychology, Görükle/Bursa, Türkiye [2]Institute of Cognitive Neurosicence, Ruhr University, Faculty of Psychology, Bochum , Almanya

Summary

Objective: The aim of this study was to investigate hormone-asymmetry relationships during the menstrual cycle for both hemispheres using verbal dichotic listening task.
Method: This study was conducted with thirty-two normally cycling women; all of them were native German speakers and right-handed with no use of hormonal medication in the previous 6 months. STCI-S18, a questionnaire to assess current mood, the Edinburgh Handedness Inventory, a background questionnaire to collect demographic information, the Symptom-Checklist 90-R and a verbal dichotic listening task were administered to all participants /completed by all participants.
Result: Statistical analysis indicated that the main effect of ear was significant (p=.007). A right ear advantage was observed, but neither the main effect of cycle (p=.303) nor the interaction of ear and cycle (p=.955) was significant. We did find, however, a significant main effect of cycle on auditory recognition when we analyzed the data of the 17 participants with validated estradiol changes (p=.047).
Conclusion: The results of the dichotic listening task data showed that the degree of language asymmetry as revealed by dichotic listening did not change during the three menstrual phases. We did find, however, that the main effect of cycle was significant when we analyzed the data of 17 participants with available estradiol levels. Estradiol seems to affect overall auditory recognition without altering asymmetry.

Key words: Verbal dichotic listening, language asymmetry, hormonal fluctuations, menstrual cycle

Dil Asimetrisi ve Menstrüel Siklusta Hormonal Değişiklikler

Özet

Amaç: Çalışmanın amacı sözel dikotik dinleme görevi kullanarak her iki hemisfer için menstrual siklüs sırasında hormon- asimetri ilişkilerini incelemektir.
Yöntem: Bu çalışma son 6 ay içinde hormon içeren ilaç kullanmamış, sağ elini kullanan ve hepsi Alman vatandaşı olan 32 normal menstrual siklüs gösteren kadın katılımcı üzerinden yürütülmüştür. Tüm katılımcılara bir mod değerlendirme anketi olan STCI-S18, Edingburgh El Tercihi Envanteri, demografik bilgileri içeren özgeçmiş formu, Semptom Tarama 90-R and sözel dikotik dinleme görevi uygulanmıştır.
Bulgular: İstatistiksel analiz kulak temel etkisinin anlamlı olduğunu göstermiştir (p=.007). Sağ kulak avantajı gözlenmiş; ancak ne siklüs temel etkisi (p=.303) ne de kulak ve siklüs etkileşimi (p=.955) anlamlı bulunmamıştır. Yine de 17 kişilik grubun verisi üzerinden yapılan analizde siklüs temel etkisi anlamlı bulunmuştur (p=.047).

Sonuç: Dikotik dinleme (sözel) görevi veri sonuçları, dikotik dinleme görevinde ortaya çıkan dil asimetrisi derecesinin, menstrüel siklüsün üç fazında da değişmediğini göstermiştir. Ancak yine de, uygun östradiol düzeylerine sahip 17 katılımcının veri analizinde, siklüs etkisi anlamlı bulunmuştur. Östradiol asimetriyi değiştirmeden işitsel tanımayı etkiler gibi gözükmektedir.

Anahtar Kelimeler: Sözel dikotik dinleme, dil asimetrisi, hormonal dalgalanmalar, menstrual siklüs

INTRODUCTION

Cerebral asymmetries affect most aspects of the cognitive architecture of the human brain. To some extent asymmetries are sex-dependent, with differences between the right and left hemispheres being more pronounced in men than in women. Although these differences are not evident in all studies, meta-analyses clearly reveal their existence[40]. Some of the sex effects on lateralization are possibly related to gonadal steroid hormone levels in women[13]. Consequently, sex hormonal fluctuations during the menstrual cycle modulate left-right differences[19,18]. Several hypotheses have been proposed to explain the influence of sex hormones on functional cerebral asymmetries (FCAs). Heister et al.[21] suggested that increased levels of sex hormones in the menstrual cycle were associated with reduced FCAs in both the right and the left hemisphere. On the other hand, McCourt et al.[30] provided evidence that high levels of sex hormones cause an increase in FCAs in tasks that are dominated by the left (LH) or the right hemisphere (RH). The author of another previous study about the influence of hormones on human cognitive and motor skills[16] proposed that high levels of estrogen led to opposite effects for each hemisphere, causing an increase of LH and a decrease of RH performance. In one study that controlled for hormone concentration and for repeated measures, the authors[19] identified interactions between the cycle phase and FCAs for both right- and left-hemispheric dominant tasks. Hausmann and Güntürkün[19] proposed that high levels of progesterone (P) are related to a reduction of lateralization. Because this effect is present for left- and right-hemispheric tasks, they assumed that P modulates the interhemispheric inhibition via the corpus callosum[19,18]. This transcallosal interaction is thought to be an essential mechanism in causing functional asymmetries[6,11].

The effects of sex hormones have been explored in normally cycling women in several studies[7,4,8,19,18], but with partly conflicting findings. Some of the contradictions reported above could result from a lack of measuring the actual hormonal levels of the participants. Instead, researchers had simply estimated the day of the menstrual cycle by counting backwards from the expected start date of the next menstrual bleeding[22]. Thus, only studies that actually obtain hormonal assays should be conducted[2,43,17,10,19,18,31,35,12].

The second possible explanation for the discrepancies in the results of the previous studies may be related to the fact that the effects of hormones on FCAs may be task-dependent[15,16,21,31,35,37]. Previous studies have used figure recognition[4], cognitive and motor tests[15,16] and spatial bisection[30] and found greatest asymmetries during the midluteal phase. Other studies, however, included figural comparisons[35] and decisions about faces[21] and discovered the most prominent asymmetries during menses.

In the present study, we examined functional cerebral asymmetries using the dichotic listening task. Similar to our study, the cycle-related change of FCAs during the menstrual cycle has already been investigated in previous studies using dichotic listening[41,37,12]. We investigated cycle-related change in FCAs with a detailed analysis of relevant hormones to verify the three relevant cycle phases (menses, follicular and midluteal). To this end, we collected saliva from all of the participants to measure estradiol (E) and progesterone (P) levels. We also aimed to investigate hormone/asymmetry relationships during the menstrual cycle. For this aim, we performed verbal dichotic listening as a left-hemispheric dominant task.

MATERIAL AND METHODS

Participants

This study was conducted using thirty-two normally cycling women with a mean age of 25.23 years (S.D.=4.57, age range: 19-38) and a regular menstrual cycle of 25 to 31 days. All participants were German citizens and were right-handed. Right-handedness was controlled using the Edinburgh Handedness Inventory (EHI; 32). The asymmetry index (LQ) provided by this test was calculated using [R-L)/(R+L)] x 100, leading to values between -100 and +100. Dextrality was indicated by positive values, whereas sinistrality was indicated by negative values in this index. The mean handedness score was 84.11 (S.D.=15.08; range: 47-100). None of the participants had used hormonal pills or medication in the previous 6 months. All participants had normal or corrected-to-normal visual acuity; none of them had a hearing threshold higher than 30 dB, and the interaural difference was never higher than 10 dB. The participants were recruited using an announcement and were paid for their participation. Participants were randomly assigned to the experimental groups, and written informed consent was obtained from every participant.

Materials

In this study, both paper-pencil tests and computerized tasks were used. A German mood questionnaire, the Edinburgh Handedness Inventory, a background questionnaire to collect demographic information, family, hormonal, medical and educational history, and the Symptom-Checklist 90-R[14] were completed by all participants at the beginning of the first session. The computerized dichotic listening (DL) task was administered at each of the three sessions (during the menstrual (days 2-5), follicular (days 8-11) and midluteal phases (days 20-22).

The verbal DL task usually reveals a right ear advantage that corresponds to left hemisphere superiority. In this task, pseudorandomly arranged syllable pairs that were presented dichotically through closed system headphones at 80 dB were presented. The stimulation set also included diotic (homonym) stimuli, which consisted of two identical sounds. The stimuli were digitally recorded, natural, complex speech sounds that were produced by a male, German, adult voice. The classical vowel (CV) syllables “BA”, “DA”, “GA”, “KA”, “PA” and “TA” with a mean duration of 350 ms were used. The basic sound characteristics, such as the intensity of the auditory stimuli/CV syllables, were controlled and balanced. While forming the dichotic syllables, spectral temporal envelopes of the syllables were matched. All of the possible combinations of the syllables pairs were presented to both ears, resulting in 36 possible combinations. To observe the possible differences between the right and left hand responses, the participants were presented 72 (one round for the right hand and one round for the left hand 2 x 36 x 2 CV pairs) dichotic syllable pairs per hand, leading to a total of 144 stimuli. Participants were tested three times (during their menses, follicular and midluteal phases) during their cycle.

The State-Trait-Cheerfulness Inventory (STCI-S18; 36) was used to assess the current mood of the participants during different phases of their menstrual cycle. STCI-S18 is an instrument that measures the three concepts of cheerfulness, seriousness and bad mood. Each concept include six items, and the responses were given on a 4 point rating scale (strongly disagree, 1; moderately disagree, 2; moderately agree, 3; and strongly agree, 4).

Procedure

Participants started with their first testing session independent of their individual cycle day, and the date of the first experiment was planned according to the information given by the participant. Every participant was tested three times: once during the menstrual phase (between the second and the fifth day of their cycle), once during the follicular phase and once during the midluteal phase. To control for potential repeated measures effects, the women were tested in a counterbalanced order, starting with either the menstrual, follicular or midluteal phase of the menstrual cycle. All of the participants completed all of the three sessions during a single menstrual cycle, with the exception of three participants who could not come to their appointments because of personal reasons, and who completed the sessions in the subsequent menstrual cycle. All of the three sessions were performed at the same time of the day for each participant to control for circadian variability in hormone releases. In addition, all of the participants were requested not to eat or drink anything, except for water, for at least one hour before the experiment.

Prior to the first experimental session, the background questionnaire created by Biopsychology Department of Ruhr University, a mood questionnaire (STCI–S18), the Edinburgh Handedness Inventory, a hearing acuity measurement and the Symptom Checklist 90-R[14] were performed for all participants with a consent form, and the STCI–S18 was repeated during each of two other sessions. After the completion of the paper-pencil tests, a saliva sample was collected from all participants two times: once before and once after each session. To account for the hormonal changes during the session, the two saliva samples were mixed, and this mixture was used for the hormonal analysis. Immediately after the collection of sample, these saliva samples were stored at -22°C until all of the participants completed all of the three sessions. Saliva E and P levels were determined using Chemiluminescence assay (CLIA) by an independent professional hormone laboratory that used commercial hormone assays. This study was approved by the Ethics Committee of the Faculty of Psychology at the Ruhr-University Bochum, Germany.

RESULTS

Salivary Assay

We first calculated the percent increase of the E and P levels during the follicular and the luteal phase compared to the menstrual phase. We defined that subjects had to display a 45% increase during the follicular and the luteal phase for E and P, respectively. All together, 20 participants had to be excluded. The mean level of serum P in the remaining 12 women was 156.38 pg/ml during the menstrual phase and 571.39 pg/ml during the midluteal phase. A paired t-test revealed a significant difference in the mean saliva P levels between the menstrual and follicular phases ($t(11) = 6.13$, $p<.001$). The mean level of serum E was 1.47 pg/ml during the menstrual phase and 6.94 pg/ml during the follicular phase. A paired t-test revealed a significant difference in the mean serum E levels between the menstrual and follicular phases ($t(11)=5.14$, $p<.001$).

Verbal Dichotic Listening

The data from the 12 normally cycling women that met the E and P level criteria were analyzed using parametric statistics because the Kolmogorov–Smirnov Goodness-of-Fit test showed normal distributions for all variables. First, the data were calculated with a one-way analysis of variance (ANOVA) with repeated measures and then we performed a 2 x 3 (ear and cycle) analysis of variance (ANOVA) with repeated measures to the data. The Greenhouse-Geisser procedure with epsilon corrected degrees of freedom was used if the data showed significant deviations from sphericity. Neither the main effect of cycle (F (2, 22)=1.25, p=.303) nor the interaction of ear and cycle (F (2, 22)=.04, p=.955 ns) was significant. However, a 2 x 3 (ear and cycle) analysis of variance (ANOVA) with repeated measures indicated that the main effect of ear was significant (F (1, 11)=10.90, p=.007). A right ear advantage (REA) was observed; the percentage of correct answers obtained from the right ear was higher than that obtained from the left ear during all the three cycles (Table 1; Figure 1). A 2 x 3 (ear x cycle) analysis of variance (ANOVA) with repeated measures was also conducted on reaction time (RT) mean value data. the result of this analysis indicated that neither the main effect of ear F (1, 11)=3.57, p=.09) nor cycle (F (2, 22)=.131, p=.817 ns) was significant. The interaction of ear and cycle (F (2, 22)=2.31, p=.138 ns) was not significant, either. Additionally, the results of the one way ANOVA with repeated measures conducted over laterality index (LI), the percent correct scores, RT mean, RT median and RT variance indicated that the main effect of cycle over these data was not significant.

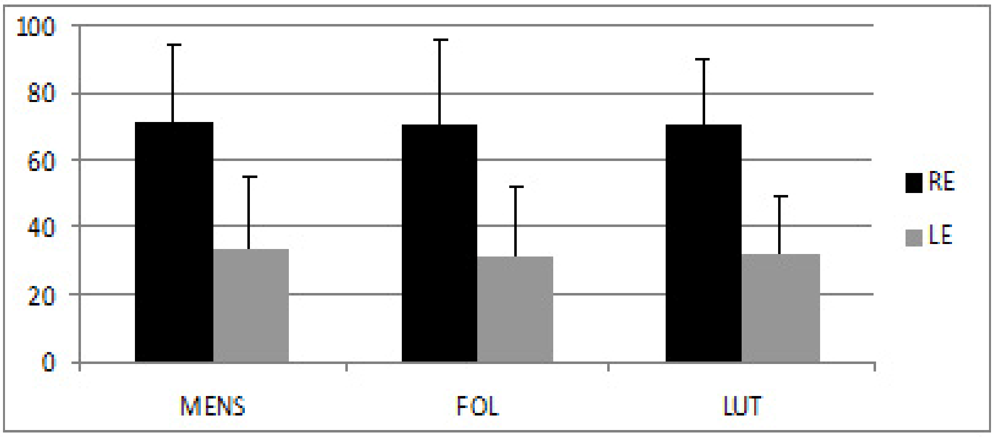

Figure 1: *Main Effect of Ear over Correct Answers of 12 Subjects in DL (verbal) Task Three Phases*

Table1. Main Effect of Ear over Correct Answers of 12 Subjects in DL (verbal) Task Three Phases

	CYCLE					
	MENSTRUAL		**FOLLICULAR**		**LUTEAL**	
EAR	Mean	SD	Mean	SD	Mean	SD
RE	71.25	23.02	70.50	24.60	70.42	19.76
LE	33.25	21.77	31.67	20.42	32.00	17.27

We then identified the participants with confirmed P levels during the menstrual and midluteal phases and conducted the data analyses with 20 participants that met the required criteria. A paired t-test revealed a significant cycle-phase difference in mean serum P level ($t(19)=7.54$, $p <.001$). The data from the 20 normally cycling women were analyzed using parametric statistics because the Kolmogorov–Smirnov Goodness-of-Fit test showed normal distributions for all variables. The data were calculated using a 2 x 2 (ear x cycle) with repeated measures. Neither the main effect of cycle ($F(1,19)=2.74$, $p=0.114$ ns) nor the interaction of ear and cycle ($F(1,19)=0.19$, $p=0.666$ ns) was significant. However, a 2 x 2 (ear x cycle) analysis of variance (ANOVA) with repeated measures again indicated that the main effect of ear was significant ($F(1,19)=36.25$, $p<.001$). This was due to an REA with the percentage of correct answers obtained from the right ear being higher than those from the left ear (Table 2; Figure 2). A 2x 2 (ear x cycle) analysis of variance (ANOVA) with repeated measures was also conducted on RT mean value data (Table 3; Figure 3). The result of this analysis indicated that the main effect of ear was significant ($F(1,19)=4.91$, $p=.040$). This was due to the RT mean value obtained from the right ear being faster than those from the left ear (Table 3; Figure 3). However, again, neither the main effect of cycle ($F(1,19)=2.61$, $p=0.123$ ns) nor the interaction of cycle and ear ($F(1,19)=0.35$, $p=0.563$ ns) was found to be significant. And the results of one way ANOVA with repeated measures conducted over LI, the percent correct, RT mean, RT median and RT variance indicated that main effect of cycle over these data was not significant.

Table 2. Main Effect of Ear over Correct Answers of 20 Subjects in DL (verbal) Task during Two Phases

	CYCLE			
EAR	**MENSTRUAL**		**LUTEAL**	
	Mean	SDr	Mean	SD
RE	78.30	21.55	77.05	19.69
LE	28.15	19.32	27.85	16.03

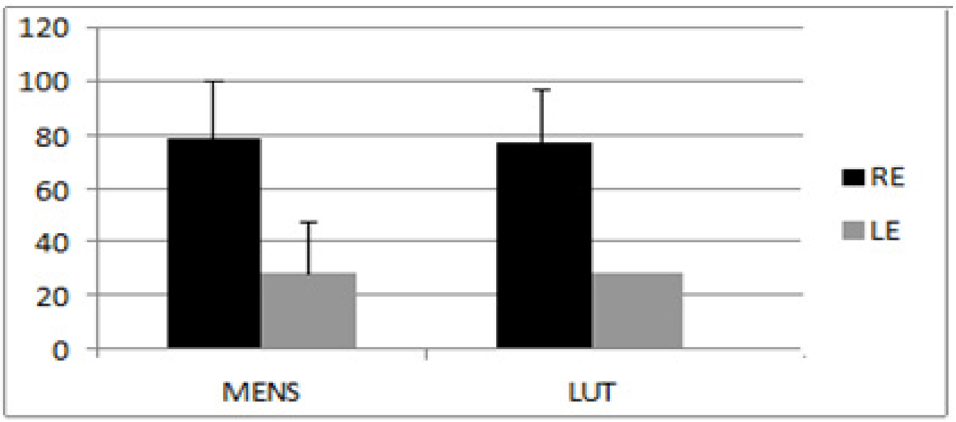

Figure 2: *Main Effect of Ear over Correct Answers of 20 Subjects in DL (verbal) Task during Two Phases*

Table 3. Main Effect of Ear over RT Mean of 20 Subjects in DL (verbal) Task during Two Phases

EAR	CYCLE			
	MENSTRUAL		LUTEAL	
	Mean	SD	Mean	SD
RE	1158.91	141.03	1188.34	138.04
LE	1186.37	158.64	1226.68	172.58

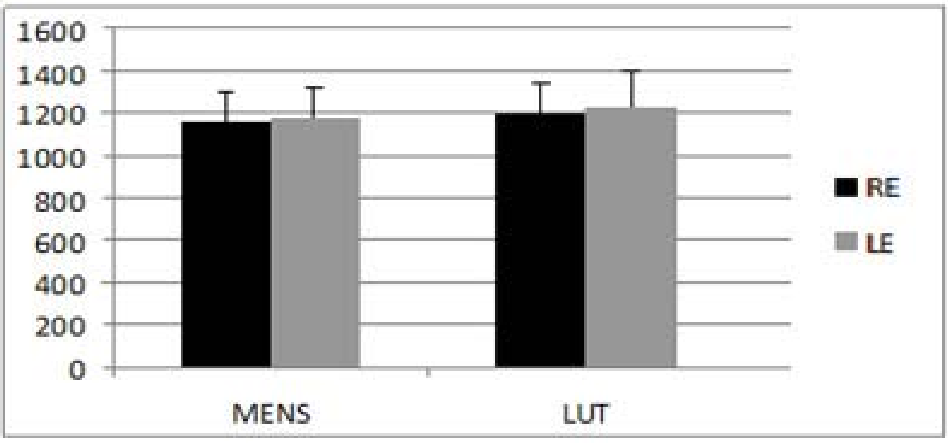

Figure 3: *Main Effect of Ear over RT Mean of 20 Subjects in DL (verbal) Task during Two Phases*

We also examined whether an analysis conducted using those participants with available E levels would yield clearer results. For this aim, we identified 17 participants whose E levels were significantly higher during the follicular phase than during the menstrual phase. We confirmed these levels using a hormone assay and analyzed the data of these participants. A paired t-test revealed a significant cycle-phase difference in mean serum E levels (t (16)=5.26, p<.001). We analyzed the data using 2 x 2 (ear x cycle) analysis of variance (ANOVA) with repeated measures. This analysis indicated that the main effect of ear (F (1,16)=24.07, p<.001) (Table 4; Figure 4) and cycle (F (1,16)=4.63, p=.047) (Table 5; Figure 5) was significant. We did not observe a significant interaction between ear and cycle (F (1,16)=.018, p=896). An REA was again indicated because the percentage of correct answers obtained from the right ear was higher than that from the left ear during all three cycles. The results of a 2 x 2 (ear x cycle) analysis of variance (ANOVA) with repeated measures conducted for the RT mean values also indicated that the main effect of ear was significant (F (1,16)=10.25, p=.006). This was again due to the RT mean value obtained from the right ear being faster than those from the left ear (Table 6; Figure 6). However, neither cycle (F (1,16)=0.63, p=.438) nor the interaction of ear and cycle was significant (F (1,16)=0.10, p=.997). The results of one way ANOVA with repeated measures conducted over LI, the percent correct, RT mean, RT median and RT variance indicated that main effect of cycle over these data was not significant.

Table 4. Main Effect of Ear over Correct Answers of 17 Subjects in DL (verbal) Task during Two Phases

	CYCLE			
	MENSTRUAL		**FOLLICULAR**	
EAR	Mean	SD	Mean	SD
RE	75.18	20.90	74.18	21.64
LE	30.35	18.93	29.06	17.67

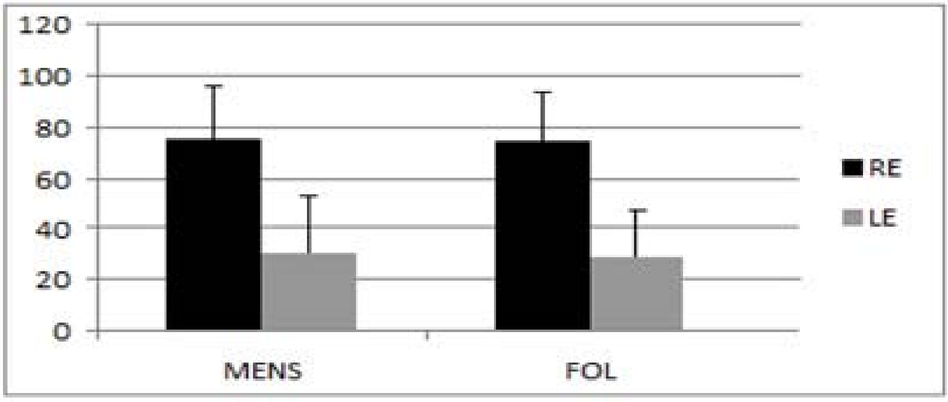

Figure 4: Main Effect of Ear over Correct Answers of 17 Subjects in DL (verbal) Task during Two Phases

Table 5. Main Effect of Cycle over Correct Answers (RE, LE) of 17 Subjects in DL (verbal) Task during Two Phases

	EAR			
	RE		**LE**	
CYCLE	Mean	SD	Mean	SD
MENSTRUAL	75.18	20.90	30.35	18.93
FOLLICULAR	74.18	21.64	29.06	17.69

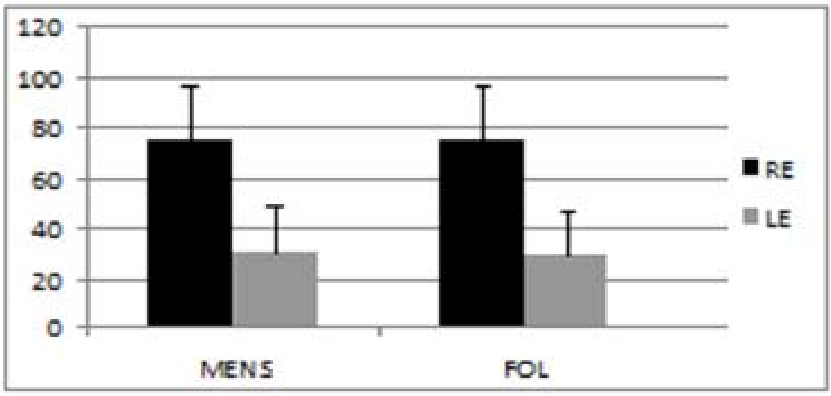

Figure 5: *Main Effect of Cycle over Correct Answers (RE, LE) of 17 Subjects in DL (verbal) Task during Two Phase*

Table 6. Main Effect of Ear over RT Mean of 17 Subjects in DL (verbal) Task during Two Phases

	CYCLE			
	MENSTRUAL		**FOLLICULAR**	
EAR	Mean	SD	Mean	SD
RE	1178.63	153.16	1152.01	178.77
LE	1239.22	167.95	1212.69	240.28

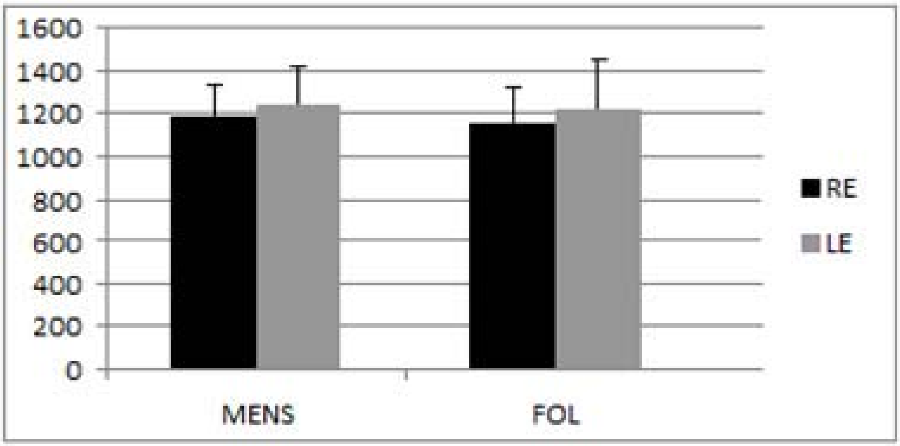

Figure 6: *Main Effect of Ear over RT Mean of 17 Subjects in DL (verbal) Task during Two Phases*

Mood

Because cycle-dependent fluctuations in mood can affect interhemispheric processes[9], STCI-S18 was performed. We analyzed cheerfulness (CH), seriousness (SE) and bad mood (BM) scores separately using ANOVA with the cycle phase as the repeated measure. A significant effect of cycle phase was not observed for the CH ($F(1,12)=2.04$, $p<.163$, ns), SE ($F(1,12)=1.13$, $p<1.98$, ns) and BM ($F(1,12)=.91$, $p<.41$, ns) scores. First, we conducted the analysis for the 12 participants whose E and P levels met our criteria. Then, we repeated the same analysis over the 17 participants with available E levels and the 20 participants with available P levels. However, no significant main effect of cycle on the CH ($F(1,17)=0.78$, $p<.39$, ns), SE ($F(1,17)=3.41$, $p<.08$, ns) and BM ($F(1,17)=.66$, $p<.43$, ns) scores of 17 participants with available E levels was found. The result was similar for the 20 participants with available P levels in that the main effect of cycle on CH ($F(1,19)=0.510$, $p<.48$, ns), SE ($F(1,19)=.850$, $p<.37$, ns) and BM ($F(1,19)=.152$, $p<.70$, ns) scores was not significant.

DISCUSSION

In the current study, we investigated the change in cerebral asymmetry related to hormonal fluctuations during the menstrual cycle by means of a verbal dichotic listening task. Although obtaining stable asymmetries with a superiority of the right ear, we did not see alterations of this lateralization with respect to estradiol or progesterone.

Verbal Dichotic Listening Task

Throughout our analysis, we obtained a stable right ear advantage (REA). A REA was observed using accuracy data from 12 participants with confirmed P and E levels. The same significant result was also obtained with the analysis performed using 20 participants with confirmed P levels and the 17 participants with confirmed E levels. On the average they always showed a clear REA and in most subtests, including a RT advantage for the right ear. Thus, our technique to study language asymmetry was successful.

The results of the dichotic listening task data showed that the degree of language asymmetry as revealed by dichotic listening did not change during the three menstrual phases. We did find, however, that the main effect of cycle was significant when we analyzed the data of 17 participants with available E levels. This result indicated that the total number of correct responses (RE, LE) differed between the menstrual and follicular phases. But since we have not provided evidence for an interaction of asymmetry with cycle phase, estradiol seems to affect overall auditory recognition without altering language asymmetry.

REA is typical for right-handed participants and indicates that more items are correctly reported from the right ear when compared to the left ear. Possibly, an REA reflects the linguistic specialization of the left hemisphere[23]. An REA has been reported to be a result of hemisphere superiority in the processing of language-related materials[28]. Similar findings have been confirmed by many DL studies[3,23,26,27,33,38]. When speech sounds are presented, the DL task reveals an REA that highly correlates with the WADA-test[25]. The perception and the production of the syllables are known as functions that are associated with the laterality of LH[5,24,34]. A recent study with a trial-by-trial analysis of event related potentials could reveal that the overall REA is a time-bound effect, which can be explained by the late transfer of syllabic information from the right to the left hemisphere[1]. The results of the current study are in accordance with the results of these previous studies.

In previous studies, a change in the asymmetry of the numbers of right and left ear responses during cycle phases were shown[37,42,41,12]. We could not replicate this finding. This was clearly not related to mood effects which were carefully controlled by additional tests. The present study differs from previous studies because we also studied the RT as a dependent variable. We indicated that the main effect of ear over RT mean was significant when we analyzed the data of 17 participants with available E levels and 20 participants with available P levels, separately. However, also in this variable we did not see a change of asymmetry over the cycle. Thus, neither accuracy nor speed measures could show that language asymmetries as measured with dichotic listening are subject to menstrual cycle changes.

Negative findings are always more difficult to interpret than positive ones. Certainly the most important limitation of our study is the sample size. However, this resulted from the fact that we used very strict criteria for subject inclusions and therefore exclude many women. This could in principle result in a Type II error. With a larger sample size, it might be possible to indicate an interaction of menstrual cycle and ear.

However, also a larger sample size would not increase the effect size. Due to this small effect size, only very large samples can reveal an interaction of hormones and asymmetry changes in dichotic listening. The theory on progesterone dependent variation of cerebral asymmetry[19] assumes that hormones change brain asymmetry by altering cortico-cortical interactions. This cortico-cortical interaction via the corpus callosum is primarily mediated by glutamatergic fibers that mostly synapse on AMPA and NMDA receptors on pyramidal neurons in the other hemisphere. These pyramidal neurons subsequently activate inhibitory GABAergic interneurons which induce a widespread inhibition. Thus, the corpus callosum does not simply exert excitatory or inhibitory action on the contralateral hemisphere, but rather induces brief glutamate-mediated excitatory postsynaptical potentials (EPSPs), followed by a prolonged GABA-mediated inhibition (IPSP). Progesterone suppresses in a dose dependent fashion the glutamate-induced excitatory responses of neurons by about 87%,[39]. Thus, the release of progesterone would result in a decrease of non-NMDA glutamate receptor responsiveness. Due to the reduction of corticocortical transfer, a reduction of functional cerebral asymmetries follows[20].

So then, why was the effect size of our study so small? It is possible that it is related to the unusual property of callosal fibers that connect the auditory cortical fields and that are possibly involved in the generation of dichotic listening effect[1]. LaMantia and Rakic[29] revealed that the axons crossing between the auditory cortical areas are unusually large and heavily myelinated to possibly ensure exceptionally fast conduction speed. It is possible that this anatomically distinct callosal pathway is less prone to be modified by hormonal fluctuations. By combining several large data sets of subjects as in Cowell et al.[12], this effect then becomes significant. This is not so in cases like the present one that utilizes highly selected and thus smaller subject numbers. Taken this issue into account, it will likely be possible to get a clearer picture in the future studies investigating the change of FCAs during menstrual cycle.

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Correspondence to:
Handan Can
E-mail: Handancan@uludag.edu.tr

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