

Effects of Biofeedback Training on Resting-State Electrophysiology and Emotion: Evidences from the Females with Premenstrual Syndrome

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Abstract

Aim

To investigate the effect of biofeedback stress dysfunction training on the psychophysiological and neural activity of women with or without premenstrual syndrome (PMS).

Methods

The present study recruited thirty women (18~30 years old, 22 ± 2.19) and fifteen women belong to PMS group (23 ± 1 years old), while the left formed the non-PMS group (22 ± 2 years old). There were nine women in each group (22 ± 2 years old) took part in the stress dysfunctional biofeedback training, which strengthens the sensorimotor rhythm (SMR) of EEG (12-15Hz) and decreases the surface electromyogram (SEMG) which lasts for two weeks (five days each week), while the left six women in each group (23 ± 1 years old) didn't receive biofeedback training but they had to finish the pretest and posttest just like the training women did (in the luteal or follicular phases). The tests include two minutes frontal EEG asymmetry (eyes closed and open) task and emotional scales.

Results

The results showed that in the pretest, in the control group, compared with the women without training, the women with biofeedback training had higher scores on self-report of emotion, stronger electrodermal response (EDA) and higher heart rate (HR); compared with training women in the control group, the training women in the PMS group had higher negative affect. In addition, after the training, compared to healthy women, the women with PMS had higher EEG asymmetry scores which turned the negative score (bad coping and dysregulation) to the positive score (normal coping and regulation). Compared with the healthy women, after training, the PMS women had lower negative emotion.

Conclusion

These findings suggest that the biofeedback of stress dysregulation effectively improve the stress coping capacity of women with PMS and improve their negative emotion as well.

Keywords

Biofeedback training, Premenstrual Syndrome, Resting-state, Frontal EEG asymmetry, Emotion

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Introduction

The hormone fluctuations under menstrual cycle were considered to have a vital effect on premenstrual syndrome (PMS), which was marked by a variety of emotional, physical, and behavioral symptoms that occur during the late luteal phase of the menstrual cycle [1]. The variations of the gonadal hormone level would affect the brain regions which were related to emotional regulation ability. The recent research suggests that the stress turns to be an underlying moderator variable, because the fluctuations of progesterone and estrogen have important effects on females' mood disorders and sensitivity to stress [2]. The depression syndrome which caused by the hormone fluctuations under menstrual cycle would lead to PMS [3]. The premenstrual phase was also related to stronger reactivity to mental stress which in turn to induce the occurrence of negative mood [4], while these strengthen stress reactivity was more obviously performing on females with PMS [5]. These studies highlight how the interaction between hormone fluctuations under menstrual cycle and stress was used to investigate its effect on brain activity.

In consideration of the effects of menstrual cycle on the prefrontal cortex (PFC) function which related to reward circuit [6,7], while the dysfunction of PFC would reflect on psychophysiological variables [8] like cardiovascular activity (representative of using resources) and frontal EEG asymmetry (motivation tendency). The study of Ossewarrde, *et al.* found that the increased negative emotion in the premenstrual phase would affect the regulation of mood and the sensitivity to stress [9]. Similarly, the activation of medial-prefrontal cortex (mPFC) to the anticipation or experience of painful stimuli in the luteal phase was lower than that in the follicular phase [10]. The study of autonomic nervous system (ANS) from Matsumoto, *et al.* also found that, in the luteal phase, the changes of ANS level may be related to the occurrence of physical-psycho and behavior syndromes and may be one of the reasons for PMS. Moreover, when the syndrome turned to be more severe, the sympathetic and vagal function would change regardless of the phases of menstrual cycle [11]. This means, the physiological tests which reflected the ANS level would help us to distinguish the physiological sensitivity to stress between women with PMS and normal women.

Though studies analyzing the application of biofeedback to PMS are sparse, biofeedback as a treatment for PMS has been demonstrated in some earlier study [12-14]. The study performed by Konandreas and Kolokithas showed that biofeedback and relaxation have a positive effect on mood states during the luteal phase of the menstrual cycle for PMS [12]. What's more, from the perspectives of methodology and theoretical construction, the review of the effects of neurofeedback on optimal performance held a view that, the EEG asymmetry (alpha, 8-13Hz) could be a marker of individual cognition and behavior improvement [15]. The neurofeedback is the effective way to treat many mood disorders. Generally, by means of the operant conditioning network to help individuals to accept the visual or auditory signal feedback in order to regulate their own cortex EEG activity. For example, the changes of asymmetry between left frontal alpha and right frontal alpha activity through neurofeedback training were considered to be effective tools to treat the major depressive disorder (MDD) [16]. The values of the EEG alpha asymmetry could predict the improvement of social anxiety [17], depression [18] and PTSD syndrome [19]. In addition, the more left EEG asymmetry induced by stress could predict the aggression or tendency of aggression caused by stress [20]. Whether or not the PMS which related to abnormal reactivity to stress and mood regulation could be treated through the neurofeedback and would reflect on the improvement of EEG asymmetry was to be determined. Therefore, we may focus on the normal females whose hormone fluctuations of menstrual cycle were normal and the PMS whose hormone fluctuations of menstrual cycle were abnormal and from the perspective of hormone fluctuation pattern was normal or not to investigate their basic stress reactivity. We chose the resting state electrophysiology activity and emotional self-reports as our stress reactivity indices to evaluate the effectiveness of biofeedback stress dysfunction training on females with or without PMS.

Above all, our purpose was to investigate the effect of neurofeedback stress dysfunction training on the psychophysiological and neural activity of normal females and females with PMS. Training was the stress dysfunctional biofeedback training, which strengthened the sensorimotor rhythm (SMR) of EEG (12-15Hz) and decreased the surface electromyogram (SEMG). We adopted the mixed experimental design together with the

subjective emotional measurement, resting state physiological recording as well as the frontal EEG asymmetry to evaluate the changes of different groups (control, PMS) of women before and after the training. The stress and menstrual cycle would both affect the PFC functions which related to reward circuit, while performing at the level of neural activity was the abnormal of EEG asymmetry and at the level of physiology were the changes of cardiovascular activities. Therefore, if we conducted the biofeedback of stress dysfunction training on PMS, the PMS's PFC would be improved or not? Specifically, if the frontal EEG asymmetry could reflect the PFC function and further to be predictive variable for the improvement of PMS's stress sensitivity.

Methods

■ **Participants**

In order to confirm the participants were healthy and had no medical and surgical diseases, all participants were checked by the gynecological examination and B-ultrasonic wave before the experiment. At the same time, we adopted the premenstrual syndrome scales [21], the self-compiled basic information on the women's menstrual cycles, Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) to screen and group the 86 females (18-30 years old). The participants were recruited via flyers in the University and campus network. Exclusion criteria were being currently pregnant or lactating, taking oral contraceptives or being under medical treatment; taking medicine which would affect the stress reactivity; clinical anxiety and depression; being obviously psychological abnormal syndrome and no regular menstrual cycles.

The final sample was comprised of 30 participants (22 ± 2.19 years old), including 15 females in the PMS group (23 ± 1 years old) and 15 females in

the non PMS group (22 ± 1 years old). There were nine women in each group (22 ± 1 years old) took part in the biofeedback training, which lasts for two weeks and five days in each week, while the left six women in each group (23 ± 1 years old) didn't have biofeedback training but they finished the pretest and posttest just as the training women did (in the luteal or follicular phases).

All participants had normal or corrected-to-normal vision. They were all right-handed, as determined by Chapman and Chapman's scale [22]. The demographic information of participants is shown in **Table 1**. All participants provided written informed consent to participate in this experiment. The study was performed in accordance with the Declaration of Helsinki.

Materials

■ **Frontal EEG asymmetry procedure**

Participants were comfortably seated 60 cm from the screen in an electrically shielded, air-conditioned and dimly lit room. Participants were asked to close their eyes, keep a comfortable and relaxing posture, relax their whole body, and avoid eye and body movements. There were eight blocks of the EEG procedure. Each block lasts for 15 seconds, while the participants kept eyes closed (C) for four blocks and eyes open (O) for four blocks. There was counterbalance between eyes-open blocks and eyes-closed blocks (O-C-O-C-O-C-O or O-O-C-C-O-C-C-O), and the whole procedure lasts for two minutes.

■ **Emotional Scales**

Seven-point emotion self-reports: We adopted the seven-point emotion self-reports to evaluate the current emotional states of participants ('-3' means extremely unhappy; '0' means neutral; '3' means extremely happy; the lower the scores, the less happy the participants' feeling). The

Table 1: Sociodemographic characteristics (mean ± S.D.) of both groups.

	PMS	Control
<i>N</i>	15	15
Age (years)	23 ± 1	22 ± 2
Menophania (years)	13 ± 1	13 ± 1
Examined phase of Pretest	9 luteal, 6 follicular	6 luteal, 9 follicular
Examined phase of Posttest	7 luteal, 8 follicular	7 luteal, 8 follicular
Cycle Length (days)	29 ± 2	28 ± 3
<i>Note:</i> PMS = premenstrual syndrome, luteal = luteal phase of menstrual cycle (1~3 days before the menstruation), follicular = follicular phase of menstrual cycle (1~3 days after the menstruation). No significant difference in age, menophania, menstrual cycle length or phases of tested		

emotional evaluation method was in accordance with the related emotional evaluation research in which there was significant correlation between emotional self-report and physiological indices [23].

Positive affect and negative affect scale (PANAS): The PANAS includes 20 items and contains two emotion dimensions (positive, 10 items; negative, 10 items). The participants are requested to make decisions according to their current emotional state [23]. The PANAS is a Likert-style questionnaire (from 1, indicating “very slightly or not at all,” to 5, indicating “extremely”). The sum of the positive affect and negative affect scores are utilized separately for data analysis. The Chinese version of the PANAS has well-established validity and reliability [24].

Procedure

■ Pretest and posttest

The participants in the present study should accept the pretest and posttest, at an interval of two weeks. The tests include the resting-state electrophysiology measurement (five minutes resting physiological recording for the electrodermal activity, heart rate, respiration and pulse rate; two minutes frontal EEG asymmetry task for the alpha EEG rhythm) and emotional scales (self-report for emotion; PANAS).

■ Biofeedback training tasks

The participants who accepted the biofeedback training should finish two weeks, each week five days, each day 30 minutes training tasks. Generally, the biofeedback training should include three parts which were the baseline test (pretest), feedback pattern/training and then the posttest. Because the PMS was one of the stress related disorder, the present study chose the stress dysfunctional biofeedback training to train the women with PMS in which our focus circuits were electroencephalogram (EEG) and electromyography (EMG). Therefore, our program for biofeedback training was to strengthen the sensorimotor rhythm (SMR) of EEG (12-15Hz) and decrease the surface electromyogram (SEMG).

The program was used to record the participants' EEG and EMG, meanwhile showing various pictures and voices to conduct real-time feedback. A training task included 3 sub-parts which were the scenery relaxation (3 minutes), smiling faces practice for decreasing EMG (8 minutes)

and scenery animation for strengthening SMR (10 minutes). Each sub-part was comprised of 5 interface manipulations which were ① the choose of electrodes (Cz); ② the strengthen or weaken of EEG frequency band or amplitude (the SMR was related to the relaxation state, the choice of amplitude was based on the participants' baseline values of SMR); ③ the settings of feedback threshold; ④ the settings of the ratio of reward; ⑤ the settings of feedback interfaces, the sequences (scenery relaxation, part A; smiling faces practice for decreasing EMG, part B; and scenery animation for strengthening SMR, part C) of each training within the two weeks were arranged as follows: ABC – ACB – BCA – BAC – CAB – CBA.

Data Recording

■ Frontal EEG asymmetry data recording

According to the previous studies, we mainly measured EEG alpha (8-13Hz) asymmetry in the frontal area (F3 and F4) and the EEG was referenced on-line to the left mastoid and re-referenced off-line to the Cz electrode. Throughout the EEG recording, the impedance of the electrodes was maintained under 5 kΩ. The electroencephalogram (EEG) was recorded by 40 Ag/AgCl electrodes mounted on a custom-made cap (ECI; Eaton, Ohio) according to the extended 10-20 system and continuously sampled at 1000 Hz by a Neuroscan NuAmps Amplifier. The band-pass filter range of 0.01 to 200 Hz was used during the EEG recording. The artifact-free EEG was analyzed with discrete Fourier transforms (DFT) which use a Hanning window of one second width and 5% overlap. Power was extracted from the 8-13Hz frequency band and measured with mean square microvolts as its unit. The raw data of power was then transformed in the natural log (ln) in order to normalize the data distribution. The value of the frontal EEG asymmetry was calculated by subtracting the value of the left EEG power from the value of the right EEG power ($\ln[\text{right alpha}] - \ln[\text{left alpha}]$).

■ Physiological data recording

The physiological reactivity was recorded, transformed, amplified and stored by the BioNomadix Remote Physiological System (BIOPAC MP150, Biopac Systems, Inc., Goleta, CA). A BioNomadix device consists of two components, a wireless transmitter that is worn by the subject to amplify and send the

physiological data and a receiver module. The range of motion for participants was 10 meters. The bipolar electrodes that were used to collect the wireless electrodermal activity (EDA100C) were attached to the ring and middle fingers of the subjects' left hands (VIN+ and VIN-, respectively). The amplifier gain of the EDA100C was $5\mu\text{mho/V}$, the high-pass filter was DC and the low-pass filter was 0.1Hz. The sample rate was 250 Hz, and the units were in $\mu\text{mho/V}$.

The pulse rate (PR) was recorded by the BN-PULSE-XDCR amplifier which has a filter of DC to 10Hz and sampling rate of FSR/4096(4.88mV). The electrode of PR was connected to the left index finger. The respiration was recorded by the RSP100C amplifier which gain was 10 and has a filter of DC to 10Hz, sampling rate was 2000Hz. The electrode of respiration was wrapped around the abdomen. The Dual Wireless electrocardiogram (ECG) BioNomadix Pair consists of a matched transmitter and receiver module specifically designed to measure ECG data on one or both channels. ECG signal data are transmitted at a rate of 2,000 Hz. Raw data from the pair are band-limited from 0.05 Hz to 150 Hz. The heart rate (HR) of each participant was obtained on the basis of the R-R interval, which was immediately extracted from the ECG signal. The unit of the HR was beats/minute (bpm). The ground (GND) was connected to the right abdomen, the VIN+ was connected to the left fourth and fifth intercostal spaces, and the VIN-, which showed the electrode connections to the ECG for the lead measurements, was connected to the left collarbone underneath (Precordial Lead).

■ Biofeedback data recording

The biofeedback training was used the multi-parameters biofeedback Infiniti4000C (ProComp Infiniti, Thought Technology; Montreal, Canada) system which including the Bioneuro Infiniti encoder, data recording interconnecting component and the sensors of EEG and EMG. The training room temperature maintained around 20°C, well-ventilated and quiet, the relative humidity is not more than 80% and the supply voltage was AC220V (50Hz). The participants were in relaxed position and eliminate the physical and mental stress emotion to accept the training. The EEG-Z sensor of Infiniti4000C was unipolar lead (three electrodes, an acting circular electrode, a clip reference electrode and a clip group electrode). According to the international 10-20 system

electrode setting method, the acting circular electrode was put at the Cz point (the placement of electrode was based on anatomical landmarks: nasion (Nz), inion (Iz), and left and right pre-auricular points: LPA and RPA). The sensor of EMG was headset unipolar lead (including positive electrode, negative electrode and reference electrode) and placing in the frontal muscle.

Data Analysis

The SPSS16.0 software (SPSS Inc., Chicago, IL) was used to process and analyze data in the present study. We conducted a mixed-factor ANOVA on the effects of training on females' emotional and electrophysiological reactivity for which the test time (pre-training and post-training) was the within-subjects variable. All of the significant analyses used the two-way test ($p < 0.05$), and the partial eta squared (η^2_p) was the effect size. Paired-sample t tests were used for significant tests for the main effects, and the simple effect analysis was used to test significant interactions. For within-subject analysis, the Greenhouse-Geisser correction was used where appropriate. The data were all presented as the mean \pm S.D.

Results

■ Subjective emotion of control and PMS groups before and after the biofeedback training

A mixed-factor ANOVA was performed on the scores of the seven-point self-report scale and positive affect and negative affect scale (PANAS). The within-subjects variable was the TIME (pre-training and post-training) and the between-subject variables were PMS (PMS group and no PMS group) and TRAINING (training and no training). In addition, the females' testing phases of menstrual cycle (luteal and follicular) were used to as the concomitant variable. The dependent variables were scores of emotion self-report scale (ES), positive affect (PA) and negative affect (NA).

The results showed that for PA, the main effect of PMS ($F_{(1,24)}=12.403$, $p=0.002$, $\eta^2=0.347$) was significant, while the main effect of TIME ($F_{(1,24)}=3.683$, $p=0.067$, $\eta^2=0.133$) was marginal significant. The main effect of TRAINING was not significant ($F_{(1,24)}=0.167$, $p=0.687$, $\eta^2=0.007$). However, for ES and NA, the main effects of PMS, TIME and TRAINING were not significant ($F_{(1,24)} < 2.82$, $p > 0.05$).

The only significant interaction was the TIME×TRAINING on the NA ($F_{(1,24)}=6.658, p=0.016, \eta^2=0.217$). Simple effect analysis revealed that compared to the training females in control group ($M=13.72, SE=2.08$), the training females in PMS group ($M=19.71, SE=1.90$) had higher scores on NA ($F_{(1,27)}=4.41, p=0.045$). The specific trends are presented in **Figure 1A**. In addition, compared to no training females in control group ($M=-0.06, SE=0.35$), the training females in control group ($M=0.77, SE=0.31$) got relatively higher scores on ES before the training, $F_{(1,27)}=3.05, p=0.092$ (marginal significance). The specific trends are presented in **Figure 1B**.

Moreover, the interaction of TIME×PMS on NA was marginal significant, $F_{(1,24)}=3.513, p=0.164, \eta^2=0.079$. However, other interactions were not significant ($F_{(1,24)}<1.88, p>0.05$).

■ Frontal EEG asymmetry of control and PMS groups before and after the biofeedback training

We adopted the mixed-factor ANOVA analysis on the scores of alpha rhythm frontal EEG asymmetry which the independent variables were TIME (pre-training and post-training, within-subjects variable), PMS (PMS and no PMS, between-subject variable) and TRAINING (training and no training, between-subject variable). The testing phases of female participants were used as the concomitant variable. The dependent variable was the alpha values of EEG asymmetry.

The results showed that, the interaction of PMS×TIME was marginal significant, $F_{(1,24)}=3.516, p=0.073, \eta^2=0.128$. In addition, the interaction of PMS×TIME×TRAINING was significant, $F_{(1,24)}=4.355, p=0.048, \eta^2=0.154$. Simple effect analysis revealed that compared the alpha value before training for training females in PMS group ($M=-0.21, SE=0.30$), the alpha value after training ($M=0.90, SE=0.34$) increased significantly, $F_{(1,27)}=6.50, p=0.017$. Other interactions were not significant ($F_{(1,24)}<0.06, p>0.05$). The specific trends are presented in **Figure 2**.

Resting state physiological reactivity of control and PMS groups before and after the biofeedback training.

Mixed-factor ANOVAs were conducted on the resting state physiological data: electrodermal activity (EDA), heart rate (HR), respiration rate and pulse rate for females in different groups and different treatment before and after the training. The testing phases of female participants were used as the concomitant variable. The dependent variable was physiological activity (EDA, HR, respiration rate, pulse rate). The between-subject variables were PMS (PMS and no PMS) and TRAINING (training and no training), while the within-subjects variable was TIME (pre-training and post-training).

The ANOVA analysis found that, the main effect of PMS was significant on HR ($F_{(1,24)}=4.793, p=0.039, \eta^2=0.166$), respiration rate

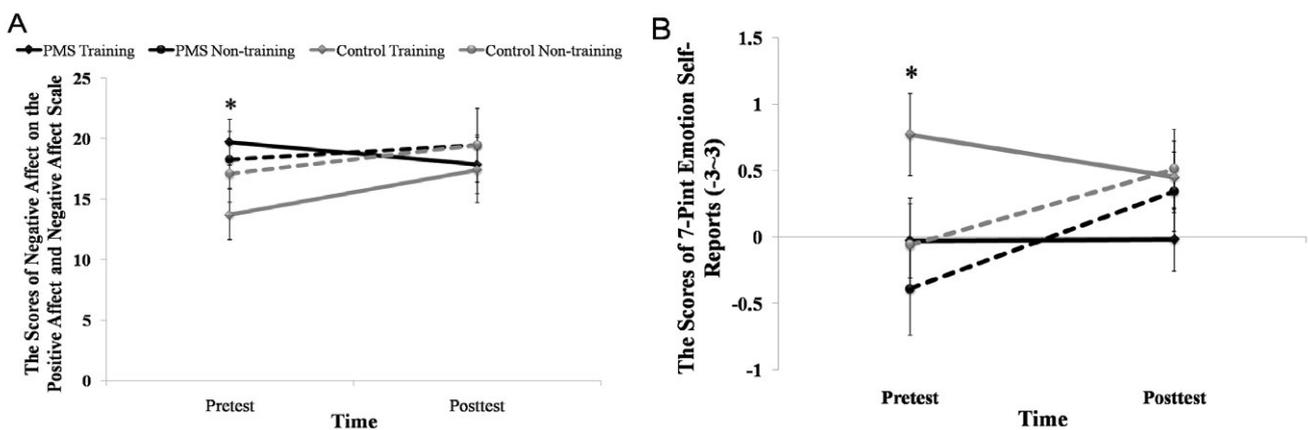


Figure 1: The scores of the 7-point emotion self-report and the positive affect and negative affect scale (PANAS) for PMS ($n=15$) and control ($n=15$) groups under different treatments (training and non-training) at pretest and posttest. (A) The scores of negative affect on PANAS for PMS ($n=15$) and control ($n=15$) groups under different treatments (training and non-training) at pretest and posttest; (B) The scores of the 7-point emotion self-report for PMS ($n=15$) and control ($n=15$) groups under different treatments (training and non-training) at pretest and posttest.

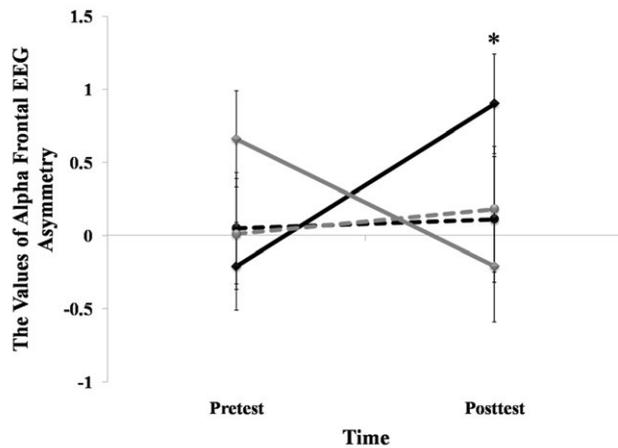


Figure 2: The values of alpha frontal EEG asymmetry for PMS ($n=15$) and control ($n=15$) groups under different treatments (training and non-training) at pretest and posttest.

($F_{(1,24)}=4.116, p=0.054, \eta^2=0.146$) and pulse rate ($F_{(1,24)}=6.446, p=0.018, \eta^2=0.212$) which you can see in **Table 2**. But the main effect of PMS on EDA was not significant, $F_{(1,24)}=0.239, p=0.630, \eta^2=0.010$. The main effect of TRAINING on HR was marginal significant, $F_{(1,24)}=3.27, p=0.083, \eta^2=0.120$; Other main effects were not significant, $F_{(1,24)}<2.07, p>0.05$.

The only significant interaction was the TIME \times TRAINING on the EDA, $F_{(1,24)}=4.608, p=0.042, \eta^2=0.161$. In addition, the interaction of PMS \times TRAINING on HR was marginal significant, $F_{(1,24)}=2.963, p=0.098, \eta^2=0.110$. Further simple effect analysis revealed that in the pretest, the females within no PMS group had significant difference on EDA ($F_{(1,27)}=6.36, p=0.018$) and HR ($F_{(1,27)}=6.52, p=0.017$). Specifically, in the pretest, compared to the females without training (EDA, $M=-3.19, SE=1.20$; HR, $M=67.35, SE=4.07$), the females

who participated in training (EDA, $M=0.20, SE=1.05$; HR: $M=79.78, SE=3.18$) within the control group got stronger EDA and higher HR. The specific trends are presented in **Figure 3**. Other interactions were not significant ($F_{(1,24)}<1.86, p>0.05$).

Discussion

The present study was the first to improve the abnormal stress sensitivity of PMS through the training of biofeedback. Specifically, the biofeedback training improved the frontal EEG asymmetry activity of PMS females. At the same time, we found that the effect of anticipation of training was separated on control females and females with PMS. The negative anticipation of training increased the negative emotion of PMS, while the positive anticipation of training strengthened the subjective feeling and autonomic nervous system activity of females

Table 2: The respiration rate (bpm) and pulse rate (bpm) for PMS ($n=15$) and control ($n=15$) groups under different treatments (training and non-training) at pretest and posttest (mean \pm S.D.).

Index	Group	Treatment	Test Time	
			Pretest	Posttest
Respiration Rate (bpm)	PMS	Training	15.56 \pm 0.67	15.19 \pm 0.69
		Non-Training	16.13 \pm 0.83	14.94 \pm 0.86
	Control	Training	14.80 \pm 0.73	14.17 \pm 0.75
		Non-Training	13.81 \pm 0.83	14.15 \pm 0.86
Pulse Rate (bpm)	PMS	Training	79.19 \pm 3.44	86.27 \pm 4.75
		Non-Training	80.99 \pm 4.28	81.84 \pm 5.92
	Control	Training	80.32 \pm 3.77	74.54 \pm 5.21
		Non-Training	67.63 \pm 4.28	66.88 \pm 5.92

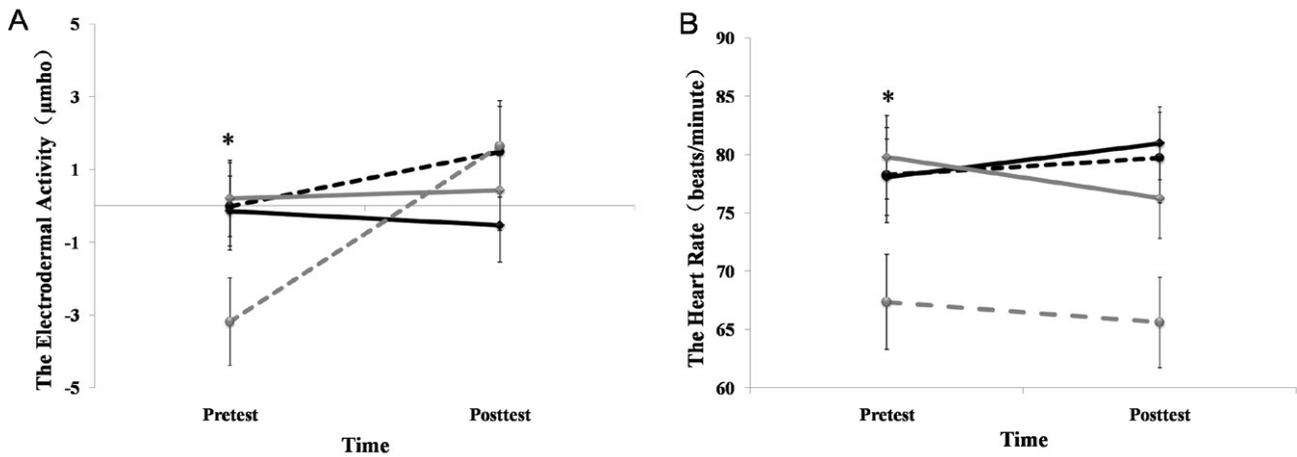


Figure 3: The electrodermal activity (EDA, µmho) and heart rate (HR, bpm) for PMS (n=15) and control (n=15) groups under different treatments (training and non-training) at pretest and posttest. (A) The electrodermal activity (µmho) for PMS (n=15) and control (n=15) groups under different treatments (training and non-training) at pretest and posttest; (B) The heart rate (bpm) for PMS (n=15) and control (n=15) groups under different treatments (training and non-training) at pretest and posttest.

without PMS. This suggests when we investigate the etiology and clinical performance of PMS, the variable of anticipation should be taken into consideration.

First, the emotional feelings before the training for the control group changed because of the anticipation of training. Specifically, compared to those who did not participate in the training, those who participated in the training had higher scores on the subjective self-reports on emotion within the control group. This result was similar to the study of Choi, *et al.* [10]. Choi and his colleagues found that the prefrontal functions of females under different phases of menstrual cycle would be affected by the anticipation of stimuli. In addition, we observed that compared to the females participated in training in the control group, the females participated in training in the PMS group reported more negative emotion before the training. This result was in accordance with the study of Epperson, *et al.* [5]. They found that, as one of the subjective stress reactivity, the increased negative mood was obvious performing on females with PMS. These results indicate the performance on self-report emotion, positive affect and negative affect would be separated on females with or without PMS because of the anticipation of biofeedback training.

Moreover, we found that compared to those who did not participate in the training, females who participated in the training in the control group had stronger EDA and higher HR before the training. However, there were no significant

differences on cardiovascular activity because of anticipation of training within the PMS group. This was consistent with the study of Matsumoto, *et al.* [11], which found the sympathetic and vagal tone for PMS females had downturn changes which were independent of testing phases of menstrual cycle. This result suggests that the abnormal hormone fluctuations during the menstrual cycle of PMS made them have problems on the mobilization of physiological resources that actually reflect their dysfunctional prefrontal states.

Finally, in the present study, compared to those who did not participate in the training, females who participated in the training within the PMS group had increased scores on the frontal EEG asymmetry after training. Specifically, the scores of EEG asymmetry went on from pre-training to post-training which means the PMS group turned to be more left EEG asymmetry through biofeedback training. This result was in accordance with the studies of Moscovitch, *et al.* [17] and Kim, *et al.* [19]. Moscovitch and his colleagues found that under resting state, the left EEG asymmetry could be improvement markers for patient syndrome and should be the final state of effective psychotherapy on patients with social anxiety. Kim and his colleagues held a view that the EEG asymmetry was nonlinear which means compared to the control group, the PTSD patient would perform more left EEG asymmetry activity. This indicates that the abnormal

functional connectivity for PTSD could be found by means of EEG measurement and performing as the nonlinear interdependency phenomenon. Based on these, besides the patients with social anxiety and PTSD, our study found that EEG asymmetry also could be predictive variable for the stress reactivity improvement of women with PMS.

This result also found evidence from the study of stress disorders and confirmed the viewpoints of Verona and Sadeh [23]. They found the participants would have more left than right prefrontal activity under stress, which means the stress reactivity related to approach activation representing a behavioral dysfunction phenomenon. In the present study, we observed the improvement of EEG asymmetry for stress-related patients (PMS females) through the training of biofeedback stress dysfunction program. This indicates that the etiology of PMS may connect to the dysfunction stress reactivity of PMS females.

As a tentative preliminary study to explore the effect of biofeedback stress dysfunction training on the psychophysiological and neural activity of PMS females, there were some limitations in our study. First, we didn't strictly control the testing phases of females. Although we used the testing phases as the concomitant variable to conduct the statistical analysis, we have imported the effects of uncontrollable sequence. Second, the biochemical reaction samples were missing in our study to confirm the stress sensitivity of females which should be the next possibility needs to investigate in the future. Besides, the sample size in this study was small, which limits the generalizability of the study, so a larger

sample study is needed to explore this question further. Above all, the present result reflected the improvement of stress reactivity of PMS females after the biofeedback training which performing on the increases of EEG asymmetry values. In addition, the anticipation of training would have separate effects on emotion and stress sensitivity for females with or without PMS. Specifically, the negative anticipation of PMS produced more negative affect before training, while the positive anticipation of normal females increased their self-report emotion, strengthened the EDA and improved the HR level. This suggests the abnormal stress sensitivity caused by anticipation to some extent has connections with PMS etiology.

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Disclosure Statement

The authors have declared that no competing interests exist.

Author Contributions

Authors Qing Liu and Wenjuan Zhang did the conception and design of the study, acquisition and analysis of data, drafting the manuscript or figures.

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