Correlative Study of EEG and Body Hydration across the Menstrual Cycle

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Abstract

Evidence exists for physical and psychological changes across the 28 days of menstrual cycle. Variation in the hormonal level have physical symptoms as oedema, breast tenderness, muscle pain, weight increase, vomiting and most notably water retention or body hydration in women. Significant changes in behavioral across the menstrual cycle such as mood swings, anxiety, depression, confusion, emotional liability, irritability, loss of concentration, lethargy, and aggression/hostility, have been associated with the menstrual cycle. Present study is design to examine whether the ovulatory cycle is associated body hydration and is there any correlation of body hydration with EEG pattern. Healthy females between the ages of 18-23 years of age were allowed to participate. Body hydration, Brain activity (EEG) and hormonal level during a normal menstrual cycle were determined using multi-frequency body impedance analysis (MFBIA), Data acquisition system (BIOPAC MP36) and ELISA procedure respectively. Comparison of brain signal and hydration with both the sex hormone we found a correlation between the EEG wave forms, hydration status and the hormonal level. Progesterone seems to be in phase with alpha followed by the delta and theta while beta goes inversely. Delta and theta seems to be in phase with estrogen and out phase with alpha. Result of present study shows that ovulatory cycle is associated body hydration and there is a correlation of body hydration with EEG pattern.

1. Introduction

In normal condition menstrual cycle last for 28 days and divided in Menstrual, Follicular, and Luteal [1] Ovarian hormone Estrogen and Progesterone fluctuates throughout the mentioned phases of the normal menstrual cycle [2]. In the menstrual phase there is a sudden reduction in estrogen and progesterone which lasts for approximately the first 5 days of the cycle [3]. The follicular phase stays from day 6 to 13 and during this phase the developing follicle increases its secretion of estrogens [3]. The luteal phase of the menstrual cycle is the longest in duration and it starts from 15th day of cycle to onset of new cycle [3]. The luteinizing hormone stimulates the development of the corpus luteum. The corpus luteum then secretes increasing quantities of estrogens, progesterone, and relaxin. Significant and sustained change in the levels of sex hormones during the menstrual cycle may have profound effect on alteration in brain functioning and body hydration. [4] There are number of physical symptoms have been found in women during the cycle includes oedema, breast tenderness, muscle pain, weight increase, vomiting and most notably water retention or body hydration in women [5]. Several workers have found significant changes in behavioral changes across the menstrual cycle such as mood swings, anxiety, depression, confusion, emotional liability, irritability, loss of concentration, lethargy, and aggression/hostility, have been associated with the menstrual cycle [6-10, 11].

Studies indicate that there is a relationship between ovarian hormones and functioning of central nervous system. Ovarian Hormone may cause changes in our emotions and brain functioning by binding to specific docking sites (receptors) on specific brain cells in specific areas of the brain. When estrogen binds to its

receptor on a brain cell, the brain cell fires faster and can use more glucose (sugar) and oxygen. Estrogen also increases the flow of blood to the brain cell so more fuel can be delivered faster so higher estrogen can bring anxiety, agitation and even seizures. Progesterone decreases the number of estrogen receptors on the cell, therefore directly blocking estrogen's effects and give calming, relaxing, and anti-seizure. [12]

Estradiol and progesterone primarily control reproduction but they also affect the body fluid regulation [3] and understanding of cyclic changes in the reproductive hormone throughout the menstrual cycle may be useful to understand the changes in the body fluid .[13] One mechanism by which estrogen may impact physiological system is through regulation of body fluid and sodium content. Receptors for estrogen and progesterone are found in non reproductive tissue involved in fluid regulation such as hypothalamus [14, 15] cardiovascular [16, 17] and kidney tubules [16]. Both estrogen and progesterone can influence the complex and integrated neural and hormonal system that have evolved to control thirst, fluid intake, sodium appetite, and renal fluid and sodium regulation. [3].

Regulation of extracellular sodium ion concentration controls the distribution of water between extracellular fluid and intracellular fluid and maintains the cell volume, ensuring normal physiologic function, Regulation of extracellular sodium ion concentration controls the distribution of water between extracellular fluid and intracellular fluid and maintains the cell volume, ensures normal physiologic function. [12] Estrogen dominance alters the normal physiologic condition and allows the influx of water and sodium into cells and increases ICW volume.

Many clinical studies of biological signals reveal correlation between the effect of estrogen, progesterone and brain signals. Present study is design to examine whether the ovulatory cycle is associated body hydration and is there any correlation of body hydration with EEG pattern.

2. Materials and Methods

All subjects were recruited voluntarily from Shobhit University, Meerut. Written informed consent was obtained from all individuals who agreed to participate. Females between the ages of 18-23 years of age with a consistent menstrual cycle and no missed cycles within the last twelve months were allowed to participate. Subjects were also required to be in good health with no known disease or disabilities and none of them were under any type of medication nor were taking or have taken oral contraceptives. Subjects were informed that the study would last approximately four to five weeks. Female students with a regular menstrual cycle (mean ± SD; age = 21 ± 1.56 yr, height = 160 ± 5.35 cm, body wt = 53 ± 5.95 kg, menstrual cycle = 25 ± 1.73 days), were taken for study EEG and body hydration over all the day at 15.00 hrs of menstrual cycle by MP36 and MFBIA respectively. All measurements were performed after the subjects had fasted for 8 hrs.

Estimation of Brain Signal using MP36: Data acquisition system (BIOPAC MP36, BIOPAC Systems, Inc., Goleta, California) was used to record EEG of women. The system records electrical signals from the heart, muscle, nerve, brain, eye, respiratory system, and tissue preparations [6]. Biopac MP36 is an integrated set of hardware and software for data acquisition and analysis; it includes data acquisition hardware with built-in universal amplifiers. The data acquisition system receives extremely small electrical signals in microvolt amplitudes and the hardware amplifies these signals, filters out unwanted electrical noise or interfering signals.

The Biopac disposable vinyl electrodes (EL 503) are placed on the FP1 and F3 region in the 10-20 International electrode system. The reference electrode is placed on the earlobe. The lead set SS2L connects the electrode to the Channel 1 (CH-1) of the MP36 system which is further connected to the computer via USB port. The CH-1 of the Biopac MP36 system is set up as 'Electroencephalogram (EEG), 0.5-35.0 Hz' mode. In this mode the gain of the amplifier is 25000. Two hardware filters, a 0.5 Hz high pass filter and a 1 kHz low pass filter, are used in this configuration. Also a digital low pass filter having 66.5 Hz cut-off and a 0.5 Q ratio is employed. This ensures the noise free picking up of EEG signals from the scalp electrodes. The sampling frequency is set at 200 samples per second. Channels 40, 41, 42 and 43 have been selected to acquire the alpha, beta, delta and theta wave.

Absolute power was obtained by averaging the frequency bins and quantified the value at following broad bands: delta (0.5 – 3.5 Hz), theta (3.5 – 8 Hz), alpha (8 – 13) Hz and beta (13 –30) Hz. (Dressler. O et al (2004)). We have used Fast Fourier Transform (FFT) to calculate the absolute power values of each band. [7-10, 18-21].

Estimation of Body Hydration Using BIA: The electrical impedance of the body is measured by introducing a small alternating electrical current into the body and measuring the potential difference that results. The impedance magnitude Z is the ratio of the magnitude of the potential difference to the magnitude

of the current. Body water compartments were estimated by multiple frequency bioelectrical impedance analyzers, made by the Bodystat, QuadScan 4000, British Isles. The device is quick in, easy, economical and non-invasive in working. The principle of measuring the flow of current through the body (impedance) is dependent on the frequency applied. The subjects were weighed in standardized light clothes and without shoes on a platform manual scale balance. BIA measurements were carried out with the subject lying in a supine position on a flat, nonconductive bed. Two electrodes were placed on the right wrist with one just proximal to the third metacarpo-phalangeal joint (positive) and one on the wrist next to the ulnar head (negative). Two electrodes were placed on the right ankle with one just proximal to the third metatarso-phalangeal joint (positive) and one between the medial and lateral malleoli (negative).

At low frequencies, the current cannot bridge the cellular membrane and will pass predominantly through the extra-cellular space. At higher frequencies penetration of the cell membrane occurs and the current is conducted by both the extra-cellular water (ECW) and intra-cellular water (ICW). By measuring the impedance at 5 kHz and 200 kHz and by applying predictive equations. It was possible to estimate both ECW and TBW (Total Body Water). ICW was calculated by subtracting the TBW with ECW.

Estimation of Estrogen and Progesterone: Plasma estrogen and progesterone were assayed at Biotechnology Lab, Shobhit University; samples from only 30 women were measured. The laboratory assayed the urine samples for 2- and 16a-hydroxyestrone and for creatinine. The ratio of 2-hydroxyestrone to 16a-hydroxyestrone was calculated.

Estradiol [22] and estrone [23] were assayed by organic extraction, celite chromatography and RIA. Reported values are corrected for procedural losses. This method is highly specific and is the 'gold standard' for estimating steroid levels in plasma. Estrone sulfate was assayed by RIA (of estrone) after initial extraction of estrone, enzyme hydrolysis, organic extraction, and separation by column chromatography [24]. Progesterone was assayed by RIA preceded by organic extraction [25]. Urine samples were assayed for 2-hydroxyestrone and 16ahydroxyestrone by means of a new ELISA procedure, as detailed elsewhere [26]. Because urine samples were not collected over a 24-h period and total urinary output was unknown, creatinine levels were measured for each sample with a Beckman manual creatinine analyzer. All of the urinary metabolite levels are thus presented as standardized values (estrogen metabolite value divided by creatinine level in each sample) to account for differences arising from variations in urine concentration.

Statistical analysis: Averaging the frequency bins and quantified the value at following bands: delta (0.5 – 3.5 Hz), theta (3.5 – 8 Hz), alpha (8 – 13) Hz and beta (13 –30) Hz. Fast Fourier Transform (FFT) was used to calculate the absolute power values by averaging the frequency bins of each band. [6-10,18-21]. Reproducibility in data related to hydration and hormonal level is calculated by dividing the between-person variance by the sum of the between-person and within-person variances [2]. Comparison of two groups was performed by using one-way ANOVA followed by post hoc analysis by Bonferroni test. P values less than 0.05 were accepted as significant.

3. Results

Brain signal during menstrual cycle: The variation in the power of EEG signal was observed across the 28 days of menstrual cycle. I was found that the Delta wave was depress at 7th day have power 326.5±12.981 while at 9th day it was having highest power 392.6±9.738. Theta wave has highest power 372.3±10.453 at 20th but at the 21st day it will depress rapidly with power 308.2±6.374. During the menstrual phase alpha wave has higher power then others and it will depress at 5th and 21st day have power 264.7±2.638 and 284.9±5.67. Beta wave has smallest depression at 7th day with power 142.5±3.478 and has highest power 186.5±6.289 at 24th day of menstrual cycle. During the ovulatory period all the waveforms will depress (Figure 1).

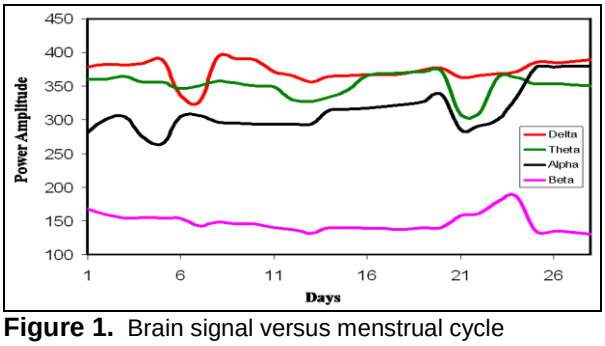

Figure 1. Brain signal versus menstrual cycle

Impedance at different frequencies during menstrual cycle: Impedance at 5 KHz has higher amplitude during the menstrual and postmenstrual cycle than the premenstrual cycle. Impedance at 50 KHz has varying amplitude throughout the menstrual cycle while impedance at 100 KHz has highest amplitude 1300±20.2 Ohm at 4th day of menstrual cycle.

Impedance at 200 KHz frequency has higher amplitude during the postmenstrual cycle than premenstrual cycle. During the ovulatory period impedance at all four 5, 50, 100 and 200 KHz is dipressed (Figure 2).

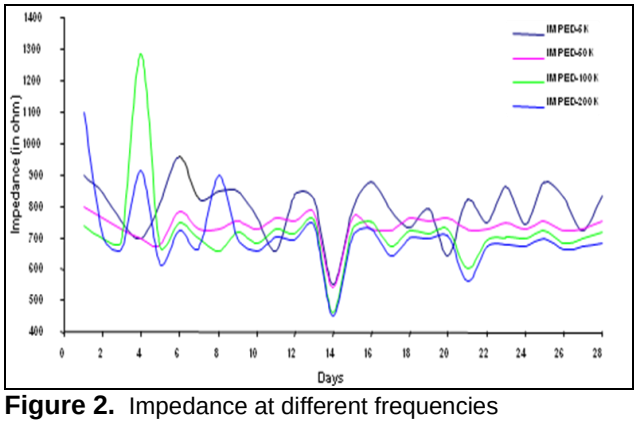

Figure 2. Impedance at different frequencies

ECW, ICW, and TBW during menstrual cycle: Intracellular water is in highest amount 13.9±0.002 at 5th day of menstrual cycle and lowest concentration 6±0.005 at 20th day of menstrual cycle. Extracellular water has higher concentration during the premenstrual cycle while lower concentration during the postmenstrual cycle. ECW have highest concentration 18.5±3.68 at 20th day of menstrual cycle and lowest concentration 9.8±0.001 at the 4th day of menstrual cycle. TBW has variation throughout the menstrual cycle .During the ovulatory period at 14th day there will be relative decrease in the concentration of the ECW, ICW, and TBW (Figure 3).

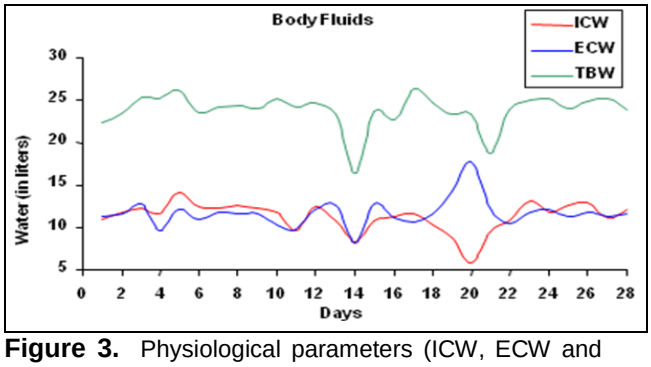

Figure 3. Physiological parameters (ICW, ECW and TBW) across the menstrual cycle

Estrogen and progesterone hormone versus menstrual cycle: Estrogen hormone have higher concentration during the menstrual and post menstrual period while progesterone have higher concentration during the pre menstrual cycle. The concentration of Estrogen was found highest 170±10.872 at 12th day while progesterone was at 22nd 13± 0.02 day of the menstrual cycle (Figure 4).

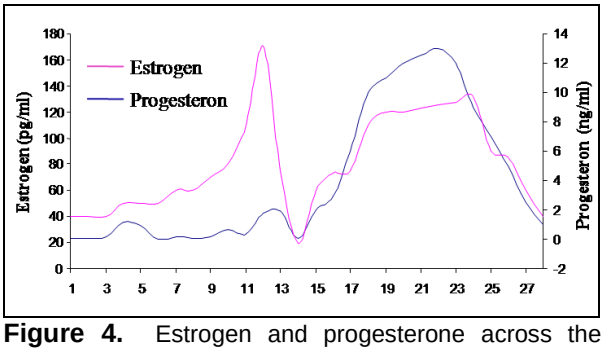

Figure 4. Estrogen and progesterone across the menstrual cycle

Comparing each brain signal and body hydration with both the sex hormone we found a correlation between the EEG wave forms, hydration status and the hormonal level. Progesterone seems to be in phase with alpha followed by the delta and theta while beta goes oppositely. Delta and theta seems to be in phase with estrogen while oppositely with alpha.

4. Discussion

Mood, cognition and social behavior may fluctuate during the phases of menstrual cycle. Many research characterized the variation in physical, physiological and behavioral symptoms occurring up to 14 days period to menses and dissipating soon after the menstrual period Greene and Dalton (1953) to describe the psychological and physical symptoms which regularly occur during the luteal phase (days 15 to 28 of a 28-day cycle) of the menstrual cycle. It is characterized by serious emotional symptoms such as depressed mood, self-deprecating thoughts, marked anxiety and tension, affective liability (suddenly feeling sad or tearful), anger and irritability, difficulties in concentration, lack of interest in activities, lethargy, sleep disturbances, a sense of being overwhelmed, and suicidal ideation, anxiety, aggression, avoidance of social activity, breast pain and bloating.

The absolute power of EEG profile of women with normal menstrual cycle [21, 28] and variation in estrogen and progesterone have also been previously studied. The study shows that, in premenstrual period progesterone is relatively higher as compared to estrogen and alpha signal seems to be dominant followed by the delta and theta, during the menstrual period the progesterone is considerably high and Delta seems to be dominant followed by Alpha and Theta and in Post menstrual, the progesterone goes high and

estrogen is relatively low and Alpha is prominent followed by Delta and Theta. Studies of brain signal associate the hormonal variation with functional abilities [5, 29]. Theta oscillations are involved with perceptual and memory encoding processing, verbal and nonverbal task [30] and it is also related to women anxiety [31]. Alpha oscillations have been observed in memory processes and mental relaxation [22] and Delta and Beta oscillations are observed in attention [23]. Several studies have also reported the possible relation of the different brain signal with the sex hormones. The release of the estrogen and progesterone hormones is divided into three phases that is premenstrual, menstrual and postmenstrual states. The frequency patterns of the brain signal and hormones are showing the correlation.

Fluctuation of steroid hormone is accompanied with the behavioral change in the menstrual cycle. [32] Biological signals reveal correlation between the effect of estrogen, progesterone and brain signals captured in the form of Alpha, Beta, Theta and Delta by Electro Encephalography (EEG) recordings. [24] EEG waveforms are generally classified according to their frequency, amplitude, and shape, as well as the sites on the scalp at which they are recorded. The most familiar classification uses EEG waveform frequency (e.g., alpha, beta, theta and delta).Comparing each brain signal with both sex hormones signals, we found a characteristic profile of coincident periods and typical relative phases. For the corresponding coincident periods the progesterone is in phase with theta, alpha, while delta and beta is out phase, whereas the estrogen is in phase with delta and theta and show opposite phase with alpha.

Result of present study shows that ovulatory cycle is associated body hydration and there is a correlation of body hydration with EEG pattern. Leutal phase (Premenstrual phase) progesterone is relatively higher as compared to estrogen. Dominance of the progesterone hormone increases the concentration of the ECW that shows the impedance at 5 KHz is relatively low during this period and there is a relative increase in the concentration of ECW and alpha signal seems to be dominant followed by the delta while theta while beta goes oppositely.

Follicular phase (post menstrual period) estrogen hormone has higher concentration as compared to the progesterone and delta and theta seems to be in phase with estrogen while oppositely with alpha and estrogen also increases the influx of the sodium ion inside the cell that causes the higher amount of ICW.

Menstrual phase as estrogen have its higher concentration so delta will dominate followed by theta and beta while alpha will decreases relatively. During the ovulatory period with the depression in the level of estrogen and progesterone there will be a relative decrease in the power of EEG signal and water concentration also.

Comparing each brain signal and hydration level with both the sex hormone we found a correlation between the EEG wave forms, hydration status and the hormonal level. Progesterone seems to be in phase with alpha followed by the delta and theta while beta was out phase. Delta and theta seems to be in phase with estrogen and alpha was out of phase .

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