Effects of Hormonal changes on Temporal Perception and Speech Perception in Noise in Females

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13AUD029

A Dissertation submitted as part fulfillment
for the Degree of Master of Science (Audiology)
University of Mysore

ALL INDIA INSTITUTE OF SPEECH AND HEARING

MANASAGANGOTHRI, MYSORE - 570006

May, 2015

CERTIFICATE

This is to certify that this dissertation entitled **"Effects of Hormonal changes on Temporal Perception and Speech Perception in Noise in Females"** is the bonafide work submitted in part fulfillment for the degree of Master of Science (Audiology) of the student (Registration number 13AUD029). This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This is certifying that dissertation entitled **"Effects of Hormonal changes on Temporal Perception and Speech Perception in Noise in Females"** is the result of my own study under the guidance of Mrs. Chandni Jain, Lecturer of Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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May, 2015

Dedicated To

Beloved Mummi-Papa

Di -Jiju

Bhaiya

&

My Guide

Acknowledgments

Dear ***Mummi-Papa*** today I want to say thank you for your's endless loving support. My dear brother, thanks for being my perfect ***Bhaiya*** and also ***Di-Jiju*** for your loving care and sharing knowledge which makes possible to complete this dissertation. *I love u all…………..*

I want to express my sincerely thank to my guide **Mrs. Chandni Jain** for her guidance, knowledge, motivation, positive inspiration, strong supports & friendly nature from selection of topic throughout the end of study. Mam, you helped me immediately whenever I need, showed me right path and relief me from dissertation tension. Mam, I just have heartful thanks to say, for being my guide, your's efforts and expending your precious time for complete my dissertation in your busy working schedules. Thanks to you once again mam for enable me for this position and blossom my carrier. Mam, please apologize me for my mistakes.

I sincerely thank to our director **Dr. S.R. Savithri**, AIISH, Mysore for giving me opportunity for successful completion of this study.

I would like to thank **Mr. Sarath Kumar** sir for calibrate my instrument and **Dr. Ajith Kumar U.** sir and **Dr. Vijay Kumar Narne** for provided guidance about rules of dissertation writing and use of needed software. Thank you, sir.

I would like to thank **Dr. Vasantlaxmi** mam for helping me for statistical analysis of my collected data of this study. Thank you, mam.

I am heartfully thankful to **Usha Shastri** mam and **Reeny Roy** di for her friendly supports.

I am also thankful to awsome special friends ***Vaishnavi, Zeena, Priyanka, Vinodini, Swati, Rohan, Padma, Somya, Sneha, Vinitha, Ayesha, Preeta, Supreeth*** *and* ***Himanshu*** for being my wonderful friends for make this journey beautiful. It is impossible to forget and harder to leave for me. *Miss you all our fun together*…………

Piyu, **Vasu** and **Vinodini -** Thank you for special care for eating food and provided needed supports. Thank you so much *Vaishnavi* and *Priyanka* for being with me during my hard time. *Miss all of you so much…….*

Vaishnavi and Zeena - My special thanks to both of you for searching participants for me. *Thank you once again my dear.*

I would like to thank ***Devdutta sir, Preeti mam*** & ***Dr. Versa*** mam for your educational guidance and supports.

From my depth of heart, I am thankful to all my ***participants***, for expending your unique time for me. Thanks all of you.

Finally, I want to thank all our respected excellent ***staffs,*** respected ***seniors*** *and* dear ***juniors*** and all my ***classmates.***

Abstract

The menstrual cycle is a cyclic fluctuation of ovarian hormonal level in females. Studies have shown that changes in gonadal steroids (estrogen and progesterone) can affect auditory abilities. However, there are lack of studies on the effect of these hormones on temporal perception and speech perception in noise. Therefore, the aim of the current study was to assess the effect of hormonal changes on temporal processing and speech perception in noise in females (across three phases of the menstrual cycle). A total of 20 female participants with an average 28 days of regular menstrual cycle in the age range of 19-24 years were included in this study. Temporal abilities were assessed using gap detection test and modulation detection test and speech perception in noise was assessed through Quick-SIN in Kannada. All the participants were tested three times during a single menstrual cycle i.e., menstrual phase (cycle days of 1-5 days), ovulation phase (cycle days of 12-15 days) and luteal phase (cycle of 18-25 days). The results showed poorest gap detection and modulation detection threshold during the menstrual phase followed by luteal phase and significant better thresholds were obtained during the ovulation phase. Speech perception in noise test also showed a significant better threshold during ovulation and luteal phase compared to menstrual phase. To conclude, hormonal fluctuation affects temporal perception and speech perception in noise across the menstrual cycle and better thresholds were noted during the ovulation phase. Further, the present study highlights the importance of considering the different phases of menstrual phase while studying the female participants.

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Chapter 1

Introduction

Hormones are chemical messengers that are produced in one part of the body, travel through the blood stream, and affect other parts of the body in both males and females. Estrogens and progesterone are female's ovarian hormones and testosterone is a male hormone. In females, hormonal fluctuations of these ovarian hormones occur during the menstrual cycle (Farage, et al., 2008).

The menstrual cycle is a periodic virginal bleeding cycle of physiological changes that occurs in females. There are three phases in 28 days of menstrual cycle, i.e. follicular phase or menstrual phase (cycle of 1-5 days, with lowest estrogen and progesterone), ovulation or mid cycle phase (cycle of 12-15 days, with high estrogen and low progesterone) and luteal phase (cycle of 18-25 days, with moderately high estrogen and high progesterone) (Elliott-Sale & Martin, 2013). During the first half of 28 days cycle, the follicles grow and mature under the dominant influence of follicle stimulation hormone and some luteinizing hormones thus is termed as the follicular phase. Early in this phase, follicular estrogen secretion is low, but towards the middle of the cycle, there is a burst of estrogens from the dominant follicle which is called ovulation phase. After ovulation, corpus- luteum is formed, causing progesterone hormone to dominate over estrogen. This final level of the menstrual cycle is called the luteal phase. Afterwards falling levels of progesterone triggers the next menstrual cycle (Ferin, Jewelewicz, & Warren, 1993; Franz, 1988). So, there are changes in estrogen and progesterone concentration in each stage of the menstrual cycle within females.

These hormones play important role in numerous physiological functions like estrogen regulates or directly alters auditory processing of acoustic signals in the brain (Remage-Healey, 2012; Tabuchi et al., 2011; Tremere, Jeong & Pinaud, 2009; Yoder & Vicario, 2012), interprets auditory information, enhances the representation of sounds in auditory cortex (Remage-Healey, 2012) which is transmitted to sensory-motor parts of the brain (McCarthy, 2008; Mcewen, 2002). It also affects neurotransmission, cellular processes, neural plasticity and biochemistry in the brain (Gawali, Rokade, Janvale & Mehrotra, 2009). Neuroimaging F-MRI studies also support for structural changes that alters brain volume during the menstrual cycle. During the ovulation phase, there are significant changes in blood-oxygen-level-dependent (BOLD) responses in gray matter and CSF volume in females (Hagemann, 2011). Transcranial magnetic stimulation also supports above findings and suggests that there is more central inhibition with high progesterone level (luteal phase) than low progesterone level (follicular phase) (Smith et al., 1999).

Estrogens and progesterone can also alter neuronal functioning through receptors distributed throughout the different parts of the central nervous system and by influencing different neurotransmitter systems. Studies have shown that there are significant changes in latencies of various auditory evoked potentials during menstrual cycle, indicating changes at the level of the central auditory pathway (Mann, Singh, Sidhu & Babbar, 2012; Natarajan, Dharshni, Ukkirapandian & Lakshmi, 2014; Walpurgera, Pietrowskyb, Kirschbaumc & Wolf, 2004; Yadav, Tandon, & Vancy, 2002;). The Excitatory nature of estrogen makes the auditory system sensitive and it becomes more sensitive when estrogen circulation is in highest peak in ovulation phase (Al-Mana, Ceranic, Djahanbakhch & Luxon, 2008).

Psychoacoustics studies have also shown fluctuations in various parameters during menstrual cycle. A study done to assess perception of binaural beats showed that the perception was best during the mid phase of menstrual cycle compared to other phases. In the same study auditory perception was also assessed using octave matching task, click lateralization task and frequency just noticeable difference (JND) task. Results showed that for octave matching task and click lateralization task, there was significant changes across the menstrual cycle and better performance was noted post-period. The reason for the same was speculated to the biochemical changes that occur during normal cyclic hormonal fluctuations which results in auditory acuity changes during menstrual cycle. The changes in synchronous neural firing affect temporal coding, pitch extraction and conduction velocity of processing auditory information. This could be due to the alteration in sodium and potassium metabolism, which is important for axonal conduction and synaptic transmission results (Haggard & Gaston, 1978).

Temporal processing is an important auditory skill that is necessary for the complex auditory task necessary for higher level auditory processing. Effect of ovarian hormones on temporal processing, by itself has not been studied; however, estrogen levels in brain regions have shown to have influence on auditory processing. The neuromodulatoy action of estrogen modulates neural coding of acoustic signals and cortical plasticity, so the auditory processing area of brain cell becomes sensitive to encode acoustic feature of sound. In a study, auditory perception abilities declined in zebrafish when the action of estrogen was blocked through injecting the auditory cortex. (Remage- Healey, 2012). It was also reported that increased amount of estrogen causes the brain cells to identify more subtle sound components and strengthens the auditory encoding, so auditory perception became better (Remage-

Healey, Coleman, Oyama & Schlinger, 2010). Similar results were also seen in the duration discrimination task, where thresholds improve after estrogen injection (Pleil, Cordes, Meck & Williams, 2011).

Ovarian hormone has shown to have an influence on speech perception in noise also. It is reported that progesterone interferes more in the perception of speech in background noise**.** In a study, hearing in noise test (HINT) was done among post-menopause women, those taking estrogen plus progestin, those taking estrogen alone, and those not taking any hormones. Results showed that women taking both estrogen and progestin had a poorer speech perception in background noise than women in the other two groups. This finding suggests that increased estrogen shows benefit on speech recognition in noise and increase progesterone, show opposite effects (Guimaraes et al., 2006).

Speech perception is lateralized to the left hemisphere (Hugdahl & Westerhausen, 2010) and high level of ovarian hormone during menstrual cycle increases the coherence of speech perception and production within the dominant left hemisphere (Wadnerkar, Cowell & Whiteside, 2006; Wadnerkar, Whiteside & Cowell, 2008). High-estrogen phases of the menstrual cycle is associated with enhanced left-hemisphere processing (greater right ear advantages) and low-estrogen phases are associated with better right-hemisphere processing, thus showing cerebral asymmetry during menstrual cycle in young healthy women. This supports a role of ovarian hormones in shaping hemispheric laterality of speech perception (Cowell, Ledger, Wadnerkar, Skilling & Whiteside, 2011; Wadnerkar, Whiteside & Cowell, 2008) and changes in perceptual asymmetry for dichotic consonant-vowel (CV) listening in women within the menstrual cycle (Altemus, Wexler, & Boulis, 1989). The efferent auditory pathway is a feedback mechanism of auditory system which also plays an important role in speech perception in noise. Studies have shown that blockage of estrogen increases contralateral suppression of DPOAE affecting the auditory integrity (Thompson, Xiaoxia & Frisina, 2006). Thus, hormonal fluctuations during the menstrual cycle in healthy females affect Neuro-anatomy as well as neurophysiology of peripheral and central auditory nervous system which results in changes in auditory behavior.

1.1.Need for the Study

Studies have shown that hearing sensitivity in women is poorest during menses, (McFadden, 1998) and as reported in the literature ovarian hormones have an influence on central auditory processing also (Remage-Healey, 2012; Tabuchi et al., 2011; Tremere, Jeong & Pinaud, 2009; Yoder & Vicario, 2012). However, there are lack of studies on the effect of these hormones on temporal perception and speech perception in noise. Studies done on animals have shown that estrogens enhance auditory perception and helps in subtle sound perception, but there are no studies to compare the effects of these hormones on temporal perception abilities in humans. Speech perception in noise has been studied in females taking hormones; however, whether the speech perception abilities changes during the different phases of the menstrual cycle has not been studied. Thus, this study is designed to study the effect of ovarian hormones on temporal processing and speech perception in noise in females with normal hearing sensitivity across three phases of the menstrual cycle.

1.2.Aim of the Study

To assess the effects of hormonal changes on temporal perception and speech perception in noise in females across three phases of the menstrual cycle (average 28 days of normal menstrual cycle).

1.3.Objectives of the Study

1) To compare gap detection thresholds (GDT) in white noise across three phases of the menstrual cycle in females.
2) To compare, modulation detection thresholds (MDT) across three phases of the menstrual cycle in females.
3) To compare speech perception in noise (SPIN) across three phases of the menstrual cycle in females.

1.4.Hypothesis

Null hypothesis were assumed for the present study stating:-

1) There is no significant difference in GDT across three phases of the menstrual cycle.
2) There is no significant difference in MDT across three phases of the menstrual cycle.
3) There is no significant difference in SPIN across three phases of the menstrual cycle.

Chapter 2

Literature Review

The menstrual cycle is a cyclic fluctuation of ovarian hormonal level in every female. Typically, single regular menstrual cycle is of average 28 days (27- 31 days) in length (Cox, 1980). Hormonal relationship is maintained between hypothalamus, pituitary gland, ovaries and reproductive tract, resulting in a regular normal menstrual cycle. The hypothalamus secretes gonadotropin-releasing hormone (GnRH) which stimulates the pituitary gland to secrete follicle stimulating hormone (FSH) and luteinizing hormone (LH). FSH results in maturation of follicles and results in secretion of higher level of estrogen resulting in ovulation. After ovulation, LH rupturing follicle called corpus luteum releases higher level of progesterone. So depending on the changing concentration level of hormones with timing, menstrual cycle is divided into three phase, i.e. menstrual phase, ovulation phase and luteal phase. Thus, sequential changes in the ovaries and mucous uterus wall results in varying estrogen and progesterone output level during menstrual cycle in females (Elliott-Sale & Martin, 2013).

2.1.Different phases of menstrual cycle

2.1.1. *Menstrual /Follicular Phase (1-5 days of cycle)*

Menstrual phase is the first stage of the menstrual cycle, which starts from the first day of bleeding and lasts for around 4 -5 days. During this phase, production of GnRH from hypothalamus results in production of FSH through pituitary gland which stimulates egg to grow in the ovaries called follicle. In this phase, lower concentration of both estrogen and progesterone are seen and gradually there is an increase level of estrogen which leads to preparation of ovulation.

2.1.2. *Ovulation / Midcycle Phase (12-15 days of the cycle)*

It is the second phase of the menstrual cycle, which is around 12-15 days in length starting from the first day of menstrual phase. As the follicles mature, the level of estrogen also increases, thus when follicles are completely matured, concentration of estrogen reaches its peak level. In this phase higher FSH and LH are secreted from the anterior pituitary gland and LH surge causes dominant follicle rupture, which results in release of mature egg from the ovary in around 14 days from the beginning of the menstrual cycle and this phase is called ovulation phase. After ovulation, the released egg enters into the Fallopian tube and there is a decline of FSH and LH hormone levels. In this phase higher levels of estrogen and lower levels of progesterone are seen.

2.1.3. *Luteal Phase (18-25 days of cycle)*

It is the last stage of regular menstrual cycle, which starts after the end of ovulation till the starting of the next menstrual cycle. In this phase, there is a formation of corpus luteum, which produces a significant amount of hormones, particularly progesterone and to a lesser extent estrogen. Thus, within 18-25 days, higher progesterone and moderately high estrogen levels are seen. After 25 days of menstrual phase, estrogen and progesterone levels gradually decline and FSH gradually increases. This drop in estrogen and progesterone triggers the end of the luteal phase and leads to the beginning of the next menstrual cycle.

As there are hormonal fluctuations occurring during the menstrual cycle, studies have been done to see the effect of these fluctuations on various aspects such as cognition, hearing, auditory processing etc.

2.2.Effects of hormonal changes on hearing abilities

2.2.1. *Pure tone audiometry (PTA)*

Effects of hormones on hearing abilities have been assessed using PTA. Baker and Weiler (1977) reported better hearing threshold from 250Hz to 8000Hz during first half of the menstrual cycle compared to second half of the menstrual cycle. Davis and Ahroon (1982) support these findings and reported a fluctuation of around 1.6 to 6.8 dB across different phases of the menstrual cycle. In the same study, they even noticed the poor recovery rate of temporary threshold shift post 115 dB (A) white noise exposure for 10 min during the menstrual phase. Swanson and Dengerink (1988) also reported poor hearing threshold at 4000Hz during the menstrual phase compared to ovulation and luteal phase. This could be because lower estrogen and progesterone levels lead to reduced blood supply in the cochlea (Laugel, Dengerink; & Wright, 1987) mainly at 4000 Hz region of the cochlea (Crow, Guild, & Polvogot, 1934).

Petiot and Parrot (1984) also reported, poorer hearing sensitivity during the menstrual phase compared to post-ovulatory phase in normal menstrual cyclic females. In another study, Rakhi (2003) reported poor hearing threshold at 4000Hz and better hearing threshold at 500Hz, 1000Hz, 2000Hz and 8000Hz during menstrual cycle compared to midcycle and luteal phase. It can be concluded that hormonal fluctuation changes, biochemical and metabolic activity of the organ of Corti and also alter the auditory nerve function and thus hearing sensitivity changes across different phases of the normal menstrual cycle in females.

2.2.2. *Immittance*

Tympanometry: Cox (1980) measured middle ear pressure across three phases of two consecutive menstrual cycles. He reported higher middle ear pressure during initial three to four days of menstrual phase. It was concluded that interstitial fluids which alter Eustachian tube functioning results in variation of middle ear pressure. However, Swagatika (2010) in her study did not found any significant tympanometic peak pressure differences across three phases of the menstrual cycle in females. But, higher static compliance was obtained during the luteal phase than menstrual and midcycle phase (Rakhi, 2003; Swagatika, 2010).

Acoustic reflex thresholds: Laws and Moon (1986) reported changes in acoustic reflex threshold (ART) due to fluctuating hormonal concentration during each phase of the menstrual cycle. They reported that, 6dB extra intensity is required for broadband noise to elicit ART during the menstrual phase compared to ovulation and luteal phase. This may be due to auditory sensory-neural level changes occurring during menstrual cycle. Swagatika (2010) assessed ipsilateral ART at 500Hz, 1000Hz, 2000Hz and 4000Hz across three phases of the menstrual cycle. The results showed lowest ART during the menstrual phase except for 4000Hz and highest during the luteal phase. The reason attributed to this was that estrogen can influence the release of GABA inhibitory neurotransmitters which can affect the electro motility function of outer hair cells (OHC) and thus resulting in slightly greater acoustic reflex threshold during midcycle. Poor acoustic reflex thresholds at 4000Hz during the menstrual cycle may be due to reduced blood supply (Crow, Guild & Polvogot, 1934).

It was also reported in the same study that hormonal fluctuation easily affects the ipsilateral acoustic reflex pathway than contralateral acoustic reflex pathway which could be attributed to the stronger contralateral acoustic reflex pathway. To conclude, hormonal fluctuation during normal menstrual cycle shows influence on both tympanometry and ART.

2.2.3. *Oto-acoustic emissions (OAE)*

Haggerty, Lusted and Morton (1993) recorded spontaneous oto-acoustic emissions (SOAE) daily, weekly and monthly in males and across regular menstrual cycle in females. The result showed significant SOAE amplitude fluctuations in females and not in males. This could be due to hormonal fluctuation in females. However, hormonal fluctuation during menstrual cycle does not show any influence on the transient and distortion product otoacoustic emission (Arruda & Silva, 2008; Yellin & Stillman, 1998).

Al-Mana et al. (2010) recorded SOAE, transient otoacoustic emission (TEOAE) and contralateral suppression of OAE during menstrual cycle in females. Greatest SOAE frequency shift and higher TEOAE amplitude level were noted during late follicular/ovulation phase. Higher medial olivocochlear (MOC) suppression of OAEs was seen during menstrual cycle compared to ovulation and luteal phase. This could be due to the lower estrogen level during menstrual cycle, which results in greater suppression of oto-acoustic emission leading to reduction in OAE. The medical olivococohlear bundle is also responsible for improved hearing sensitivity during the ovulation phase. It may be due to the excitatory efferent activity of estrogen, which enhances response to transient stimuli in noisy condition (Kawase et al., 1993). However, Rakhi (2003) found better signal to noise ratio (SNR) values during the menstrual phase compared to midcycle and luteal phase. The reason reported was a larger release of GABA neurotransmitter which inhibits outer hair cell functioning resulting in reduction of DP & TE oto-acoustic emission amplitude during midcycle and luteal phase. Thus, it may be concluded that ovarian hormones affects cochlear blood supply (Laugel et al., 1987), metabolic activity and electrolytic balance of the cochlear fluids (Lee & Marcus, 2001) and thus resulting in altered amplitude of otoacoustic emission and auditory efferent pathway functioning mechanism during normal menstrual cycle in females.

2.2.4. *Electrophysiological tests*

Auditory Brainstem Response. Electrophysiological studies also showed changes during the regular menstrual cycle in females. Auditory brainstem response (ABR) for click stimuli during four phases of menstrual cycle i.e. menstrual phase, midcycle/ovulation phase, mid-luteal and premenstrual / late luteal phase showed increased absolute latency for wave III and V and also increased I-V interpeak latency during midcycle phase. Smallest latencies were noted during the luteal phase of menstrual cycle, indicating that higher progesterone level results in faster central neural conduction. However, there were no changes noted for wave Ist peak latency. These findings suggest that effects of hormones fluctuation are more pronounced in the rostral brain side of the central auditory neural pathway than peripheral auditory neural pathway (Elkind-Hirsch, Stoner, Stach, & Jerger 1992; Yadav, Tandon & Vaney 2002). The longer wave V peak latency may be due to greater release of GABA inhibitory neurotransmitter during the late follicular phase when the estrogen level is higher which inhibits auditory nerve and thus resulting in slower transmission of auditory information (Disney & Calford, 2001; Majewska et al., 1986).

Al-Mana et al. (2010) also reported shorter wave Vth peak latency, wave III-V and V-I interpeak latency during the luteal phase compared to follicular phase in normal menstrual cycle of females. They concluded that higher estrogen level may excite auditory nerve and would change neural conduction time for transmission of auditory information through the brainstem. However, Rakhi (2003) reported slightly delayed wave III and V peak latencies during the luteal phase compared to menstrual phase, but did not find any significant differences for V peak latency across all phases of the menstrual cycle. This could be because Na+ and K+ metabolism change axonal conduction time during the menstrual cycle (Haggard & Gaston, 1978). It is also reported that absolute auditory brainstem response latencies delays at higher peak of estrogen level (midcycle phase) is seen compared to menstrual phase and shortest latencies during luteal phase, but no significant differences for interpeak latencies across different phases of regular menstrual cycle in females (Kaur, Bansal, Manchanda & Maheshwari, 2013; Natarajan, 2014). Upadhayay, Paudel, Singh and Bhattarai (2014) measured auditory brainstem response during the pre-ovulatory and post-ovulatory phases. They found shorter Vth peak wave latencies and interpeak latencies (III-V & I-V) during the post-ovulatory phase (higher progesterone level) than compare to pre-ovulatory phase. It may be due to higher progesterone levels, which modulates central auditory pathway at the level of the brainstem as reported.

Middle Latency Response. Yadav, Tandon and Vaney (2002) measured middle latency responses (MLR) by using click stimuli across four different phases of the menstrual cycle. They found all the MLR peak latencies were shorter during luteal phase and delayed during midcycle phase. It was hypothesized that higher estrogen level may decrease acetylcholine release in the central auditory pathway causing delayed central conduction time resulting in delayed latencies during midcycle.

Late Latency Response. Yadav, Tandon and Vaney (2003) measured late latency response (LLR) by using click stimuli during four phases of the single menstrual cycle. They found significant delayed N1 and P2 peak latencies during midcycle and relatively better during the midluteal phase. It was concluded that Estrogen may be influencing GABA release at the level of auditory association areas, resulting in delayed central axonal conduction time.

Walpurger et al. (2004) measured early and late auditory event-related potential using tones during three phases (menstrual, follicular and luteal phases) of the normal menstrual cycle. They did not find any significant differences in amplitude and latency of early stages of auditory information processing component, i.e. N1 and P2 across different phases of the menstrual cycle. However, in late ERP components N2 latency was shorter during the menstrual phase compared to other phases. These findings suggest that cortical arousal responses to deviant stimuli were reduced during luteal phase, which may be due to Neuro-inhibitory action of higher progesterone.

To conclude from above review studies, there is no clear agreement among several studies, but it is evident from all the studies that hormonal fluctuation during the regular menstrual cycle influences brainstem structures as well as cortical auditory processing. Effects of hormonal changes were more in the central auditory neural pathway compared to peripheral auditory pathway. Also, estrogen and progesterone hormonal variation lead to changing central conduction time, which affects auditory processing (Elkind-Hirsch et al., 1992).

2.3. Role of ovarian hormone in auditory processing

Effect of ovarian hormones by itself on auditory processing has not been studied; however, estrogen levels in brain regions influence auditory processing. Auditory processing includes processing of various skills such as auditory closure, binaural integration, binaural interaction and temporal processing.

2.3.1. *Temporal Processing*

Temporal processing is an important auditory skill that is necessary for the complex auditory task necessary for higher level auditory processing. Haggard and Gaston (1978) studied auditory perception during pre-period (6 to 9 days before the start of the ovarian cycle), period (two days before and after menstrual cycle), post-period (six to nine days after the onset of menstrual phase) and mid-cycle (12 to 15 days after the onset of menstrual phase) in females.

In this study 704 Hz and 701 Hz continuous tone was mixed together for tone modulation and stimulus was presented in three conditions i.e. without beats, very faint beats and beats. The Psychoacoustic beat detection task was given to the participants and results showed better beat detection during the mid - phase of menstrual cycle compared to other phases. It was also reported that beat perception threshold varies during the menstrual cycle and the highest score was seen during initial two days of the menstrual cycle in females (Haggard, & Gaston, 1978). In the same study, auditory perception changes for the octave matching task, click lateralization task and just noticeable differences in frequencies was assessed across the four cycles in females. For octave matching task 203/406 Hz and 1.53 / 3.06 Hz pair frequency was taken. There were significant differences in octave matching task across the menstrual cycle seen for both the frequency stimulus and more accuracy was noted during the period (two days before and after onset of the cycle) and also better accuracy was seen during mid-cycle phase than the pre - period phase of hormonal fluctuation cycle. The same results were also noted for click lateralization task with interaural time delays of 100 microsec. For just notificable difference task better score was noted during the mid - phase of cycle for 7000Hz but it did not show any significant difference across the menstrual cycle for frequencies 206 Hz, 3000Hz and 7000Hz.

In another study, it was reported that estrogen enhances central auditory processing of complex sound in songbirds. Estrogen is a neuorosteroid hormone which changes synaptic connection, biochemical reaction, releases neurotransmitter, synaptic enzyme action, neural conduction time, dendritic potential and central auditory circuits for processing auditory information. Estrogen is excitatory in nature which excites auditory nerve and cortical circuits for auditory processing. Higher estrogen level at the cortical level leads to rapid neural firing (spike) for complex auditory stimuli resulting in rapid encoding and increased frequency selectivity (fine tuning), which lead to better perception of song in songbirds. It was also reported that injecting estrogen suppression injection in left hemisphere disturbs rapid auditory neural firing (axonal conduction) and auditory cortex circuits so processing of auditory information and auditory perception of complex sound perception become poorer in songbirds. To conclude, estrogen shapes and enhances auditory recognition in songbirds (Remage-Healey, Jeon & Joshi, 2013).

Pleil et al. (2011) assessed duration discrimination test in female rats. Duration of tone was varied from 2sec to 8sec and results showed better duration discrimination scores after estrogen injection. It was hypothesized that acute estrogen level, increases dopamine release and also contributes to multiple cortical mechanism, which increases auditory processing for temporal perception.

Hagemann et al. (2011) reported alteration of brain structure during the regular menstrual cycle in females but not in males. Magnetic resonance imaging was done in females during menstrual phase, ovulation phase and mid-luteal phase and only one time in males. The results showed that gray matter and cerebro-spinal fluid volume changes across hormonal fluctuation for females during the regular menstrual cycle only but no such changes seen in males. The greatest change in gray matter volume is due to changes in progesterone level and changes are more significantly different during the ovulation phase. It was concluded that brain structure changes during menstrual cycle leading to multiple cortical functional changes.

Cibian and Pereira (2014) studied temporal resolution in female participants with menstrual migraine using gap in noise test during two distinct phases of menstrual cycle i.e. menstrual phase and luteal phase. The results showed poor gap detection threshold (mean threshold of 5 msec) during the menstrual phase for the left ear and significantly poorer gap detection threshold for females with the migraine group then compared to without menstrual migraine females group.

Thus, hormonal fluctuation during the regular menstrual cycle affects psychoacoustic performance. This may be due to various changes in biochemical synaptic transmission and metabolism (Na^+ and K^+) concentration which alters neurophysiological processes for acoustic stimuli. The changes in synchronous neural firing affect temporal coding, pitch extraction and conduction velocity of processing auditory information due to alteration in sodium and potassium metabolism, which are important for axonal conduction time and synaptic transmission (Haggard & Gaston, 1978).

2.3.2. *Speech Perception in Noise*

Ovarian hormones have shown to have an influence on speech perception in noise. Smith et al. (1999) studied hormonal fluctuation effects on cortical function. They measured transcranial magnetic stimulation (TMS) during the follicular phase and luteal phases of regular menstrual cycle in females. The results indicated more cortical inhibition during the luteal phase than follicular phase. It may be due to high estrogen action release of glutamate neurotransmitter which excites auditory neural circuits and high progesterone level lead to more releases of GABA which inhibits neural circuits of auditory cortex. It was concluded that fluctuating hormones during menstrual cycle changes in neural circuits of the brain, which may alter speech recognition, as speech is processed in auditory cortex.

It is also reported that progesterone interferes in the speech perception in the presence of background noise. Guimaraes et al., (2006) studied estrogen and progesterone hormonal therapy effects on hearing and speech perception in noise. In this study conventional pure tone audiometry, distortion product oto-acoustic emissions and hearing in noise test was done for each ear in three postmenopausal female groups. The groups consisted of those taking hormonal replacement therapy, i.e. estrogen treated group, estrogen and progesterone treated group and no hormonal therapy treated group. Results showed poorer scores on females with estrogen and progesterone treatment group compared to other groups. It was concluded that progesterone affects peripheral and central auditory system which leads to poorer hearing sensitivity and also a poorer speech perception in noise and quiet.

Gonadal steroid hormones are neuromodulators which alter Neuro-physiological processes of auditory nerve, i.e. synaptic connection, enzyme activity, neural plasticity, dendritic potential and Na+ and K+ biochemical ionic processes. This changes axonal conduction and action potential for temporal coding and processing of auditory information.

Chapter 3

Method

3.1.Research design

The time series design was used to fulfil the aim of the present study.

3.2.Participants

To fulfil the objectives of the study, 20 female participants with an average 28 days of regular menstrual cycle were taken. The age range of all female participants was 19-24 years (Mean age: 20.61 years, SD: 1.88).

3.2.1. *Participant selection criteria*

1) Regular menstrual cycle of 27 to 31 days of length (Cox, 1980).
2) No otological and medical history.
3) No history of use of steroids.
4) Normal hearing sensitivity (pure tone thresholds within 15dB at octave frequencies between 250Hz to 8000Hz. Speech recognition threshold of up to 25 dBHL, and speech identification of monosyllables of at least 88%).
5) All the subjects had "A" type tympanogram, with reflexes present.
6) No neurological abnormality as reported.
7) Females taking any hormonal pills were excluded from the study.
8) No lactation and no pregnancy during the last year.
9) No diagnosed premenstrual syndrome.
10) All the subjects were native speakers of Kannada language.

3.3.Test environment

All the basic experiments were conducted in an acoustically treated room where the noise levels were within permissible limits as per ANSI S3.1; (1991) standards. All the experimental testing was done in a quiet room.

3.4.Instrumentation

- A calibrated GSI-61 audiometer coupled with an acoustically matched headphone (TDH-39) and bone vibrator (Radio ear B-71) was utilized to estimate pure tone threshold, speech recognition threshold and speech identification score.
- A calibrated immittance meter GSI-33 /GSI-TYS (Version-2) middle ear analyzer was used for measuring tympanometry and acoustic reflex threshold.
- MATLAB Version R2010a software installed in a laptop (HP 2000) was used for performing temporal perception tests. Stimuli were presented via laptop (HP 2000) connected to PC310 headset. The headphone was calibrated at the beginning of the experiment to produce 80dBSPL output.

3.5.Procedure

Written consent was taken from all the subjects for willingly participating in the study.

3.5.1. *Case History*

To confirm the candidacy criteria all the subjects were assessed with a detailed case history like no otological and neurological complains and irregular pre or post menstrual complains (shorter or longer than average 28 days of the menstrual cycle) etc.

3.5.2. *Otoscopic Examination*

Otoscopy was done to assess for a clean ear canal and healthy tympanic membrane.

3.5.3. *Routine Audiological Evaluation*

Conventional puretone audiometry was done to estimate pure tone thresholds for each octave frequency ranging from 250Hz to 8000 Hz for air conduction and 2 dB step size was used at near threshold by using modified Hughson- Westlake procedure (Jerger and Carhart, 1959) in each ear. Average pure tone air-conduction threshold at 500Hz, 1000Hz, 2000Hz and 4000Hz was considered as a pure tone average threshold in each ear.

Speech audiometry i.e. Speech recognition threshold (SRT), speech discrimination score (SDS) was done for each participant. For SRT testing, spondee word lists in Kannada (Rajashekar, 1976) were used. Phonemically balanced monosyllable word lists (Yathiraj & Vijayalaxmi, 2005) were used for estimation of speech discrimination score in Kannada.

Tympanometry and reflexometry was performed using 226Hz probe tones bilaterally, and both ipsilateral and contralateral acoustic reflex thresholds at 500Hz, 1000Hz, 2000Hz and 4000Hz were measured. During immittance measurement subjects were instructed to sit comfortably, don’t swallow, don’t move the head, jaw and also don’t have to talk.

After routine audiological evaluation, temporal abilities were assessed through gap detection test (GDT) and temporal modulation detection test (MDT). Speech perception in noise was assessed through Quick – SIN in Kannada. All participants were tested three times during a single menstrual cycle i.e., follicular phase or menstrual phase (cycle days to 1-5 days, with lower estrogen and progesterone), ovulation or midcycle phase (cycle days of 12-15 days, with high estrogen and low progesterone) and the luteal phase or premenstrual phase (cycle days of 18-25 days, with moderately high estrogen and high progesterone).

3.5.4. *Temporal Tests*

Temporal perception tests (gap detection test and modulation detection test) were carried out by using Maximum Likelihood Procedure (MLP) toolbox, which implements an MLP in Matlab (Grassi & Soranzo, 2009). MLP stimuli were generated at 44,100 Hz sampling rate and three-interval, alternate forced-choice method was used to track threshold. A 79.4% correct response criterion of psychoacoustic function was used to track the threshold. 5-6 practice items were given for both the tests before the beginning of the actual test.

Gap Detection Threshold. The gap detection threshold was measured binaurally by asking the client to detect a variable temporal gap in the center of a 500 ms duration broadband noise. Broadband noise was used as stimulus as its spectrum does not change with the insertion of the gap (Moore, 2003). This noise had cosine rise and fall time of 0.5msec. Gap duration was varied according to listener's performance using maximum likehood procedure (MLP) and the participant's task was to identify which noise contained a gap.

Modulation Detection Threshold. The modulation detection threshold was estimated by presenting modulated and unmodulated stimuli binaurally. The participant's task was to identify which block had the modulated noise. A 500 ms duration and 10 msec cosine rise and fall time Gaussian noise which was sinusoidal amplitude modulated at modulation frequencies of 8 Hz, 20 Hz, 60 Hz and 200 Hz were used as stimuli

(Bacon & Viemeister, 1985). The modulation detection thresholds were expressed in dB by using the following formula:-

Modulation detection thresholds in dB = 20 log10 m.

Where;

m = modulation detection threshold in percentage.

3.5.5. *Speech Perception in Noise*

Speech perception in noise testing was done to measure understanding of 50 % of the words in sentences (SNR-50). Three equivalent sentence lists of Kannada Quick Speech in Noise test (Avinash, Methi, & Kumar, 2010) were used as stimuli. Each list contains 7 sentences and each sentence has five key words mixed with 8-talker speech babble noise at different signal to noise ratio (SNR). The SNR varied from +8 dB to -10 dB in 3 dB steps in each successive subtest in a list. Each sentence was presented binaurally through a laptop connected with calibrated headset (PC310). Before starting of the test, subjects were instructed to listen, and then repeat the presented sentence and 1 point was awarded for each correctly repeated keyword. The presentation of the list was randomized across three phases of menstrual cycle. The total possible score of each list was 35 points. The SNR-50 was calculated using the Spearman- Karber equation (Finney, 1952) as:-

SNR-50 = i+1/2 (d) - (d) (# correct) / w

Where;

i = the initial presentation level

d = the attenuation step size

w = number of keywords per decrement

Correct = total number of correct keywords

3.6. Statistical analysis

The obtained data were subjected to statistical analysis using SPPS software (version 17). Descriptive statistics were used to estimate the mean and standard deviation. To analyze the data across three phases of the menstrual cycle, repeated measures ANOVA was done.

Chapter 4

Results

The main aim of the present study was to assess the effect of hormonal changes on temporal perception and speech perception in noise in females across three phases of menstrual cycle (average 28 days of regular menstrual cycle). The SPSS software version 17.0 was used for statistical analysis. The following statistical tools were carried out to analyze the obtained data across three phases of regular menstrual cycle in females.

- Descriptive statistics were carried out to estimate the mean and standard deviation for all the parameters.
- Repeated measures ANOVA was done to estimate the differences in temporal perception and speech perception in noise across the three stages of the menstrual cycle.
- Bonferroni test was done for pairwise comparison across three phases of single menstrual cycle only when repeated measures ANOVA indicated significant differences across three phases of menstrual cycle.

The results of the current study are discussed in following headings:

- Effect of hormonal changes on temporal perception.
- Effect of hormonal changes on speech perception in noise test (SPIN).

4.1.Effect of hormonal changes on temporal perception

Temporal perception was assessed across three phases of the menstrual cycle in females through gap detection in noise test and modulation detection test.

4.1.1. *Gap Detection Test*

Figure 1 shows the mean GDT score across three phases of the menstrual cycle along with a single standard deviation (SD) error bar. In the figure, x-axis represents different phases of single menstrual cycle and the y-axis represents the gap detection threshold (ms). It is evident from the figure that menstrual phase shows poorest gap detection threshold followed by luteal phase and best threshold was obtained during the ovulation phase.

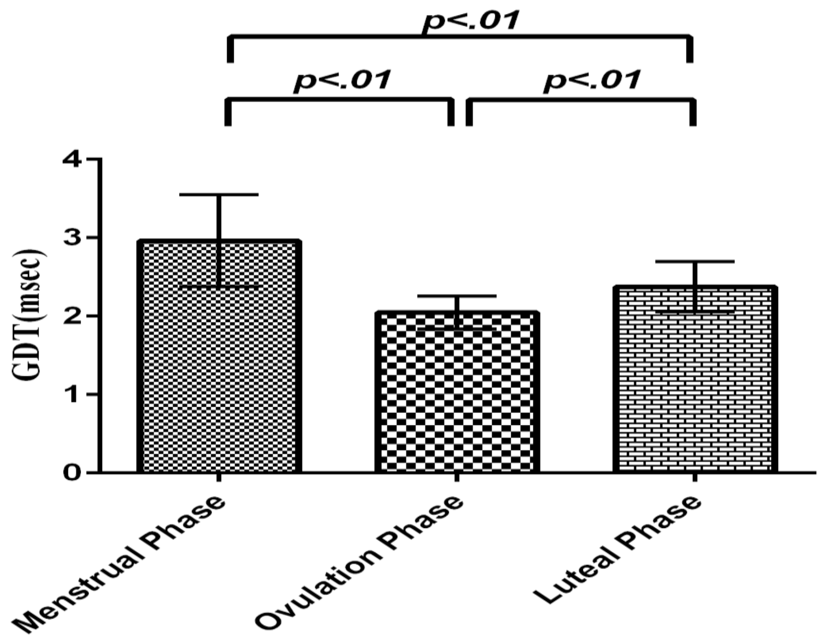

Figure 4:1: Mean scores and one standard deviation (SD) error bar for GDT across three phases of single menstrual cycle.

Repeated measures ANOVA was done to assess the significance in GDT across three phases of the menstrual cycle. The results indicated a significant main effect of menstrual cycle on GDT ($F = 24.396$; $p<.01$). Later, Bonferroni test was done to see a pairwise comparison among three phases of the menstrual cycle. The result showed that GDT was significantly different between all pairs of the menstrual cycle. Table 4.1 shows pairwise comparison results for all the phases.

Table 4.1: *Bonferroni test for pairwise comparison of GDT among three phases of menstrual cycle*

	Menstrual Phase	Ovulation Phase	Luteal phase
Menstrual Phase	_	.914*	. 588*
Ovulation Phase	-.914*	_	-.327*
Luteal Phase	-.588*	.327*	_

* indicate the mean difference is significant at the P<.01 levels.

4.1.2. *Modulation Detection Test*

The modulation detection threshold was carried out for four different modulation frequencies (8Hz, 20Hz, 60Hz & 200Hz) across three different phases of the menstrual cycle. Figure-2 shows the mean and standard deviation of modulation detection threshold at all modulation frequencies across three phases of the menstrual cycle in females. In this figure, x-axis indicates modulation frequencies in Hz and y-axis indicates modulation detection threshold (dB) for each phase of the menstrual cycle. From the figure it can be inferred that menstrual phase shows poorest modulation detection threshold followed by luteal phase and best threshold were obtained during the ovulation phase.

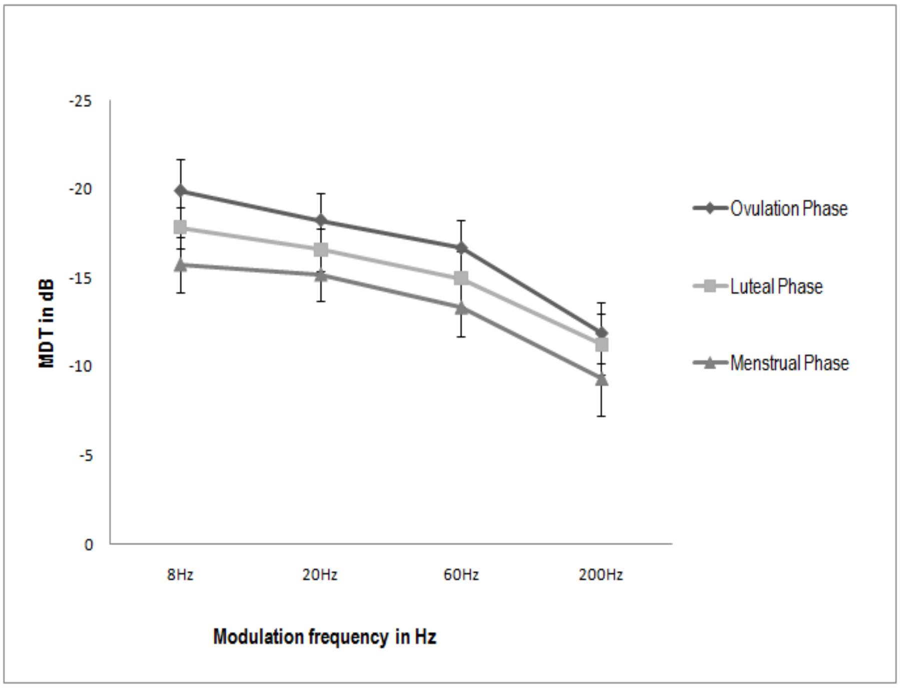

Figure 4:2: Mean MDT at 8Hz, 20Hz, 60Hz and 200Hz across three phases of menstrual cycle, Error bars depict one standard deviation (SD) of errors.

Repeated measures ANOVA results indicated a significant main effect of menstrual cycle on MDT for all the modulation frequencies (Table 4.2).

Table 4.2: *F-value and significant level for MDT frequencies across three phases of menstrual cycle*

MDT frequency	8Hz	20Hz	60Hz	200Hz
F-value	80.784*	35.535*	39.569*	12.386*

* indicate p<.01 level of significant.

Pairwise comparison using Boneferroni's test showed statistically significant (p<.01) mean differences between all pair phases of the menstrual cycle for all modulation frequencies. However, there was no significant difference noted between ovulation and luteal phase for 200Hz modulation frequency (p >.05).

4.2. Effect of hormonal changes on Speech Perception in Noise

Figure 3 shows the mean and standard deviation of the SNR-50 value across three phases of the single menstrual cycle. In this figure, x-axis represents three phases of single menstrual cycle and the y-axis represents SNR-50 (dB) value. From the figure it can be concluded that menstrual phase shows poorest SNR-50 (dB) followed by luteal phase and best SNR-50 was obtained during the ovulation phase.

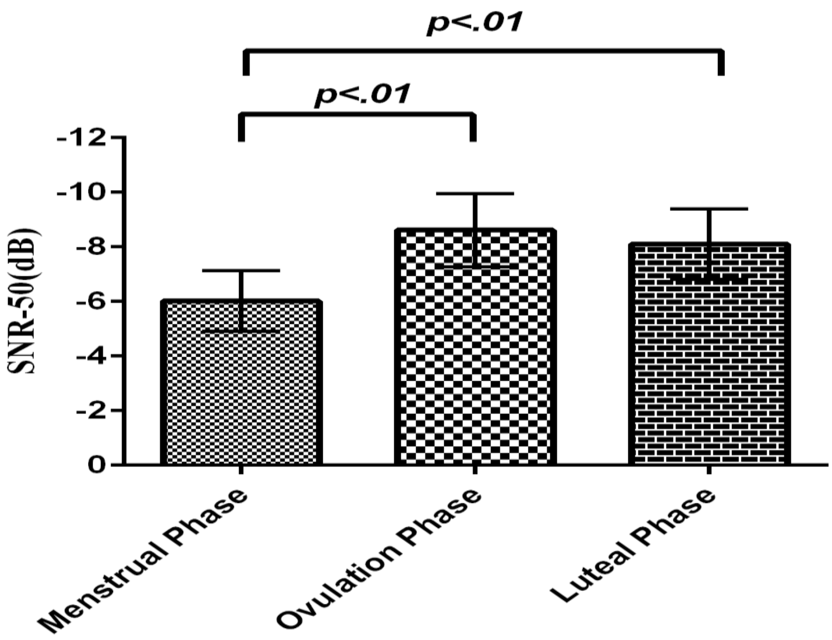

Figure 4:3: Mean scores and one standard deviation error bar of SNR-50 across three phases of single menstrual cycle.

Repeated measures ANOVA indicated that there was a significant main effect of menstrual cycle on SNR-50 (F = 24.284, P<. 01). Later, the Bonferroni test showed that there were significant mean differences between menstruation and ovulation phase (p<.01) and menstrual phase and luteal phase (p<.01), but such significant differences did not exist between ovulation and luteal phase (p>.05) (Table 4.3).

Table 4.3: *Bonferroni test for pairwise comparison of SNR-50 among three phases of menstrual cycle*

Phases	Menstrual Phase	Ovulation Phase	Luteal Phase
Menstrual Phase	_	2.600*	2.086*
Ovulation Phase	-2.600*	_	-.514
Luteal Phase	-2.086*	.514	_

* indicate the mean difference is significant at the p<.01 levels.

Chapter 5

Discussion

The current study was conducted with the aim to assess the effects of hormonal changes on temporal perception and speech perception in noise in females across three phases of the menstrual cycle (average 28 days of normal menstrual cycle). To fulfil the aim, 20 female participants with an average 28 days of regular menstrual cycle were tested across three different phases of single menstrual cycle i.e. menstrual phase (cycle of 1-5 days) ovulation or mid cycle phase (cycle of 12-15 days) and luteal phase (cycle of 18-25 days). Discussion of obtained results is given in following headings:

- Effect of hormonal changes on temporal perception.
- Effect of hormonal changes on speech perception in noise test (SPIN).

5.1. Effect of hormonal changes on Temporal Perception

The GDT findings of the current study showed that the larger silent interval was required to detect gaps in noise during the menstrual phase compared to ovulation and luteal phase. Similar findings were noted for MDT also wherein larger modulation depth was required for modulation detection in noise at four different modulation frequencies during the menstrual phase when compared to ovulation and luteal phase. Thus, the findings of both GDT and MDT suggest the poorest temporal resolution ability during menstrual phase, followed by luteal phase and best temporal resolution ability during the ovulation phase. These findings may be attributed to the fluctuation in estrogen and progesterone level across different phases of the menstrual cycle, which affects peripheral as well as central auditory processing.

Similarly, Pleil et al. (2011) found better duration discrimination scores post estrogen injected in female rats. It was hypothesized that rapid and acute estrogen level, increases temporal processing of auditory information. Al-Mana et al. (2008) reported that during ovulation phase best cochlear acuity is noted and auditory system is most sensitive. Higher levels of estrogen during the ovulation phase excites auditory nerve resulting in faster axonal conduction of auditory processing at the cortical level. It is also believed that acute estrogen level increases glutamate excitatory neurotransmitter which would result in better auditory processing for temporal perception during the ovulation phase compared to menstrual and luteal phase.

Moreover, possible explanation for poor scores during the luteal phase could be due to the extra release of neuro-inhibitory neurotransmitter i.e. GABA due to higher progesterone levels which inhibits temporal processing of auditory information in auditory cortex (Smith et.al., 1999).

In the present study it was also noted that MDT at 200 Hz modulation frequency did not show a significant difference during ovulation and luteal phase. This could be because of the higher modulation rate itself, which is difficult to be detected in the auditory system. Also, slight differences in estrogen level between ovulation and luteal phase would have resulted in the similar excitation and central conduction.

5.2. Effect of hormonal changes on Speech Perception in Noise

The results of the present study showed speech perception in noise thresholds during ovulation and luteal phase better when compared to menstrual phase. Similar results were reported by Guimaraes, et al. (2006), in which study hearing in noise test

(HINT) was done for each ear in three postmenopausal females groups taking hormonal replacement therapy i.e. estrogen treated group, estrogen plus progesterone treated group and no hormonal therapy treated group. The findings showed poor HINT score obtained in estrogen plus progesterone taking group compared to estrogen alone and control group. It was concluded that presence of progesterone interferes speech perception in noise and higher estrogen results in better speech perception in noise. In the present study also better speech perception in noise was noted during ovulation and luteal phase which could be due to the relatively higher estrogen level compared to menstrual phase. It is also hypothesized that neural synchronization at the level of the brainstem and cortical level are important for speech perception in noise (Anderson, Skoe, Chandrasekaran & Kraus, 2010). This synchronization might increase when there is an increase in the level of estrogen because it is excitatory in nature which could excite auditory nerve and cortical circuits leading to rapid neural firing (spike) and resulting in the rapid temporal processing of auditory information (Remage-Healey, Jeon & Joshi, 2013; Smith et.al. 1999).

Another outcome of the present study was that SNR-50 did not differ significantly between ovulation and luteal phase. This could be explained based on the functioning of medial olivocochlear bundle. The MOC system plays an important role in speech perception in noise (Mishra & Lutman, 2014). Animal studies on “MOC antimasking” hypothesis suggested that activation of the MOC system result increases the response of transient signals embedded in continuous noise contralaterally at a moderate level (Kawase et al. 1993). Al-Mana, Ceranic, Djahanbakhch, and Luxon (2010) studied contralateral suppression of OAE during four different phases of regular menstrual cycle i.e. early and late stages of follicular luteal phase. They found reduced MOC suppression during the late follicular phase (ovulation) but opposite effect was seen during the luteal phase. So, excitatory effects of estrogen during ovulation reduced MOC supression which would result in increased cochlear response to noise as reported in the same study. Thus, this reduction in MOC supression would have lead to reduced speech perception in noise during the ovulation phase. Thus no significant difference was noted in SPIN between ovulation and luteal phase.

To conclude, current temporal perception tests i.e. GDT and MDT finding show significant better temporal perception during the ovulation phase compared to menstrual and luteal phase. It may be hypothesized that higher estrogen level increases glutamate excitatory neurotransmitter resulting in faster axonal conduction of auditory processing at the cortical level. In this study, significant poorer temporal processing was seen during the luteal phase compared to ovulation phase. It may be believed that higher progesterone level during this phase, releases more amount of GABA inhibitory neurotransmitter which inhibits temporal processing of auditory information. Moreover, poorest temporal processing during the menstrual phase could be due to lower estrogen level compared to the other two phases. The SNR-50 finding in the current study also showed significant better speech perception in noise during ovulation and luteal phase compared to menstrual phase. It could also be contributing to the increase in the level of estrogen, which provides better synchronization of auditory nerve and cortical circuits. Thus, hormonal fluctuation during menstrual cycle affects temporal perception and speech perception in noise in females as seen in the current study. Thus, the null hypothesis is rejected in the present study.

Chapter 6

Summary and Conclusion

The menstrual cycle is a periodic fluctuation of the ovarian hormonal level seen in every female, which affects peripheral as well as central auditory processing. Studies have shown that the auditory system is influenced by hormonal fluctuation during menstrual cycle. However, studies related to the effect of hormones on temporal perception and SPIN are limited.

The aim of the current study was to assess the effects of hormonal changes on temporal perception and speech perception in noise in females across three phases of the menstrual cycle (average 28 days of normal menstrual cycle). In the present study, 20 normal hearing female participants with an average 28 days of regular menstrual cycle were taken. The following tests were carried out for all female participants across three phases of the menstrual cycle: –

- Temporal processing test, i.e. gap detection test and modulation detection test at 8Hz, 20Hz, 60Hz and 200Hz modulation frequencies assess temporal resolution ability of the auditory system.
- Quick- SIN in Kannada was used to assess the ability of speech perception in the presence of noise.

Repeated measures ANOVA and Bonferroni tests were carried out for statistical analysis using SPSS software (version 17). The following results were obtained in the present study:

- Menstrual phase showed poorest threshold followed by luteal phase and best threshold were obtained during the ovulation phase for both gap detection test and modulation detection test.
- Poorest speech perception was seen during the menstrual phase compared to ovulation and luteal phase. However, the SNR-50 value did not differ significantly between ovulation and luteal phase.

Thus, it can be concluded that hormonal fluctuation during menstrual cycle affects temporal processing and speech perception in the presence of noise. This could be due to varying levels of estrogen and progesterone. The study would help in understanding which hormone has more effects on temporal perception and speech perception ability in noise. Moreover, this study provides further insight about the effects of hormone agents like steroids and contraceptive on hormonal synthesis and its effects in central processing of auditory information. Further, the present study highlights the importance of considering the menstrual phase while studying the female participants.

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