

ABSTRACT

Title of Dissertation: THE EFFECT OF THE MENSTRUAL CYCLE ON EVOKED OTOACOUSTIC EFFERENT SUPPRESSION

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The purpose of the study was to investigate the effects of the menstrual cycle on suppression of transient-evoked otoacoustic emissions. Otoacoustic emissions (OAEs) are soft sounds produced by the inner ear that can be measured in the ear canal by a sensitive microphone. OAEs may be present spontaneously or may be evoked by presenting sound(s) to the ear. Presenting a noise (in addition to the eliciting stimulus) to one or both ears during testing typically causes a change in the measured OAE levels. Because the change is most often a decrease in OAE levels, this effect has been termed "suppression." Although OAE suppression is not used routinely in audiometric evaluations, research has indicated potential clinical value for diagnosis of certain pathologies, such as auditory neuropathy (e.g., Starr et al., 1996). However, more information on sources of normal variation in OAE suppression is needed. Little information is available on how the menstrual cycle affects OAE suppression. In the present study, suppression of transient-evoked OAEs (TEOAEs) was investigated. TEOAEs are measured following the presentation of clicks to the ear. Repeated measures of TEOAE suppression were completed on 30 participants divided into three groups: (1) 10 normally-menstruating females who were not taking oral contraceptives, (2) 10 normally-menstruating

females who were taking oral contraceptives, and (3) 10 males. Participants were tested on three separate days. Female participants were tested during menstruation, pre-ovulation/mid-cycle and pre-menstruation. An ovulation prediction kit was used by female participants not taking oral contraceptives to aid in estimating the time of ovulation. Male participants were tested at intervals that corresponded in time to those for the female groups. TEOAE suppression did not differ significantly between the three groups or across the three sessions (one menstrual cycle) for any of the groups. Unsuppressed TEOAE levels were also similar between groups and stable across sessions for all groups. The findings suggest that female sex hormones do not affect TEOAE suppression. From a clinical standpoint, these results are fortuitous in that phases of the menstrual cycle would not need to be taken into account when interpreting unsuppressed TEOAE levels or TEOAE suppression results.

THE EFFECT OF THE MENSTRUAL CYCLE ON EVOKED OTOACOUSTIC
EFFERENT SUPPRESSION

By

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Dedication

I would like to dedicate this dissertation to my best friend and supporter, my husband, Mustafa, who has always believed in me when others doubted. I like to also dedicate this dissertation to my son, Adam, who has inspired me to keep working hard and believe in my dreams. Finally, I would like to thank my mom, dad, mom #2, sisters and family for their endless positive support.

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Chapter 1: Introduction

The menstrual cycle is a complicated yet organized set of changes in hormones in females. There are four hormones that are involved in regulation of the menstrual cycle: estrogen, progesterone, lutenizing hormone (LH), and follicle stimulating hormone (FSH). These hormones may have an effect on the cochlea (inner ear) and central auditory pathways. The majority of research on hearing and hormones has focused on estrogen. Estrogen receptors have been detected in the auditory system, including the inner ear, of animals and humans (e.g., Stenberg, Simonoska, Stygar, Sahlin & Hultcrantz, 2003; Stenberg, Wang, Fish III, Schrott-Fischer, Sahlin, & Hultcrantz, 2001).

The purpose of the estrogen receptors in the auditory system is not known; however, a study on mice showed the lack of estrogen receptors was related to a deterioration of cortical neurons in the brain (Wang, Andersson, Warner, & Gustafsson, 2001). One theory states that estrogen may be important in maintaining the function of the auditory system and auditory efferent system. Specifically the lack of estrogen may increase the risk of hearing loss and decrease the possible protective role of the efferent system in humans (Thompson, Zhu, & Frisina, 2006). Researchers have also speculated that estrogen may cause a change in the speed at which sensory information travels through the auditory brainstem (Elkind-Hirsch, Wallace, Stach & Jerger, 1992). In addition, estrogen may have an effect on cochlear blood flow (Laugel, Dengerink, & Wright, 1987).

Results of research on the effects of the menstrual cycle on auditory measures have been conflicting. Changes in auditory thresholds over the course of the menstrual

cycle have been documented in some studies (e.g., Baker & Weiler, 1977), but not in others (e.g., Grieze-Jurgelevicius, Chernos, & Petersik, 1990). Decreases in temporary threshold shifts (TTS) during different phases of the menstrual cycle have been documented (Davis & Ahroon, 1982; Hori, Nakashima, & Sato, 1993). In addition, a number of studies have indicated changes in physiological measures across the menstrual cycle such as the acoustic reflex (Laws & Moon, 1986), the auditory brainstem response (ABR) (e.g., Elkind-Hirsh et al. 1992), and otoacoustic emissions (OAEs) (e.g., Hurley, Hood, Berlin, & Leonard, 1996).

OAEs are soft sounds produced by the cochlea that can be measured in the ear canal using a sensitive microphone. The presence of these sounds indicates normal function of the cochlea and, in particular, of the outer hair cells (e.g., Brownell, 1990; Kemp, Ryan, & Bray, 1990). There are two main types of OAEs: spontaneous OAEs (SOAEs), which can be recorded in the absence of any stimulation, and evoked OAEs, which are recorded during or after the presentation of a sound to the ear. Evoked OAEs can be further sub-categorized by the type of stimulus used to evoke them. Transient-evoked OAEs (TEOAEs) are measured following the presentation of a short stimulus such as a click or tone-burst and were the focus of the present study.

A large body of research has indicated that OAE levels measured in the ear canal are altered during or following the presentation of an additional acoustic stimulus (typically a noise) to one or both ears during OAE testing (e.g., Berlin, Hood, Hurley, Wen, & Kemp, 1995; Liberman, 1989). Because the change is most often a decrease in OAE level, this effect has been termed OAE “suppression.” OAE suppression is mediated by the auditory efferent system, the central auditory nervous system pathways

that run from higher structures to lower or peripheral structures. In particular, evidence indicates that the medial olivocochlear (MOC) portion of the auditory efferent system mediates OAE suppression in humans (e.g., Veuille, Khalifa, & Collet, 1999). Therefore, OAE suppression has been used as a non-invasive means to study the function of the MOC system. Measurement of TEOAE suppression is not performed routinely by clinicians and is most often used as part of a test battery approach to confirm auditory neuropathy. Other clinical applications for TEOAE suppression are still under investigation.

Currently little information is available on how the menstrual cycle affects TEOAE suppression. Such information would be important in developing normative data for clinical diagnostic use of this procedure and could help explain how female sex hormones affect the functioning of the central auditory nervous system. Several research studies have reported greater fluctuation in SOAE frequency across the menstrual cycle for females not taking oral contraceptives than for females taking oral contraceptives (e.g., Bell, 1992; Haggarty, Lusted, & Morton, 1993; Penner, 1995). A pilot study by Hurley et al. (1996) investigated efferent suppression of TEOAEs across the menstrual cycle in a small sample. The researchers found no significant change in the amount of TEOAE suppression across the menstrual cycle. However, these researchers provided no information on the inclusion criteria for participants or the method of verifying menstruation or ovulation in the female participants.

The purpose of the present study was to investigate the effects of the menstrual cycle on binaural TEOAE suppression, utilizing strict inclusion criteria and multiple methods to confirm menstruation and ovulation in female participants. TEOAEs were

measured in three groups of participants: females with normal menstrual cycles not taking oral contraceptives, females with normal menstrual cycles taking oral contraceptives, and a control group of males. TEOAEs were measured both with and without the presentation of an additional, binaurally presented noise during three separate sessions scheduled over a period of one month. It was hypothesized that the unsuppressed (without noise) TEOAE levels would change across a period of one month (one menstrual cycle) in females with normal menstrual cycles not taking oral contraceptives but that the unsuppressed TEOAE levels would be stable across a period of one month (one menstrual cycle) in females with normal menstrual cycles taking oral contraceptives and in males. It was also hypothesized that the change in TEOAE levels following presentation of binaural noise would change across a period of one month (one menstrual cycle) in females with normal menstrual cycles not taking oral contraceptives but that the change in TEOAE levels following presentation of binaural noise would be stable across a period of one month (one menstrual cycle) in females with normal menstrual cycles taking oral contraceptives and in males.

Chapter 2: Review of Literature

Otoacoustic Emissions

OAEs are soft sounds that can be measured in the ear canal. OAEs reflect the normal function of the cochlea and the normal active response to sound. This active mechanism is believed to be at the level of the basilar membrane and to contribute to the sensitivity and frequency selectivity evident in the normal ear (e.g., Brownell, 1990; Kemp et al. 1990). This active mechanism of the cochlea has also been referred to as the “cochlear amplifier” (Dallos, 1992; Davis, 1983).

The cochlear amplifier provides additional energy to the incoming signal, resulting in a boost of the responses of the basilar membrane. Specifically, the cochlear amplifier enhances the peak of the basilar membrane response by approximately 100 times (Ashmore & Kolston, 1994). There is evidence to support that cochlear amplification acts immediately on all the frequency components of the stimulus (Ashmore & Kolston, 1994). Several lines of research indicate that outer hair cells contribute to the amplification process (Ashmore, 1993; Hudspeth & Markin, 1994; Pickles, 1993). Damage to outer hair cells results in elevated thresholds and broader tuning curves compared to responses from cochleae with normal outer hair cell function (e.g., Liberman & Dodds, 1984). Healthy outer hair cells also appear necessary for the production of OAEs. OAEs are absent or reduced when outer hair cells are damaged by noise exposure or ototoxic medications (e.g., Hamernick, Ahroon, Jock, & Bennett, 1998).

Until recently, all OAEs were thought to originate from the electromotile response of the outer hair cells. Recent research has led to the hypothesis that OAEs are generated

by two different mechanisms, nonlinear distortion and linear coherent reflection (Shera & Guinan, 1999). Emissions generated by either mechanism follow a similar pathway in that the backward traveling waves will propagate basally and out into the ear canal. However, the processes responsible for creating the backward traveling waves are different (Shera & Guinan, 1999). Nonlinear distortion results from the activity of the outer hair cells. Linear reflections are believed to be a result of the energy bouncing back from impedance perturbations within the cochlea (Zweig & Shera, 1995). The phase behavior of the emission assists in distinguishing between those OAEs generated by the nonlinear distortion and those generated by the linear reflection mechanisms. As the stimulus frequency changes, the phase for emissions arising from nonlinear distortion remains stable, while the phase for emissions arising from linear reflection changes rapidly (Shera & Guinan, 1999; Shera, 2004). Most OAEs are thought to arise from a mixture of linear reflection and nonlinear distortion, although the component that dominates may depend on various factors such as the type and level of stimulation used to evoke the OAE (e.g. Yates & Withnell, 1999).

Transient Evoked Otoacoustic Emissions (TEOAEs)

Transient-evoked otoacoustic emissions (TEOAEs) are one type of evoked OAE that are measured following presentation of a brief stimulus such as a click or tone-burst. The spectrum of a TEOAE depends on the spectrum of the stimulus used to evoke it (Probst et al. 1991). For example, a click contains a broad range of frequencies, while a tone-burst is more frequency specific and with a narrower band of energy (Probst, Coats, Martin, & Lonsbury-Martin, 1986). The various frequency components of the resulting

transient evoked response have different latencies (Kemp, 1978). High frequencies are emitted first from the base of the cochlea, followed by low frequencies from the apex, reflecting the tonotopic organization of the cochlea (e.g., Kemp, 1978). TEOAEs are reliable and stable for a given individual barring changes in cochlear function (e.g., Balatsouras, Kaberos, Karapantzos, Homsiloglou, Economou, & Korres, 2004; Prieve et al. 1993; Vedantam & Musiek, 1991), although some test-retest variation in levels is expected, with much of the variation probably due to differences in the placement of the probe used to measure the TEOAEs in the ear canal (e.g., Robinette, 2003).

The transient stimuli commonly used to elicit the TEOAE are clicks (e.g., Probst et al. 1991). An example of a click-evoked TEOAE is shown in Figure 1. The acoustic waveform of the TEOAE that is generated following the click stimuli is measured by utilizing time synchronous averaging (e.g., Probst et al. 1991). The first 20 milliseconds (ms) following presentation of the transient stimulus are examined for TEOAE energy. The first few milliseconds of the TEOAE response waveform are removed to omit any energy due to the stimulus. Typically the level, percentage reproducibility, and/or the signal to noise ratio (SNR) of the broad-band TEOAE or of the TEOAE filtered into frequency bands is analyzed to determine whether the output is an actual response (Kemp et al. 1990). The instrumentation used to measure TEOAEs alternately stores the responses into two different buffers, resulting in two averaged traces (see the top of Figure 1). Once the software collects an adequate number of averages in each buffer, the test is completed and the two waveforms can be compared and analyzed. The waveforms are compared to determine reproducibility using cross-correlation analysis. Higher reproducibility, that is, greater similarity between the two averaged waveforms, increases

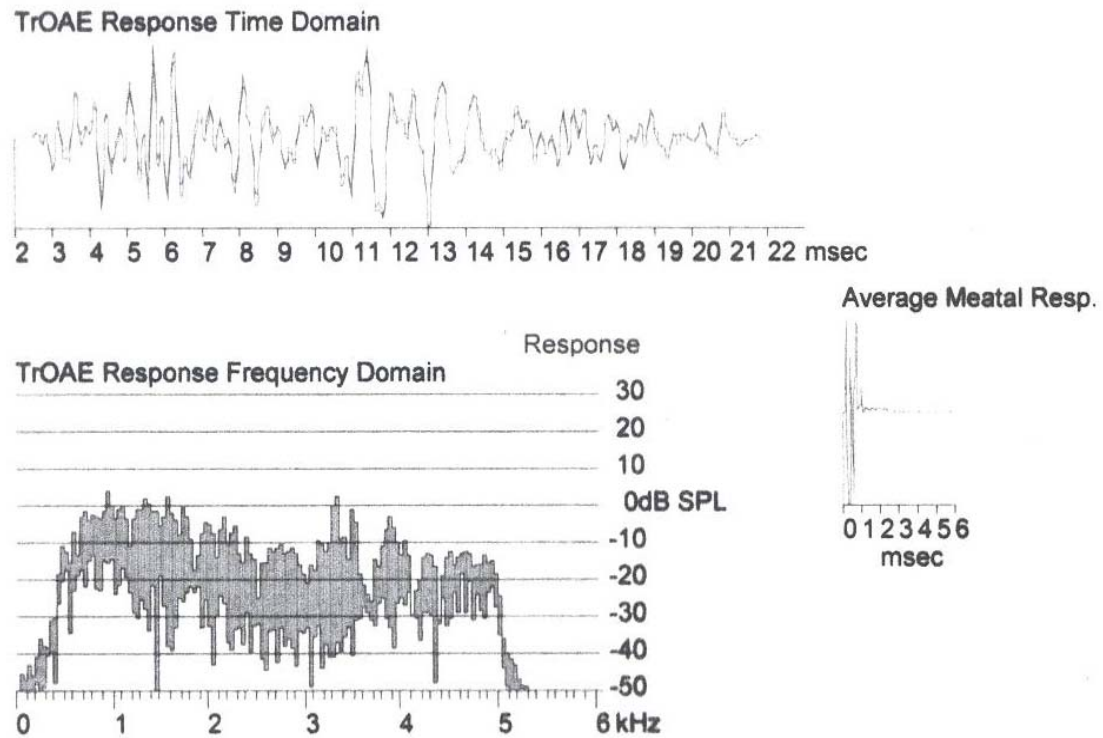


Figure 1. Example of one participant’s unsuppressed (without noise) TEOAE response recorded at 80 dB pSPL using the Intelligent Hearing Systems Smart TrOAE program. The top portion of the figure shows the TEOAE time waveforms. The two simultaneously-collected waveforms are superimposed for comparison. The first two milliseconds of the response waveforms have been eliminated to remove any artifact from the click stimulus. The bottom portion shows the measured TEOAE in the frequency domain. The TEOAE is represented by the shaded region and the noise is shown in white. On the right side of the figure is the time waveform of the stimulus in the ear canal.

the likelihood that the response reflects cochlear activity rather than noise. The averaged waveforms are also analyzed in the frequency domain in the form of a Fast Fourier Transform (FFT) to obtain levels and signal-to-noise levels in different frequency bands. When a high stimulus level is used, such as 80 dB peak sound pressure level (pSPL), a specialized mode of stimulus presentation, typically referred to as the “nonlinear” mode, is often used. The nonlinear mode was designed to eliminate stimulus artifact from the transient stimuli (typically clicks) that may interfere with the energy in the TEOAE spectrum (Bray, 1989). In this mode, the responses to subsets of four transients are sub-averaged prior to their inclusion in the overall average. Three of the transients have the same sound pressure level (SPL) and phase. The last transient is presented 180 degrees out of phase and about 10 dB higher than the other three. When the responses to the four transients are sub-averaged, the stimulus energy should cancel, resulting in less stimulus artifact in the final, averaged TEOAE response (Kemp, Bray, Alexander & Brown, 1986). Following development of the “nonlinear” mode, presentation of all transient stimuli at the same level and phase has come to be referred to as the “linear” mode. The linear presentation mode can be utilized when a low stimulus level is presented, such as 60 dB pSPL.

TEOAEs, as well as other evoked OAEs, have several clinical applications. The most well-known is use of OAEs to screen for the presence of hearing loss, particularly in newborns. The presence of OAEs is taken as a sign of normal cochlear function, while the absence of measurable OAEs indicates that further testing is necessary to rule out a hearing loss. Because they provide information about the status of outer hair cells, OAEs

can be useful as part of a test battery approach for differential diagnosis of auditory disorders. The presence of OAEs can aid in confirming normal middle ear function. OAEs also have been used to explore the function of the medial efferent system in a noninvasive manner. This has been most commonly done by presenting noise to the contralateral ear during OAE testing and examining the resulting changes in OAE level in the ipsilateral ear (e.g., Komazec, Filipovic, & Milosevic, 2003; Morand-Villeneuve, Garnier, Grimault, Veuillet, Collet, & Micheyl, 2002; Quaranta, Gandolfi, Fava, Quaranta, & Zini, 2000).

Suppression of Otoacoustic Emissions

OAE amplitudes are altered in the presence of an additional acoustic stimulus presented to the ear ipsilaterally, contralaterally or binaurally (e.g., Berlin et al. 1995; Liberman, 1989). Typically, the change is a reduction in OAE level; therefore, this phenomenon has been called "suppression." The change in OAE level is calculated by subtracting the level of the OAE measured without any additional suppressor from the level of the OAE measured in the presence of the suppressor (e.g., Brashears, Morlet, Berlin & Hood, 2003). The change in OAE level begins with the onset of the suppressor and continues as long as the suppressor is present (Liberman, Puria, Sunil, & Guinan, 1996).

In the vast majority of reports, the addition of contralateral, ipsilateral and/or binaural stimulation produces OAE suppression (e.g., Berlin, Hood, Hurley & Wen, 1994; Berlin et al. 1995; Harrison & Burns, 1993; Hood, Berlin, Wakefield, & Hurley, 1995; Liberman et al. 1996; Moulin, Collet & Duclaux, 1993). In a small number of

cases, the additional acoustic stimulation has resulted in an increase in OAE level, termed "enhancement." Enhancement of TEOAEs has been reported in isolated cases of individuals with tinnitus and hyperacusis (abnormal sensitivity to loud sounds) (Collet, Veuillet, Bene & Morgan, 1992) or acoustic neuromas (Quaranta, Gandolfi, Fava, Quaranta, & Zini, 2000). Enhancement has also been reported for distortion-product OAEs (DPOAEs) (e.g., Brown & Norton, 1990). DPOAEs are another type of evoked OAE measured during presentation of two sinusoids to the ear ("f1" and "f2" where $f_1 < f_2$). When the frequencies of the two tones are close together, they interact with each other on the basilar membrane, resulting in the production of tones at predictable frequencies that are arithmetically related to the two input frequencies (e.g., $2f_1 - f_2$, $2f_2 - f_1$). Several researchers have proposed that DPOAE enhancement may result from changes in the contributions from the two mechanisms (nonlinear distortion and linear coherent reflection). The DPOAE level measured in the ear canal for any given pair of tones is thought to depend on how the nonlinear distortion and reflection components combine. Whether they combine additively or cancel will depend on their phase relationship. If the additional stimulation results in changes to either or both components and alters their phases, how they add or cancel in the ear canal would also change, potentially resulting in enhancement or suppression (e.g. Kujawa & Liberman, 2001; Martin, Villasuso, Stagner, & Lonsbury-Martin, 2003; Meinke, Stagner, Martin, & Lonsbury-Martin, 2005).

There have been several hypotheses regarding the mechanism of suppression of OAEs. The first hypothesis is that the contraction of the stapedius muscle (acoustic reflex) is involved in the reduction of the level of OAEs. Several research studies that

have demonstrated that suppression is present and in some cases even greater in individuals with paralysis of the stapedius muscle (e.g., Berlin, Hood, Cecola, Jackson, & Szabo, 1993a; Collet, Kemp, Veuillet, Ducleaux, Moulin, & Morgan, 1990; Giraud, Collet, Chery-Croze, Magnan, & Chays, 1995; Veuillet, Collet, & Duclaux, 1991), making it unlikely that the acoustic reflex plays a major role in the OAE level decreases in humans. Furthermore, several studies have used animals with surgically severed or paralyzed middle ear muscles to rule out the middle ear muscle participation in OAE suppression (e.g., Kawase, Delgutte, & Liberman 1993; Liberman, 1991; Rajan, 1995; Winslow & Sachs, 1987).

Another hypothesis that has been proposed is that acoustic crossover may cause the suppression of TEOAEs. However, several factors make this unlikely. The intensity of the click and noise SPLs typically used are considered to be too low for acoustic crossover to occur (Hood, Berlin, Hurley, Cecola, & Bell, 1996). Today, insert earphones are most often used to present the contralateral stimulus. As a result, the interaural attenuation (the loss of intensity of sound that results when sound is presented to one ear and heard by the other ear) is much greater than for supra-aural ear phones. In addition, suppression is greater for lower intensity stimuli compared to higher intensity stimuli (Hood et al. 1996). Available evidence suggests that suppression results from the activation of the auditory efferent system, specifically the olivocochlear bundle.

The Olivocochlear Bundle

The olivocochlear bundle is the portion of the auditory efferent system that runs from the brainstem to the cochlea (Iurato et al. 1978). The olivocochlear bundle arises from the superior olivary complex, the first brainstem nucleus to receive binaural afferent

input (Moore, 2000). The olivocochlear bundle is composed of two unique neural pathways, the lateral olivocochlear (LOC) bundle and the medial olivocochlear (MOC) bundle (Warr & Guinan, 1979).

The LOC bundle is made up of thin, unmyelinated efferent neurons that originate in the lateral region of the superior olivary complex. The LOC neurons receive most of their stimulation from uncrossed afferents and project to the ipsilateral cochlea where they synapse on afferent fibers of the inner hair cells. As a result of this indirect communication, LOC neurons appear not to influence hair cell activity directly (Warr, 1992). The role of the LOC system is not well understood, because the unmyelinated axons of this pathway are difficult to stimulate (e.g., Gifford & Guinan 1987).

Researchers believe that the LOC neurons may have an acute inhibitory effect on the cochlea and may also contribute to the development of a normal cochlea (e.g., Groff & Liberman, 2003). More recent studies of the LOC system in guinea pigs have shown changes in the cochlear action potential (CAP) resulting from indirect electrical stimulation (Groff & Liberman, 2003) or from destruction of LOC neurons (Le Prell, Shore, Hughes, & Bledsoe, 2003). In either case, outer hair cell responses such as DPOAEs did not seem to be affected (Groff & Liberman, 2003; Le Prell et al. 2003).

The MOC bundle is comprised of thick, myelinated neurons that originate in the medial region of the superior olivary complex. MOC neurons receive most of their stimulation from crossed afferents. They project mainly to the contralateral cochlea, although a small number of MOC neurons project to the ipsilateral cochlea. Most MOC fibers synapse directly on outer hair cells and, therefore, are hypothesized to have a direct influence on outer hair cell activity (Lim, 1986). Electrical stimulation of the

olivocochlear bundle most likely selectively activates fibers of the MOC system (Guinan, Warr, & Norris, 1983). It is this part of the olivocochlear efferent system that is thought to be responsible for OAE suppression (e.g., Berlin et al. 1994; Collet et al. 1990). The activation of the MOC system is believed to effect a change in the outer hair cell activity that is reflected in a reduction in the level of the OAE (e.g. Collet et al. 1990; Veuillet et al. 1991). The fibers of the olivocochlear bundle travel along the vestibular nerve (Rasmussen, 1946). Vestibular neuroectomy is a procedure that involves an excision of the inferior vestibular fibers, also impacting the olivocochlear bundle. Research studies have shown that individuals who have a history of vestibular neurotomy/neurectomy showed reduced or absent OAE suppression (e.g., Giraud et al. 1995; Williams, Brookes, & Prasher, 1993, 1994).

There are several hypotheses that have been proposed regarding the functional roles of the MOC system. One hypothesis is that the system protects the inner ear from acoustic overstimulation (e.g., Liberman, 1991; Rajan, 1995). Researchers have found that electrical stimulation of the olivocochlear bundle raises the thresholds of primary afferent neurons (Guinan & Gifford, 1988; Weiderhold & Kiang, 1970) or significantly reduces the threshold shift in response to loud sound exposure (Rajan & Johnstone, 1988 a, b). When the olivocochlear bundle was sectioned it resulted in a greater permanent threshold shift due to noise exposure compared to that of the contralateral non-operated ear in the guinea pig (Attanasio et al. 1999). Permanent thresholds shifts to noise exposure were also found to be larger in guinea pigs with weak OAE suppression and smaller in guinea pigs with strong OAE suppression (Maison & Liberman, 2000). However, there have been studies that have shown no evidence of a protective effect of

the olivocochlear bundle from acoustic injury. Liberman (1991) eliminated the olivocochlear bundle in cats and measured the compound action potentials at the round window before and after acoustic overexposure and found no evidence that the activity of the olivocochlear bundle provided protection from acoustic injury.

There have been few studies that have investigated the protective effect of the MOC system in humans. Collet, Morgan, Veuillet, and Gartner (1991) conducted a study to determine if there was a difference between the functioning of the MOC system in participants with sensorineural hearing loss who had a history of noise exposure and participants with a sensorineural hearing loss who did not have a history of noise exposure. The researchers found no significant difference in contralateral suppression of TEOAEs between the two groups. The researchers also studied temporary threshold shift by exposing participants to a monaural, 180 second, 95 dB SPL puretone at 2000 Hz. No correlation was found between temporary threshold shift and contralateral suppression of TEOAEs for subjects with noise-induced hearing loss. There are several questions that arise regarding the Collet et al. (1991) study. The researchers did not provide information on the degree of sensorineural hearing loss in participants and did not provided information on the level of TEOAEs measured in the participants. Veuillet, Martin, Suc, Vesson, Morgan, and Collet (2001) studied MOC suppression in humans during auditory recovery from acoustic trauma. The researchers found no significant change in TEOAE level or MOC suppression, however, better recovery in audiometric thresholds was observed for participants with greater MOC suppression. The researchers concluded the MOC system may play an important role in post-traumatic threshold recovery.

Kirk and Smith (2003) hypothesized that the MOC system did not evolve in mammals to protect the cochlea from acoustic trauma, because ambient noise in most natural acoustic environments is significantly lower in intensity than the noise levels used in experimental conditions. Kirk and Smith (2003) state that water and wind create a low-intensity, fairly broad-band noise which is present in most natural environments. The researchers hypothesized that the MOC system developed in an environment composed of unmasking transient stimuli. Similarly, the MOC system has been hypothesized to permit more accurate detection and discrimination of signals in the presence of background noise (e.g., Dewson, 1968; Hienz, Stiles, & May, 1998; May & McQuone, 1995). Micheyl and Collet (1996) found that the greater the decrease in OAE level during contralateral stimulation, the better the performance in detection of tones in noise on psychoacoustic tests by normal hearing participants.

The third hypothesis is that the MOC bundle reduces cochlear compression, which is believed to be crucial for intensity encoding (Russell & Murugasu, 1994). The researchers hypothesize that if cochlear status is affected by olivocochlear bundle activity, then the perception of intensity would also most likely be affected. Zeng, Lehmann, Soli, and Linthicum (1994) reported that individuals who had undergone vestibular neurectomies had significantly poorer intensity and speech discrimination in noise in the surgical ear as compared to the non-surgical ear. Studies on cats with severed efferent fibers have shown performance deficits in detecting level changes in a noisy background for high frequency tones (May, McQuone & Lavoie, 1995; McQuone & May, 1993). However, this theory was not supported by the findings of Morand-Villeneuve et al. (2002). These researchers found no significant effects of contralateral

noise stimulation on psychoacoustic tests that measured loudness functions (means for tracking changes in loudness perception) and loudness integration for normal-hearing participants and vestibular neuroectomy patients.

TEOAE Suppression

When suppression of TEOAEs is measured, the decrease in the overall level of the broad-band TEOAE is reported to be relatively small, approximately -1 to -4 dB SPL in normal hearing listeners for contralateral suppression (e.g., Veuille et al. 1991). Some normal hearing individuals may appear to show little or no suppression when only the broadband TEOAE is examined (Berlin et al., 1993a). Berlin et al. (1993a) reported that in their sample of normal hearing participants, those who showed little change in the broad-band OAE level with contralateral stimulation actually showed measurable suppression when the emission was examined in the time domain. Further study has indicated that when suppression is examined across the time waveform, suppression is greatest in the later post-stimulus time periods (e.g., Berlin, Hood, Wen, Szabo, Cecola, Rigby, & Jackson, 1993b; Veuille et al. 1991). Hood et al. (1996) examined the suppression effect over the TEOAE time waveform by averaging TEOAE amplitude across the 8-18 ms post-stimulus time period. The magnitude of TEOAE suppression in the full 20 msec time window was compared to the magnitude of TEOAE suppression in the 8-18 msec time window. Contralateral TEOAE suppression was greater in the 8-18 msec time window than across the entire 20 msec time window for 39 of the 48 participants. Velenovsky and Glatke (2002) analyzed the TEOAE in 2 ms time intervals and reported statistically significant contralateral suppression effects at all time intervals

except for 2-4 ms and 18-20 ms. Greater suppression may be seen in the later time intervals as a result of the response properties of the MOC neurons. Liberman and Brown (1986) studied the response properties of the MOC neurons to acoustic stimulation by surgically exposing the neurons in cats. The researchers found the response of the MOC neurons to have a long latency (5-50 ms) to low sound levels. Berlin et al. (1993b) proposed that greater suppression may be seen in the later time intervals, because it may take at least 4 ms for the information to travel to and back from the olivocochlear neurons.

Graham and Hazell (1994) reported that there is significant variability in the magnitude of suppression. Hood (2002) stated that all normal hearing individuals show suppression in some time interval. The total absence of suppression in the amplitude, time and frequency domain is defined as an abnormality. A total absence of suppression has been reported in patients with auditory neuropathy (e.g., Berlin et al. 1993b). Reduced or absent suppression also has been documented in patients with lesions of the brainstem which can affect the efferent pathway. Prasher, Ryan, and Luxon (1994) reported reduced contralateral TEOAE suppression in participants with extrinsic (cerebello-pontine angle lesion) and intrinsic (e.g., brain-stem demyelination) lesions in the brainstem compared with normal-hearing individuals. Ototoxic drugs can also have an effect on suppression. Aran, Erre, and Avan (1994) found the suppression affect of TEOAEs disappeared when guinea-pigs were administered gentamicin.

Several research studies have investigated gender differences in TEOAE suppression. Multiple studies have found no significant differences between females and males in the amount of suppression resulting from binaural or contralateral stimulation

(e.g., Brashears et al. 2003; Khalfa & Collet, 1996; Khalfa, Veuillet & Collet, 1998).

However, Barham, Berlin, Hood, Hurley, and Wakefield (1995) found that the absolute amount of TEOAE suppression in three noise conditions (binaural, ipsilateral and contralateral) was greater for females than males. The size of the difference in the amount of suppression for females and males was not reported by the study.

Methodological Factors and TEOAE Suppression

A variety of factors affect the magnitude of TEOAE suppression, including the type, intensity, and duration of the suppressor and the intensity of the stimulus. The stimulus is defined as the signal that is used to elicit the OAE, typically clicks for TEOAEs, and the suppressor is defined as the signal that is used to elicit the suppression effect. The suppressor stimuli can be speech, pure tones, clicks, narrow-bands of noise, or broad-band noise.

Multiple studies have indicated that broad-band suppressors produce a larger contralateral suppressive effect compared to more narrow-band suppressors (e.g., Maison, Micheyl, Andeol, Gallegno & Collet, 2000; Norman & Thornton, 1993; Velenovsky & Glatke, 2002). Broad-band noise produces greater suppression than narrow-band noise or pure tones (Maison et al. 2000; Norman and Thornton, 1993), and narrow-band noise produces greater suppression than pure tones (Berlin et al. 1993b). Velenovsky and Glatke (2002) studied three noise bands centered at 2000 Hz: narrow-band, wide-band, and equalized (noise adjusted to equal the loudness of wide-band noise). Only wide-band noise produced a significant reduction in TEOAE level. Unlike the other studies, Velenovsky and Glatke (2002) used a probe microphone system to

monitor the noise stimuli and a spectrum analyzer to monitor the noise level and bandwidths.

Several research studies have reported that for a given stimulus level, the amount of suppression increases as the suppressor level increases (e.g., Collet et al. 1990; Berlin et al. 1993b; Hood et al. 1996). Berlin et al. (1993b) noted greater suppression when narrow-band noise was presented contralaterally between 60-80 dB HL and minimal suppression was found when the narrow-band noise was presented between 20-40 dB HL to the contralateral ear. Komazec et al. (2003) found a statistically significant reduction in TEOAE level when broad-band noise was presented to the contralateral ear at 40 and 30 dB SL. However, there was no significant difference in TEOAE level observed when the broad-band noise was presented to the contralateral ear at 20 and 10 dB SL.

Hood et al. (1996) performed a study to investigate the appropriate click and noise levels for contralateral TEOAE suppression in a group of 48 participants with normal hearing ranging in age from 12 to 59 years. Due to the length of time involved in testing each participant at various noise levels, different participants were used for the various click levels assessed, which may have increased the risk for greater variability to exist in the study. The stimulus clicks were presented from 50-70 dB pSPL and the suppressor noise (white noise) varied from 10 dB below the click level to 10 dB above the click level (40-80 dB SPL). The researchers monitored the SPL of the suppressor continuously during testing by using a probe microphone which was placed in the ear canal. The researchers recommended measurement of TEOAE suppression using the linear click presentation mode and a click level of 55 or 60 dB pSPL with the suppressor set 5 dB

higher than the click as suppression was found to be significantly greater at these levels compared to other levels that were assessed in the study.

Several animal studies have examined the effects of the duration of the suppressor and the adaptation of the MOC system (e.g., Brown, 2001; Liberman & Brown, 1986). Liberman and Brown (1986) demonstrated little difference in efferent discharge rate in cats when tone-burst duration was increased from 50 to 500 msec. Brown (2001) studied response adaptation of medial olivocochlear neurons in guinea pigs by surgically exposing the spiral ganglion (core of the cochlea) so that single-fiber recordings of the MOC neurons could be performed. Noise bursts were presented monaurally and binaurally. Brown (2001) found MOC response adaptation was minimal compared to that of auditory nerve fibers for tones and noise presented at durations of 500 ms and 10 s. Brown (2001) concluded that the responses of MOC neurons are relatively constant with time and more constant than the responses obtained from the auditory nerve. Suppression appears to remain stable as long as the stimulus is presented, which suggests an absence of MOC neuron fatigue.

Giraud, Collet, and Chery-Croze (1997) studied the effects of varying the noise duration on contralateral suppression of TEOAEs on human subjects. The presentation of the contralateral noise was delayed by a variable amount of time (0, 10, and 180 s) and the duration of the noise was also varied (1 min, 1 min 10 s, and 4 min). Giraud et al. (1997) found no significant change in contralateral suppression for TEOAEs when the duration of the noise was changed from 1-4 minutes. However, the researchers did not report on the purpose and possible effects of the delay of presenting the contralateral

noise. The researchers propose 4 minutes may have not been long enough to cause fatigue of the efferent nerve fibers.

Hood, Berlin, Wakefield, and Hurley (1995) studied the effects of duration of the suppressor on the efferent system in humans. Hood et al. (1995) studied four broad-band noise durations of 80, 160, 240 and 408 msec. The researchers observed suppression to progressively increase as noise duration increased. Suppression increased progressively from 80 to 240 msec but suppression was less for the noise duration of 408 msec.

Despite the results reported by Hood et al. (1995), multiple researchers have used a noise duration of 400 or 408 msec when investigating TEOAE suppression in humans (e.g., Berlin, Hurley, Hood, Bordelon, & Wen, 1996; Brashears et al. 2003; Micheyl & Collet, 1996).

The suppressor can be presented contralaterally, ipsilaterally or binaurally. Contralateral suppression is the most commonly used method of presentation reported in research studies because it is easy to perform. Ipsilateral and binaural suppression are measured utilizing a forward-masking paradigm; the suppressor and stimulus are separated in time resulting in less acoustic interaction of the two signals. Contralateral suppression involves the presentation of the stimulus through the OAE probe and the suppressor through an earphone in the opposite ear; therefore, contralateral suppression can be simultaneous or forward-masked. Berlin et al. (1995) used a forward masking paradigm when studying the effects of binaural, ipsilateral and contralateral suppression and found that binaural noise produced the greatest magnitude of suppression. Berlin et al. (1995) found the amount of suppression to binaural noise for normal hearing listeners was from -2.5 to -4 dB between 8-18 msec. Ipsilateral and contralateral noise both

produced a significant amount of suppression, but the magnitude of suppression did not differ significantly between them.

Berlin et al. (1995) also found that the suppressive effects decreased as the time separation between the offset of the suppressor and the onset of the stimulus increased. The researchers reported that 1 msec time separation between the suppressor and the stimulus was the most effective. There were no significant differences between time separation of 2, 5, 10 and 20 msec and little suppression was observed for a time separation of greater than 50 msec. However, Tavarkiladze, Frolenkov, and Kruglov (1995) found a direct masking effect may occur and interfere if the time separation between the suppressor and stimulus is less than 10 msec. As a result, a time separation of 10 msec is recommended (Hood, 2002).

The Menstrual Cycle

The menstrual cycle refers to the cyclical changes in hormones that occur in the ovaries and uterus (Sloane, 1993). The menstrual cycle is based on a hormone-feedback system that involves the central nervous system and hormones of the hypothalamus, the anterior pituitary gland and the ovaries (Golub, 1992). The four major hormones that regulate the menstrual cycle are lutenizing hormone (LH), follicle stimulating hormone (FSH), estrogen, and progesterone (Ferin, Jewelewicz & Warren, 1993). LH and FSH are produced by the pituitary gland while estrogen and progesterone are produced by the ovaries. The hypothalamus is responsible for monitoring the level of estrogen and progesterone in the blood (Golub, 1992). The hypothalamus secretes a hormone called

the Gonadotropin-releasing-hormone (GnRH) which results in the secretion of LH and FSH from the pituitary gland (Golub, 1992).

In the majority of females, the menstrual cycle lasts between 25 to 30 days (Ferlin et al. 1993). The menstrual cycle can be divided into two main phases: the follicular phase and the ovulatory phase. During the follicular phase, the ovarian follicles begin to grow under the influence of the FSH, and estrogen levels slowly rise (Golub, 1992). FSH will eventually cause a single follicle to fully develop and secrete estrogen. Based on a typical menstrual cycle of 28 days, the follicular phase extends from day 1 to day 14 of the cycle (Golub, 1992). Typically, day 1 of the cycle is defined as the first day of menstruation (discharge of blood from the uterus). The developed follicle will secrete estrogen which inhibits the release of FSH and stimulates the release of LH (Golub, 1992).

LH stimulates the development of the endometrium, which is the mucous membrane that lines the uterus. LH will cause the ovum to be released from the developed follicle. The release of the ovum begins the ovulatory phase. Immediately before ovulation, estrogen levels increase and then fall dramatically as the follicle expends its hormone-producing cells (Golub, 1992). Subsequently, the pituitary gland increases its secretion of LH which is often referred to as the “LH surge” (Golub, 1992; Sloane, 1993). There is also a small increase in FSH that is observed (Golub, 1992). The mean duration of the LH surge is 48 hours (Ferlin et al. 1993). It is estimated that ovulation occurs approximately 18 hours after the LH surge (Ferlin et al. 1993) or 34-36 hours after the initiation of the LH surge (Ferlin, et al. 1993; Sloane, 1993).

The cells left as a result of the ruptured follicle begin to enlarge and eventually become the corpus luteum (Sloane, 1993). The corpus luteum produces progesterone and estrogen, and reaches a peak of activity after ovulation. Progesterone and estrogen reach a maximum six to nine days after the LH surge (Ferin et al. 1993; Sloane, 1993).

If the egg is fertilized, it is then implanted in the endometrium of the uterus. If fertilization does not occur, the corpus luteum function begins to decline about 14 days after ovulation (Sloane, 1993; Golub, 1992). The levels of estrogen and progesterone begin to decline and the uterus lining also begins to shed away, resulting in menstruation (Golub, 1992). At this point, the pituitary gland will begin to secrete FSH due to low levels of estrogen in the blood, resulting in a new cycle (Golub, 1992; Sloane, 1993).

Oral contraceptives, commonly known as birth control pills, contain a combination of synthetic estrogen and progesterone or progesterone only and are used to prevent conception (Shapiro, 1977; Sloane, 1993). Most of the pills are available in 21-28-tablet packages. Birth control pills prevent conception by inhibiting the release of GnRH from the hypothalamus, which stops FSH from stimulating follicles to grow and LH from triggering ovulation (Shapiro, 1977). Furthermore, the estrogen and progesterone in birth control pills causes a thickening of the cervical mucus and changes in the endometrium (Shapiro, 1977). This results in a hostile environment for sperm to penetrate into the ovum. The monthly bleeding that occurs while taking birth control pills is considered a false menstruation produced by the estrogen and progesterone stimulation of the endometrium, which is followed by the withdrawal of the hormones 7 days before the onset of bleeding (Sloane, 1993).

The menstrual cycle and the time of ovulation are commonly monitored using basal body temperature, changes in cervical mucous, the menstrual calendar, or ovulation kits. A very small but statistically significant increase in body temperature is typically observed about 2 days after the peak of the LH surge (Ferin et al. 1993). Basal body temperature must be measured early in the morning before any activity and the measurement must be performed for a period of time. Furthermore, a woman may have shifts in body temperature that are difficult to recognize (Sloane, 1993). The daily variations in temperature are in the range of 0.1 to 0.2 degrees until just before ovulation (Sloane, 1993). An elevation of at least 0.4 degrees that continues for at least 3 days means that ovulation has occurred (Sloane, 1993).

The physical properties of cervical mucous change during the menstrual cycle. The cervical mucous changes as a result of different levels of hormones (Sloane, 1993). Before or near the time of ovulation the mucous is dilute, secreted in great amounts and forms a particular pattern (Sloane, 1993). After ovulation the mucous becomes thicker (Sloane, 1993).

A calendar can be used to monitor the menstrual cycle. This is done by recording the dates of bleeding. As mentioned previously, the first day of bleeding is considered the first day of the cycle. Based on an average 28 day cycle, the time of ovulation would be estimated to be around day 14. The final phase of the menstrual cycle would be estimated to be approximately 7-9 days after the estimated time of ovulation.

Ovulation kits detect changes in hormones, specifically LH. LH can be detected in urine and can assist in approximating the time of ovulation. It is recommended that urine be collected early in the morning as LH is most concentrated at that time. The

participant urinates on a test stick and the color or color intensity is compared to the color in the control window or surge guide provided with the kit. As mentioned previously, it is estimated that ovulation occurs approximately 18 hours after the LH surge (Ferin et al. 1993) or 34-36 hours after the initiation of the LH surge (Ferin, et al. 1993; Sloane, 1993).

Effects of the Menstrual Cycle on Auditory Function

Estrogen may be important in maintaining the function of the auditory system and auditory efferent system. Specifically the lack of estrogen may increase the risk of hearing loss and decrease the possible protective role of the efferent system in humans (Thompson et al. 2006). Research has shown that female mice experienced presbycusis at a faster rate after menopause than before menopause (Guimaraes, Zhu, Cannon, Kim, & Frisina, 2004). Guimaraes et al. (2004) further note that the declines in hearing did not occur until old age-after menopause. Thompson et al. (2006) found contralateral suppression was reduced when tamoxifen (an estrogen blocker) was administered to female mice compared to contralateral suppression when female mice were given a placebo.

Researchers have also speculated that estrogen may cause a change in the speed at which sensory information travels through the auditory brainstem (Elkind-Hirsch et al. 1992). Coleman, Campbell, Cooper, Welsh, and Moyer (1994) studied rats that underwent removal of the ovaries and found shorter brain wave latencies in those rats treated with estrogen replacement than in untreated ovariectomized rats. However, research conducted by Elkind-Hirsch et al. (1992) found prolonged brain wave latencies for female human subjects with premature ovarian failure who were treated with

estrogen-only replacement as compared to shorter brain wave latencies for female human subjects with premature ovarian failure treated with estrogen and progesterone replacement. Estrogen also may have an effect on cochlear blood flow. Laugel et al. (1987) found estrogen treatments significantly decreased cochlear blood flow while progesterone treatments significantly enhanced cochlear blood flow in response to phenylephrine and nicotine in ovariectomized female rats.

Multiple studies have investigated the effects of the menstrual cycle on auditory function, specifically auditory thresholds, temporary threshold shifts, acoustic reflex thresholds, auditory brainstem responses and OAEs. The studies vary widely in methodology. An additional concern is that in several studies the researchers did not define the inclusion criteria used for participants or define what constitutes a normal menstrual cycle.

Auditory Thresholds. Research studies examining auditory sensitivity in females during different phases of the normal menstrual cycle have produced conflicting results. Several studies comparing normally menstruating females not taking oral contraceptives and females taking oral contraceptives have reported no significant differences in hearing thresholds across the menstrual cycle in either group (Grieze-Jurgelevicius et al. 1990; Hori et al. 1993; Schubert, Meyer, & Washer, 1975) while other studies have shown significant changes in auditory thresholds across the menstrual cycle for females not taking oral contraceptives and for females taking oral contraceptives (e.g., Baker & Weiler, 1977; Petiot & Parrot, 1984; Swanson & Dengerink, 1988). For example, Baker and Weiler (1977) found females not taking oral contraceptives had significantly lower (better) thresholds during the first half of the menstrual cycle than during the second half.

In contrast, Swanson and Dengerink (1988) found that females who were not taking oral contraceptives showed lower (better) auditory thresholds during ovulation than during menstruation. In addition, Petiot and Parrot (1984) found that females taking oral contraceptives had higher (worse) thresholds during menstruation and lower (better) thresholds when the pill was taken, but this effect was only significant at 4000 Hz.

Comparisons of auditory thresholds between females not taking oral contraceptives and females taking oral contraceptives have also produced conflicting results. A few studies have found lower (better) thresholds for females on oral contraceptives than for females not on oral contraceptives (e.g., Baker & Weiler, 1977; Schubert et al. 1975; Davis and Ahroon 1982). However, one study found poorer thresholds for females on oral contraceptives than for females not on oral contraceptives (Grieze-Jurgelevicius et al. 1990).

The differences in findings across studies are most likely related, at least in part, to the differences in methodology. For example, several studies performed testing in a sound treated room (e.g., Petiot & Parrot, 1984; Swanson & Dengerink, 1988) while another study performed testing in a small cubicle (Grieze-Jurgelevicius et al. 1990). The equipment used to assess hearing also varied among studies. For example, the Grieze-Jurgelevicius et al. (1990) study used a portable audiometer, the Baker and Weiler (1977) study used a conventional audiometer, and the Petiot and Parrot (1984) study used Bekesy audiometry. Some studies were careful to complete all testing at the same time of day (e.g., Grieze-Jurgelevicius et al. 1990; Swanson & Dengerink, 1988) while other studies did not report on the time of day for testing (e.g., Baker & Weiler, 1977; Davis & Ahroon, 1982). The schedule of testing also differed among studies. For example, the

Baker and Weiler (1977) study tested female participants twice a week until the onset of menses for two cycles, while the Grieze-Jurgelevicius et al. (1990) study tested female participants in the middle of the premenses, menses and postmenses phases. The criteria for what constitutes a normal menstrual cycle in female participants have not always been specified among these studies and monitoring of the menstrual cycle has varied across studies. In addition, these studies have included only a small number of participants per group (typically 4-12).

Several studies have also investigated temporary threshold shift (TTS) across the menstrual cycle. TTS refers to a temporary change in hearing level as a result of a brief exposure to sound. Hori et al. (1993) studied TTS using conventional audiometry and found that males showed larger TTS at certain frequencies than females not taking oral contraceptives in all the phases of the menstrual cycle. TTS for females not on oral contraceptives were smaller during post-ovulation than during pre-ovulation and menstruation at certain frequencies. Davis and Ahroon (1982) also found less TTS during menstruation for females not taking oral contraceptives using Bekesy audiometry.

Petiot and Parrot (1984) studied the effects of the menstrual cycle and oral contraceptives on TTS using Bekesy audiometry in three groups of participants: females not taking oral contraceptives, females on oral contraceptives, and males. The study revealed that females on oral contraceptives showed greater TTS at selected frequencies than females not taking oral contraceptives. This difference was most apparent during the beginning (menstruation) of the contraceptive cycle. Furthermore, females on oral contraceptives showed a faster recovery from noise exposure than females not on oral contraceptives, particularly at 4000 Hz.

Physiological Measures. Studies have documented changes in physiological measures such as the acoustic reflex, the auditory brainstem response (ABR) and OAEs across the menstrual cycle. Acoustic reflex threshold testing assesses the function of the middle ear system and the auditory neural pathway by measuring the reflexive contraction of a small muscle (stapedius) in the middle ear in response to loud sounds. Laws and Moon (1986) found that the reflex threshold for females not taking oral contraceptives showed significantly greater variability from day to day than for male participants. Mean acoustic reflex thresholds obtained from females for one complete menstrual cycle and the mean acoustic reflex thresholds for males obtained for a period of 28 days differed only by 1.55 dB. However, females needed about a 6 dB louder stimulus level to elicit the acoustic reflex thresholds during days 1-6 (menstruation) than during days 7-26. There was a peak of sensitivity, that is, a lower acoustic reflex threshold, between days 15-19 (post-ovulation).

The ABR is a neurological test that assesses the function of the brainstem in response to auditory stimuli. Several research studies have examined the effects of female sex hormones on the latency of waves of the ABR to clicks; however, the results have been conflicting. Yadav, Tandon, and Vaney (2002) studied ABR during the different phases of the menstrual cycle in 20 normal cycling females not taking oral contraceptives. ABR waves were recorded using alternating 90 dB SPL click stimuli. All participants recorded their basal body temperature for two months to document ovulation. Participants were tested four times in one menstrual cycle: menses (1-3 days), mid-cycle (11-15 days), post-ovulation (17-22 days) and pre-menstrual (25-27 days). The results of the study revealed no significant differences in peak latencies, inter-peak latencies and

amplitudes of ABR waves during the different phases of the menstrual cycle. Similarly, Howard, Mason, Taghavi, and Spears (1992) found no change in ABR wave latencies at different phases of the menstrual cycle for 30 females with premenstrual problems and for 20 healthy female controls with no menstrual problems. Neither group in this study was taking oral contraceptives. ABR waves were recorded using clicks presented 70 dB above the participant's hearing threshold. Participants were tested during menses (days 0-5) and mid-cycle (days 12-14).

In contrast, other studies have reported increases in ABR peak and inter-peak latencies during certain parts of the menstrual cycle. Elkind-Hirsh et al. (1992) studied ABR waves in response to alternating polarity clicks presented at 70 dB nHL in nine normally cycling females not taking oral contraceptives and a group of nine females on oral contraceptives. ABR waves were measured four times during a single cycle: early follicular (days 1-3), mid-cycle (days 12-15), post-ovulation (days 17-22) and premenstrual (days 25-27). Blood samples were taken before each test to assess estrogen, progesterone, LH and FSH levels. The researchers reported a significant increase in wave III and wave V peak latencies and in the I-V inter-peak latency during the mid-cycle phase (ovulation) for females not taking oral contraceptives. The researchers believe that this may suggest that the brainstem is sensitive to the increase in estrogen that is associated with during mid-cycle. No significant differences were found in ABR wave V latency or wave I-V inter-peak latency for the females taking oral contraceptives. A gradual and significant increase in wave III peak latency was found in this group when on oral contraceptives from day 8-28 (this includes all phases of the cycle except menstruation). The researchers believe that this may have been due to the hormone

replacement. The latencies of wave I in both groups of subjects varied little across the menstrual cycle. Furthermore, no significant difference in amplitude of wave V was observed between the two groups.

Zani (1989) studied ABR waves in four female athletes not taking oral contraceptives and four female athletes taking oral contraceptives. ABR waves were recorded using click stimuli presented at 65 dB SPL. All participants recorded their basal body temperature and mood for two cycles. Testing was scheduled during the second day of menses, ninth day of the follicular phase, between the 14th and 15th day of the ovulation phase and between the 23rd and 24th day of the pre-menstrual phase. Zani (1989) found females not taking oral contraceptives showed a longer latency for wave V during menstruation compared to during ovulation and a sharp decrease in wave V latency during pre-menstruation. However, females taking oral contraceptives showed a stable trend in wave V latency during the menstrual cycle.

Still other studies have reported decreases in amplitude, peak and inter-peak latencies of ABR waves during certain parts of the menstrual cycle. Tasman, Hahn and Maiste (1999) studied ABR waves recorded using click stimuli presented at 70 dB (scale not specified) in 19 females not taking oral contraceptives. Participants recorded their mood, basal body temperature, time of menses and LH surge test results for two months. ABR waves were recorded three days a week at the same time of the day for one complete cycle. The researchers found a decrease in amplitude of ABR waves I and III and a decrease in wave V latency and the wave III-V inter-peak latency across all phases of the menstrual cycle (from the follicular phase through the ovulatory phase to the premenstrual phase). Caruso et al. (2003) studied ABR in 94 females taking a variety of

oral contraceptives. ABR waves were recorded using click stimuli presented at 100 dB pSPL. Prior to the participants taking any oral contraceptives, sonography was performed on days 10, 12 and 15 of the menstrual cycle to document ovulation. In addition, on days 21 and 25, serum hormone concentrations were taken. Once ovulation was confirmed, participants were then prescribed an oral contraceptive. All participants were tested on days 7, 14 and 21 of taking the pill. The results revealed shorter wave I latency and inter-peak latency I-V during days 13-16 than days 18-23 and the follicular phase (days 5-8). No statistically significant difference was observed in wave latencies and inter-peak latencies for the different types of oral contraceptives that were used by the female participants.

Several research studies have shown effects of the menstrual cycle on SOAEs in small groups of participants. Penner, Brauth and Jastreboff (1994) studied SOAE frequencies across the menstrual cycle in two female participants not taking oral contraceptives with regular menstrual cycles and binaural SOAEs (SOAEs in both ears). Testing was performed once daily for a single cycle, and the participants were tested approximately the same time each day to avoid changes due to the circadian rhythm (a daily rhythmic activity cycle that is based on a 24 hour interval). Monaural and binaural SOAE frequencies shifted across the menstrual cycle with a minimum SOAE frequency preceding menstruation and a maximum SOAE frequency near the time of ovulation.

Penner (1995) studied SOAEs in a female with a normal menstrual cycle from days 1-44, which was then followed by amenorrhea (absence of a period) from days 45 to 225. The subject was given an oral contraceptive from days 226 to 295 to reestablish her menstrual function. All testing was performed between 4 and 5 p.m. to rule out the

influence of circadian rhythms on SOAE frequencies. Penner (1995) found that the SOAE frequencies decreased just before menstruation and increased just after the onset of menstruation. Less fluctuation of SOAE frequencies was found when the participant used oral contraceptives. The averaged standard deviation for SOAE frequencies for both the right and left ears while the participant was on a oral contraceptive was 4.7 Hz. However, the averaged standard deviation for SOAE frequencies for both the right and left ears while the participant was not on the oral contraceptive (during the normal menstrual cycle) was 7.9 Hz.

Bell (1992) reported that both cycle and circadian rhythm affect SOAEs. Bell (1992) studied SOAE frequencies in a small group of female participants not taking oral contraceptives. The participants were monitored daily from less than a month up to seven months. The results of the study revealed regular circadian variations in the frequencies of SOAEs in two of the three participants studied. A rise in frequency of 0.6 - 1% was noted while the participant was asleep and a drop of approximately 0.6-1% was noted while the subject was awake. Similar to the Penner et al. (1994) study, Bell (1992) found that SOAE frequencies rose and fell by 0.4 - 0.6% with a minimum level near the beginning of menstruation and rising to a peak near ovulation.

Haggarty et al. (1993) evaluated eight females not taking oral contraceptives and found a significant frequency fluctuation in SOAEs. The mean fluctuation was 16.3 Hz and the standard deviation was 6.4 Hz. The majority of SOAEs (22 of the 31 SOAEs) varied by .5 to .8 %. Haggarty et al. (1993) did not find frequency fluctuation in SOAEs for males in their study. The authors hypothesize that the fluctuation in SOAE frequencies may be attributed to the monthly menstrual cycle and propose that the

frequency variation of the SOAEs may be due to a direct effect of the hormones on the auditory efferent neurotransmitters. The researchers also studied the effect of the circadian rhythm on one male and one female subject for 24 hours. The results of the study revealed a significant 24 hour variability of frequency for each SOAE for both the male and female participant. The greatest and smallest change in SOAE frequencies were seen at nine and 15 Hz. The mean fluctuation in SOAE frequencies was .7 and .6% for the female participant and the mean fluctuation in SOAE frequencies was .4 to .6 % for the male participant. The researchers believe that these results suggest the possible influence of the circadian rhythm on SOAEs.

Yellin and Stillman (1999) compared changes in body temperature to the level of SOAEs as well as to the level of TEOAEs and distortion-product OAEs (another type of evoked OAE) across the menstrual cycle. They tested the right ear only for 13 females not taking oral contraceptives aged 25-49 years. Testing was performed within 3 days of menses and thereafter at 7 day intervals over 12 weeks. Testing was completed within 2 hours of the time of the first session. Prior to OAE testing, normal middle ear function was verified by tympanometry and body temperature was taken by an oral digital thermometer. A slight increase in body temperature was observed around mid-cycle, however there was no relationship found when changes in body temperature were compared to changes in TEOAEs, SOAEs and DPOAEs. There are several questions that arise in regards to the procedure used to record body temperature. The researchers report that temperature was taken at each session but do not specify whether temperature was taken before or after activity. As mentioned previously, it is well documented that there is a very small but significant increase in body temperature approximately two days after

the LH surge (Ferin et al. 1993). Basal body temperature must be measured early in the morning before any activity and the measurement must be performed for a period of time. Furthermore, a woman may have shifts in body temperature that are difficult to recognize (Sloane, 1993). As a result, the slight increase in body temperature observed around mid-cycle reported in the Yellin and Stillman (1999) study may have been attributed to other variables that were not well controlled. In regards to the study on TEOAEs and DPOAEs, the researchers only analyzed broad-band levels and not frequencies. Yellin and Stillman (1999) found no systematic change in level in TEOAEs and DPOAEs across the menstrual cycle. However, SOAEs were found to be more numerous early in the menstrual cycle, gradually decreasing in number during the course of the cycle to a low at the end of the cycle.

To date, little information is available on how the menstrual cycle effects OAE suppression. Hurley et al. (1996) conducted a pilot study on a small sample to investigate efferent suppression of TEOAEs across the menstrual cycle. The researchers studied efferent suppression in the right ear only in six females not taking oral contraceptives and three females taking oral contraceptives. Clicks were presented at 60 dB SPL using the “linear” paradigm and white noise (400 ms in duration) was presented at 65 dB SPL binaurally in a forward masking paradigm. The time between the end of the noise and the start of the click was 10 msec. A total of four recordings were taken (two runs without any noise present and two runs with noise present). In their sample, unsuppressed TEOAE level (recorded without any noise present) was lower during menstruation than the other phases of the menstrual cycle for both groups of females. However, TEOAE suppression was stable across the menstrual cycle. No statistically

significant difference in SOAE levels by frequency or by day was found for the four participants not taking oral contraceptives and two participants taking oral contraceptives who had SOAEs. The changes observed in the Hurley et al. (1996) pilot study might be due to uncontrolled variables, such as middle ear function, particularly middle ear pressure, and noise exposure. Hurley et al. (1996) performed tympanometry only once at the beginning of the experiment. Furthermore, no information was provided on the criteria used for inclusion into the study to ensure that female subjects had a normal regular menstrual cycle. The participants were tested every weekday morning; however, verification of menstruation or ovulation by subject report, calendar counting, basal body temperature, cervical mucous monitoring, or an ovulation predication kit method were not reported.

Summary and Purpose

Several research studies have shown effects of the menstrual cycle on different auditory behavioral measures (Baker & Weiler, 1977; Davis & Ahroon, 1982; Elkind-Hirsh et al. 1992; Petiot & Parrot, 1984; Schubert et al. 1975; Tasman et al. 1999). However, this area of research is also plagued by contradictory findings likely due, at least in part, to differences in methodology. Examples of differences in methodology among the studies include the place of testing, the type of equipment used, the time of day testing was performed, and the method for scheduling of testing based on the participant's menstrual cycle. The criteria for what constitutes a normal menstrual cycle in female participants have not always been specified, and the method of monitoring the menstrual cycle has varied across studies.

Changes in SOAEs across the menstrual cycle have been reported in several studies (e.g., Haggarty et al. 1993; Bell, 1992). Little information exists on the impact of the menstrual cycle on unsuppressed TEOAE levels or TEOAE suppression other than the pilot study by Hurley et al. (1996). Hurley et al. (1996) reported that TEOAE level (without any noise present) was lower during menstruation than the other phases of the menstrual cycle but that TEOAE suppression did not change significantly across the menstrual cycle. However, Hurley et al. (1996) did not monitor for middle ear status or noise exposure and did not report on criteria for inclusion or means of monitoring the menstrual cycle.

The purpose of this study is to investigate the effects of the menstrual cycle on binaural TEOAE suppression in three different groups of participants: females with normal menstrual cycles not taking oral contraceptives, females with normal menstrual cycles taking oral contraceptives, and healthy male controls. Such information would be important in developing normative data for clinical diagnostic use of this procedure and could help explain how female sex hormones affect the functioning of the central auditory nervous system.

Chapter 3: Experimental Questions and Hypotheses

Experimental Questions

The specific experimental questions that were addressed were:

1. a. Does unsuppressed (without noise) broad-band TEOAE level change across a period of one month (one menstrual cycle) in the three participant groups: females with normal menstrual cycles not taking oral contraceptives, females with normal menstrual cycles taking oral contraceptives, and males?
 - b. If so, are the changes similar across groups?
2. a. Does unsuppressed (without noise) TEOAE level at specific frequencies change across a period of one month (one menstrual cycle) in the three groups?
 - b. If so, are the changes similar across groups?
3. a. Does the magnitude of change in broad-band TEOAE level following presentation of binaural noise (TEOAE suppression) differ across a period of one month (one menstrual cycle) in the three groups?
 - b. If so, are the changes similar across groups?
4. a. Does the magnitude of change in TEOAE level following presentation of binaural noise (TEOAE suppression) in specific post-stimulus time intervals change across a period of one month (one menstrual cycle) in the three groups?
 - b. If so, are the changes similar across groups?
5. a. Does the change in TEOAE level following presentation of binaural noise (TEOAE suppression) at specific frequencies change across a period of one month (one menstrual cycle) in the three groups?

- b. If so, are the changes similar across groups?

Hypotheses

It was hypothesized that unsuppressed broad-band TEOAE level and level of TEOAEs at specific frequencies would change across the period of one month (one menstrual cycle) in females with normal menstrual cycles not taking oral contraceptives but would be stable across a period of one month (one menstrual cycle) in females with normal menstrual cycles taking oral contraceptives and in males. This is consistent with research studies on TEOAEs, SOAEs and physiologic measures (e.g., Haggarty et al. 1993; Hurley et al. 1996; Laws & Moon, 1986; Penner, 1995).

It was hypothesized that the magnitude of change in broad-band TEOAE level following the presentation of binaural noise (TEOAE suppression) would change across the period of one month (one menstrual cycle) in females with normal menstrual cycles not taking oral contraceptives but would be stable across the period of one month (one menstrual cycle) in females with normal menstrual cycles taking oral contraceptives and in males. The change in TEOAE level following the presentation of binaural noise (TEOAE suppression) in specific post-stimulus time intervals and at specific frequencies would change across a period of one month (one menstrual cycle) in females with normal menstrual cycles not taking oral contraceptives but would be stable across a period of one month (one menstrual cycle) in females with normal menstrual cycles taking oral contraceptives and in males. This is consistent with research on SOAEs and physiological measures, which

have shown greater fluctuation of SOAE frequencies and acoustic reflex thresholds for females not taking oral contraceptives than males (Haggarty et al. 1993; Laws & Moon, 1986). In addition, Penner (1995) found less fluctuation of SOAEs when a female participant took oral contraceptives.

Chapter 4: Methodology

Participants

Three groups of adult participants aged 18-35 years participated in this study. Fifty-one participants were screened for eligibility. Of these, 21 participants were determined to be ineligible to participate (see below). Testing was completed on the remaining 30 participants. Group One consisted of 10 females with normal hearing thresholds and “normal” (25-35 days) menstrual cycles. The females in Group One did not take any hormone-based contraceptives. Group Two consisted of 10 females with normal hearing thresholds and normal menstrual cycles who were taking oral contraceptives. Group Three consisted of 10 males with normal hearing thresholds. Participants were recruited from the student body and staff of the University of Maryland, College Park, MD. All procedures were approved by the University of Maryland, College Park IRB.

Initial Testing and Screening for Eligibility

All testing was conducted in the Hearing Clinic and the Auditory Physiology Laboratory in the Department of Hearing and Speech Sciences at the University of Maryland, College Park, Maryland. Data collection on each participant was completed over several sessions. During the initial session, following completion of the informed consent (Appendix A), each participant was asked to complete a case history to assess general and otologic health (Appendix B). Female participants also completed a questionnaire on regularity of the menstrual cycle and methods of contraception

(Appendix C). The questionnaires were reviewed orally with the participant by the investigator for any necessary clarification.

Each participant was weighed on a scale and provided his/her height (self-report) so that the Body Mass Index (BMI) could be calculated. BMI was calculated using the following formula: $(weight\ in\ lbs / height\ squared\ in\ inches) \times 703$. The purpose of calculating the BMI was to ensure that female participants did not have a body fat issue that might interfere with a regular menstrual cycle. Obesity (e.g., Pasquali, Patton, & Gambineri, 2007) and low BMI (e.g. Castelo-Branco, Reina, Montivero, Colodron, & Vanrell, 2006) have been associated with irregular menstrual cycles. All participants were required to have a normal weight for their height as determined by BMI of 18.5-24.9.

Following completion of the history and questionnaire forms, routine audiometric testing was performed in a double-walled, sound-attenuated booth. Testing was completed on both ears. Otosopic inspection was performed to rule out any obvious abnormalities or pathology of the outer and middle ear. Hearing sensitivity was assessed by air conduction using pure tones from 250-8000 Hz, and by bone conduction using pure tones from 500-4000 Hz. Speech reception threshold was also determined using spondee words presented via monitored live voice. Normal hearing sensitivity was defined as pure tone thresholds less than or equal to 20 dB HL from 250-8000 Hz and the absence of any air-bone gaps greater than 10 dB at one or more frequencies.

Normal middle ear function was confirmed using acoustic immittance measures. Tympanometry and acoustic reflex threshold testing were conducted using the GSI-33 middle ear analyzer and a 226 Hz probe tone. Normal middle ear pressure was defined in

this study as -50 to $+50$ daPa, because research has shown that pressure less than -100 daPa can affect the recordings of OAEs (e.g., Trine, Hirsh, & Margolis 1993). Normal static admittance was defined in this study as .3 to 1.3 ml, slightly more conservative than the .3 to 1.5 mmho normative range defined for normal-hearing young listeners by Roup, Wiley, Safady, and Stoppenbach (1998). Acoustic reflexes were measured ipsilaterally and contralaterally using tonal stimuli at 500, 1000 and 2000 Hz and using a broad-band noise (bandwidth = 125-4000 Hz). Tones and broad-band noise were presented at levels between 50 and 110 dBHL. The acoustic reflex threshold was established by presenting the stimulus in an ascending manner in 5-dB steps to determine the lowest level at which an admittance change of at least 0.02 mmho was observed and could be repeated at least twice. Normal acoustic reflex thresholds for tones were defined as 70-100 dB HL (Gelfand, Schwander, & Silman 1990; Silman & Gelfand, 1981). Acoustic reflex thresholds for broad-band noise were required to be 60 dB HL or higher to prevent the contraction of the stapedius muscle in response to the 65 dB SPL broad-band noise that was used during suppression testing (conversion of HL to SPL is + 7dB per the GSI-33 manual).

Participants were also screened for TEOAEs and SOAEs using the Intelligent Hearing System (IHS) Smart TrOAE (version 2.60) system. For the TEOAE screening, clicks (75 usec) were presented in the non-linear mode to each ear at 80 dB pSPL, and 1024 averages were collected. Participants were required to have TEOAE signal-to-noise-ratios (SNRs) of 6 dB or greater in at least three out of four frequency bands tested (2000, 3000, 4000 and 5000 Hz) and 80 percent or greater reproducibility for the broad-band click-evoked OAE in order to be eligible to participate.

The SOAE screen was performed in the right ear only. Clicks (75 usec) were presented to the ear at 60 dB pSPL and 1024 averages were collected. An SOAE was considered present if the SOAE was 6 dB above the noise floor. SOAE screenings were originally performed using the Otodynamics ILO88 system; however, a malfunction with this equipment necessitated a switch to the IHS Smart TrOAE system. SOAE screening was performed using the Otodynamics system on 6 participants at the initial session prior to the change, and the data for these participants could not be retrieved from this system. However, a hard copy of the data was available for participant FM5 (FM: female not on oral contraceptive). SOAEs were present only in seven out of the 25 participants tested. Specifically, SOAEs were present in five females not on oral contraceptives, one female on an oral contraceptive, and one male.

Following completion of the audiometric evaluation, participants were informed of their hearing test results and their eligibility to continue in the study. Eligible participants had normal hearing sensitivity, normal middle ear function and measurable TEOAEs as indicated by the criteria outlined above. In addition, participants were excluded if they had a history of exposure to noise or ototoxic medications, a family history of hearing loss (except of history of presbycusis), dizziness, tinnitus, or a history of middle ear pathology or surgery, as determined from the case history form (Appendix B).

Female participants in Groups One and Two were required to have a normal menstrual cycle. A normal menstrual cycle was defined as ranging from 25-35 days. Participants in Group One could not have used hormone-base contraceptive (such as ‘the pill’) for at least the previous two months. Group Two participants were required to be taking oral contraceptives regularly (no missed pills within the last 90 days). Female

participants were required to have a negative history of irregular menstrual periods and of pregnancy within the last 3 months. Female participants that used other hormone-based contraceptives other than an oral contraceptive (the pill) were not included in the study to reduce potential sources of variability. Participants were also excluded from participating in the study if oral contraceptives were prescribed to regulate the menstrual cycle. All included participants had negative history for hormonal disorders or diseases such as a thyroid disorder or kidney disease, for medications that affect hormones such as Danazol (Danocrine), or for hormonal replacement therapy. The restrictions on disorders, medications and body weight that affect hormones were necessary, because these factors can interfere with the normal menstrual cycle.

Of the 51 participants originally screened for eligibility, 21 participants did not qualify. Participants were excluded from the study for the following reasons: history of depression, history of excessive cerumen, history of hearing loss, use of other form of birth control other than the “pill”, birth control taken to regulate the menstrual cycle, menstrual cycle longer than 35 days, and body-mass index outside of the normal ranged defined in this study. Table 1 lists the basic demographic information for the 30 participants who qualified to participate in the experimental portion of the study.

Unlike previous studies which have utilized basal body temperature, menstrual calendar, or subject report to monitor females with spontaneous menstrual cycles, this study used a combination of a menstrual calendar and an ovulation prediction kit. The use of an ovulation prediction kit is considered reliable in estimating ovulation. Guida et al. (1999) found the correlation between ultrasonographic diagnosis of ovulation and detection of LH levels using the ovulation prediction kit to be 1.0, while the correlations

Table 1. *Demographic information on the 30 participants included in data analysis.*

Participant Number	Menstrual Cycle Length (days)	Oral Contraceptive	Race	Auditory Thresholds for Right Ear at 1, 2, and 4 kHz (dB HL)			SOAEs for Right Ear (kHz)
FM1	28	-	White	5	5	10	No Data
FM5	32	-	Black	15	10	5	977, 1550, 1758, 1917, 2478, 2637, 3870, 4907, 1062
FM6	34	-	Asian	10	10	5	Absent
FM7	35	-	White	15	10	0	1445
FM8	30	-	Asian	5	10	10	1172, 1211, 1562
FM10	28	-	White	0	5	-5	1680
FM11	25	-	Asian	0	0	0	1055, 1094
FM12	33	-	Black	10	10	10	1445, 1484, 2031, 3008, 4140
FM14	30	-	White	10	15	10	Absent
FM16	32	-	White	15	15	15	Absent
FOC1	31	Ortho Tri-Cyclen	White	10	10	5	No Data
FOC2	29	Triphasil-28	White	10	5	0	No Data
FOC4	28	Desogen	White	10	5	5	No Data
FOC5	29	Ortho Tri-Cyclen Lo	White	10	10	0	No Data
FOC7	29	Alesse (Avian)	White	20	20	15	Absent
FOC8	29	Portia	White	10	10	10	Absent
FOC9	30	Ovcon	White	5	5	10	Absent
FOC10	30	Ortho Tri-Cyclen Lo	White	10	5	5	Absent
FOC11	29	Ortho Tri-Cyclen Lo	White	10	5	5	1523, 3515
FOC13	28	Ortho Tri-Cyclen Lo	White	5	10	10	Absent
M1	-	-	White	15	10	10	Absent
M2	-	-	Asian	10	5	5	Absent
M3	-	-	White	10	5	0	Absent
M4	-	-	White	0	5	5	Absent
M5	-	-	Black	10	5	5	Absent
M6	-	-	Asian	5	0	0	2695
M7	-	-	White	10	5	5	Absent
M10	-	-	White	15	20	20	Absent
M11	-	-	White	10	10	5	Absent
M13	-	-	White	0	10	10	Absent

Note. Participant numbers beginning with “FM” denote females not on oral contraceptives. Participant numbers beginning with “FOC” denote females on oral contraceptives. Participant numbers beginning with “M” denote male participants.

between ultrasonographic diagnosis of ovulation and prediction of ovulation using cervical mucus or basal body temperature were only .48 and .30, respectively.

Experimental TEOAE Measurement

All TEOAEs were measured using the Intelligent Hearing System (IHS) Smart TrOAE (version 2.60) system. Only the right ear was tested for each participant for experimental TEOAE measures. The OAE probe (Etymotics 10D) was placed at the start of the session and the same probe fit was maintained for all data collection. The stimuli for TEOAE measurement were clicks (75 usec) presented at a level of 60 dB pSPL. Each TEOAE recorded was the averaged response to 1024 stimulus presentations. The “linear” stimulus presentation mode was used for all TEOAE measurements. The IHS Smart TrOAE system bandpass filters the TEOAE response from 500 to 5000 Hz.

As mentioned previously, when TEOAEs are measured, response waveforms are alternately saved in two separate memory buffers such that, upon completion of testing, two averaged waveforms have been simultaneously collected. These two waveforms (A and B) are compared with one another and a cross-correlation analysis is performed. Measurement systems, including the IHS system, then provide the user with the overall level of the TEOAE, which is the peak-to-peak level of the correlated portions of the A and B waveforms. This level is referred to as the “broad-band TEOAE level” in this document. The IHS system also provides the user with the level of the noise (difference between A and B waveforms) and the TEOAE and noise levels in specific frequency bins (resolution is approximately 40 Hz).

Suppression was achieved using presentation of a broad-band noise presented binaurally at 65 dB SPL. The bandwidth of the broad-band noise suppressor varied depending on the type of transducer utilized. For the ipsilateral side using the OAE probe, the bandwidth of the noise was 50 to 16,000 Hz. For the contralateral side using an insert earphone, the bandwidth was 50 to 8000 Hz. A forward masking paradigm was used, such that the suppressor noise was always presented to both ears 10 ms before the stimulus/click in time. The suppressor noise was 400 ms in duration for both ears.

The level of presentation for the clicks was chosen based on the work of Hood et al. (1996). These researchers found TEOAE suppression to be greater when the click level was set at 55 or 60 dB pSPL and the suppressor set 5 dB higher than the click. Binaural suppression was selected based on the work of Berlin et al. (1995) who found binaural suppression to result in greater suppression than ipsilateral and contralateral suppression. Broad-band noise was chosen to be the suppressor based on the work of Maison et al. (2000) and others who found broad-band noise suppressors to produce a larger suppressive effect than narrow-band noise suppressors. A forward masking paradigm was designed to separate the suppressor and stimulus in time so less acoustic interaction of the two signals occurred. Tavarkiladze et al. (1995) found that the stimulus and suppressor may interfere if the time separation between the suppressor and stimulus is less than 10 ms. As a result, a time separation of 10 ms is recommended (Hood, 2002) and was utilized in the current study. The suppressor noise was set to a 400 ms duration based on the multiple studies that have used this setting (e.g., Berlin et al. 1995; Brashears et al. 2003; Hurley et al. 1996).

Two TEOAE responses were measured following the binaural presentation of noise (with-noise condition) and two TEOAE responses were measured without noise (without-noise condition). The order of presentation of with-noise and without-noise conditions was interleaved and the starting condition was counterbalanced across subjects, as well as for each test session. Individual test runs for conditions “-with noise-” and conditions “-without noise-” were accepted only if the artifact rejection rate was less than 50%. In addition the stimulus click waveform was visually inspected to ensure ringing did not occur after 2 msec. If a particular TEOAE measurement did not meet these criteria, then that individual test run was discarded and repeated.

Suppression of TEOAEs was repeated in the right ear at three test sessions (see below). Tympanometry and acoustic reflex thresholds for tones were also repeated at each test session to verify normal middle ear function for both ears on each day of testing. As mentioned previously, middle ear pressure had to be within -50 to +50 daPa and acoustic reflex thresholds to tones had to be within 70-100 dB HL. Middle ear pressure values were within 0-15 daPa of one another across the three sessions for all participants, with the exception of four participants (FM16 = 10-35 daPa, FOC4 = 15-20 daPa, FOC8 = 10-40 daPa, and FOC13 = 5-25 daPa). All participants had acoustic reflex thresholds within 0-10 dB of one another across the three sessions, with the exception of three participants (FOC13 = 10-15 dB, M1 = 0-15 dB, and M13 = 0-20). No participants in this study had abnormal middle ear function on any of the test days.

If the SOAE screening at the initial visit revealed present SOAEs, the SOAEs screening was repeated at the three test sessions (Note. Screening for SOAEs on five participants who were initially tested using the ILO88 system was not repeated because

their initial data was lost. However a hard copy of the data was available for participant FM5, and an SOAE screening was repeated at every session for FM5).

All participants were counseled to avoid exposure to excessive noise for 48 hours prior to each of the test sessions. To rule out noise exposure prior to suppression testing, participants were asked before each test session if they had been exposed to excessive noise in the previous 48 hours. No participants reported being exposed to excessive noise prior to each test session. In addition, auditory threshold was re-assessed at 4000 Hz in the right ear only during each of the three TEOAE suppression test sessions. The threshold at 4000 Hz for the right ear was required to be within 15 dB of the threshold obtained during the initial audiological evaluation. Thresholds at 4000 Hz for the right ear were within 0-5 dB across sessions for all female participants and within 0-10 dB for all male participants. No participants in this study were suspected of noise exposure.

Female participants were asked prior to each test session if they had become pregnant or suspected they were pregnant. No participants in this study became pregnant or suspected they were pregnant. To rule out the circadian rhythm effects, all participants were tested at approximately at the same time during the evening for all sessions, because research has shown an effect of circadian rhythm on OAEs (Yellin & Stillman, 1999).

Schedule of Testing

Participants were tested over a total of three to four sessions. The schedule of testing for each of the three participant groups is explained below.

Group One. Female participants in Group One with spontaneous normal menstrual cycles (not taking oral contraceptives) were tested for a total of four sessions. The first session consisted of the questionnaires and routine audiometric testing explained

above. Experimental TEOAE measurements were performed in three subsequent sessions. Female participants in Group One were asked to mark the start and end of menstruation on a calendar provided by the experimenter (Appendix D) for one complete cycle (first day of last menses to the first day of next menses). The experimenter scheduled the remaining appointments for testing based on the participant's menstrual calendar and LH test results. The second session was scheduled during the first three days of menstruation. During the second session, female participants of this group were be provided with an ovulation prediction kit (ClearPlan Easy Ovulation Test Pack) and were asked to monitor their LH for approximately seven days to assist the experimenter in determining the period of ovulation. LH tests have been shown to be most accurate in detecting ovulation and to be superior to basal body temperature charting, calendar calculation methods, or observation of vaginal or cervical discharge (e.g., Guermandi, Vegetti, Branchi, Uglietti, Ragni, & Crosignani, 2001). The participant was instructed to perform the testing of LH during mid-cycle based on the menstrual calendar. The participant was provided with seven test sticks and each stick was labeled with a number. For example, test stick labeled with a number "1" was used by the participant on day one. This assisted the experimenter in distinguishing between the various test sticks. Specific instructions provided by the manufacturer of the ovulation prediction kit were reviewed with the participant. The participant was instructed to perform the test in the early morning. The participant was instructed to urinate onto a test stick. The participant documented a change in color or color intensity compared with the color in the control window or surge guide provided with the kit. The participant was asked to store each test stick in a sealed zip-lock bag so that the experimenter could verify the results. An attempt

was made to schedule the third test session during the initial observation of the LH surge, which occurs just before ovulation. The LH surge is believed to last approximately 48 hours. Half of the participants were tested on the day the LH surge was detected and the other half of the participants were tested the next day. The fourth session was scheduled on a day between 7-9 days after the LH surge.

Group Two. Female participants in Group Two with normal menstrual cycles taking oral contraceptives were also tested in four sessions. The first session consisted of the questionnaires and routine audiometric testing as explained above. Female participants were then asked to mark the first day of their last menses on a calendar provided by the experimenter. Experimental TEOAE testing was completed at three subsequent sessions based on the participant's menstrual calendar: a second session within the first three days of their next menstrual period, a third session on a day between 13-15 days after the start of her period and the fourth session on a day between 7-9 days after the third session.

Group Three. Male participants in Group Three were tested for a total of three sessions; the initial session was considered the first session for experimental TEOAE testing. Therefore, for male participants, the first session included the case history questionnaire, routine audiometric testing, and experimental TEOAE testing. The experimenter scheduled the remaining two sessions with the participant for a day between 13-15 days after the first session and on a day between 7-9 days after the second session.

Data Analyses

To examine the test-retest variability, the difference between the two measurements of the broad-band TEOAE level in the without-noise condition and the difference of the two measurements of the broad-band TEOAE level in the with-noise condition were each calculated for each group and for each session using Microsoft Excel.

Unsuppressed TEOAE and noise levels (those measured in the “-without noise-” condition) were examined for differences across test sessions and across the three groups of participants. Two measurements were obtained in the without-noise condition at each session, and the average of the two measurements was computed using Microsoft Excel for use in these analyses. Both the broad-band TEOAE and noise levels and the TEOAE and noise levels at specific individual frequencies were examined. As mentioned previously, the broad-band TEOAE and noise levels represent the peak values across the entire response (500-5000 Hz). The specific individual frequencies for which the IHS system provides level and noise data were as follows: 1,562, 2,031, 3,125, and 4,062 Hz (frequency resolution was approximately 40 Hz).

Changes in TEOAE level following binaural presentation of the suppressor noise were also examined for differences across sessions and/or groups. The change in broad-band TEOAE level following presentation of the suppressor noise was calculated offline using Microsoft Excel. The mean of the two runs obtained in the without-noise condition were subtracted from the mean of the two runs obtained in the with-noise condition. Therefore, a negative result (decrease in TEOAE level when the noise is present) is

defined as suppression whereas a positive result (increase in TEOAE level when the noise is present) is defined as enhancement.

The change in TEOAE levels following presentation of the suppressor noise for specific time intervals and frequencies was calculated offline using the Kresge EchoMaster program provided with the IHS Smart TrOAE software. The two TEOAE recordings collected in the without-noise condition were loaded into one buffer and were averaged. The two TEOAE recordings collected in the with-noise condition were loaded into another buffer and were averaged. The Kresge system calculated the difference between the average without-noise condition and the averaged with-noise data. The data were loaded into the analysis program so that the TEOAE levels obtained in the without-noise condition would be subtracted from those obtained in the with-noise condition. Therefore, a negative result (decrease in TEOAE level when the noise is present) is defined as suppression whereas a positive result (increase in TEOAE level when the noise is present) is defined as enhancement. The Kresge EchoMaster program analyzes TEOAE suppression in both the time and frequency domains (Wen, Berlin, Hood, Jackson, & Hurley, 1993). Change in TEOAE level was examined in 2 msec time intervals after stimulus onset from the Kresge EchoMaster program. The following specific individual six post-stimulus time intervals were examined: 3.0-5.0, 6.0-8.0, 9.0-11.0, 12.0-14.0, 15.0-17.0, 18.0-20.0 msec. Change in TEOAE level also was examined using the Kresge EchoMaster program at the following specific individual frequencies: 1,562, 2,031, 3,125, 4,062 Hz (Note: change in TEOAE level was examined at individual frequency bins not averaged level over frequency bands).

Statistical analyses were completed using the Statistical Package for Social Sciences (SPSS) for Windows, version 15.0 and Microsoft Excel. Analysis of variance (ANOVA) with a split-plot factorial design was utilized. Changes in TEOAE level (dependent variable) were compared for two independent variables, group and session, each with three levels. The three groups were females not taking oral contraceptives, females taking oral contraceptives and male controls. The three levels for session were first session, second session, and third session. In some analyses there was a third independent variable: frequency or time. There were four levels for frequency: 1,562, 2,031, 3,125, and 4,062 Hz. There were six levels for time: 3.0-5.0, 6.0-8.0, 9.0-11.0, 12.0-14.0, 15.0-17.0, and 18.0-20.0 ms. Similar analyses were also conducted in which the dependent variable was the level of unsuppressed TEOAE. In some cases, Mauchly's test indicated that the assumption of sphericity was violated. In such cases, degrees of freedom were corrected using the Greenhouse-Geisser estimates of sphericity. If significant main effects were noted, a post-hoc paired sample 2-tailed t-test was performed. For the post-hoc paired sample 2-tailed t-test the alpha level was corrected using the Bonferroni adjustment. The standard alpha level of .05 was corrected by dividing the alpha level by the number of comparisons that were performed in the paired sample 2-tailed t-test.

Chapter 5: Results

Test-Retest Variability

As mentioned previously, two TEOAE measurements were made without noise (without-noise condition) for comparison with two TEOAE measurements were made with binaural noise presented in a forward-masking paradigm (with-noise condition). This permitted determination of test-retest variability, that is, variation in the level of the TEOAE from one test run to the next for a given individual at a given session. It should be noted that the test-retest variability reported here reflects variation obtained using the same probe fit for both measurements (The probe was not removed and re-fitted in the ear canal between measurements, however repositioning of the probe was occasionally required between measurements).

The range of test-retest variability within each session for each group was examined for broad-band TEOAE level in the without-noise condition and in the with-noise condition. For broad-band TEOAE level measured in the without-noise condition the mean variability for the FM group was +0.20 dB for session one, +0.19 dB for session two, +0.28 dB for session three. For the FOC group the mean variability was +0.02 dB for session one, +0.25 dB for session two, and +0.10 dB for session three. For the M group the mean variability was -0.39 dB for session one, -0.22 dB for session two, +0.59 dB for session three. For broad-band TEOAE level measured in the with-noise condition the mean variability for the FM group was -0.04 dB for session one, -0.05 dB for session two, and -0.4 dB for session three. For the FOC group the mean variability was -0.07 dB for session one, +0.06 dB for session two, and -0.05 dB for session three. For the M

group the mean variability was -0.45 dB for session one, +1.3 dB for session two, and -0.25 dB for session three.

Unsuppressed (without noise) Broad-band TEOAE Levels and Noise

Analyses were run to determine if unsuppressed broad-band TEOAE levels (without-noise condition) differed across groups or if changes in these TEOAE levels were seen across sessions. As noted previously, the average of the two measurements was computed to determine TEOAE levels and noise levels for use in the analyses. All participants had been required to have robust TEOAEs as determined from the TEOAE screening at the initial session.

The mean unsuppressed broad-band TEOAE level ranged from 15 to 24 dB SPL for females not on oral contraceptives, from 11 to 23 dB SPL for females on oral contraceptives and from 13 to 22 dB SPL for males. Mean unsuppressed broad-band TEOAE levels and noise levels collapsed across the three sessions for each group are shown in Figure 2. Mean unsuppressed broad-band TEOAE levels and noise levels for each session for each group are shown in Figure 3. Standard error bars were not included in Figure 3 for clarity of presentation. Means and standard deviations for unsuppressed broad-band TEOAE and noise levels for each group in each session are listed in Table 2. TEOAE and noise levels are similar for the three groups and appear stable across sessions.

To verify whether the unsuppressed broad-band TEOAE levels differed significantly across groups or changed across the three sessions (i.e., the three phases of the menstrual cycle for the female participants), a two-way analysis of variance

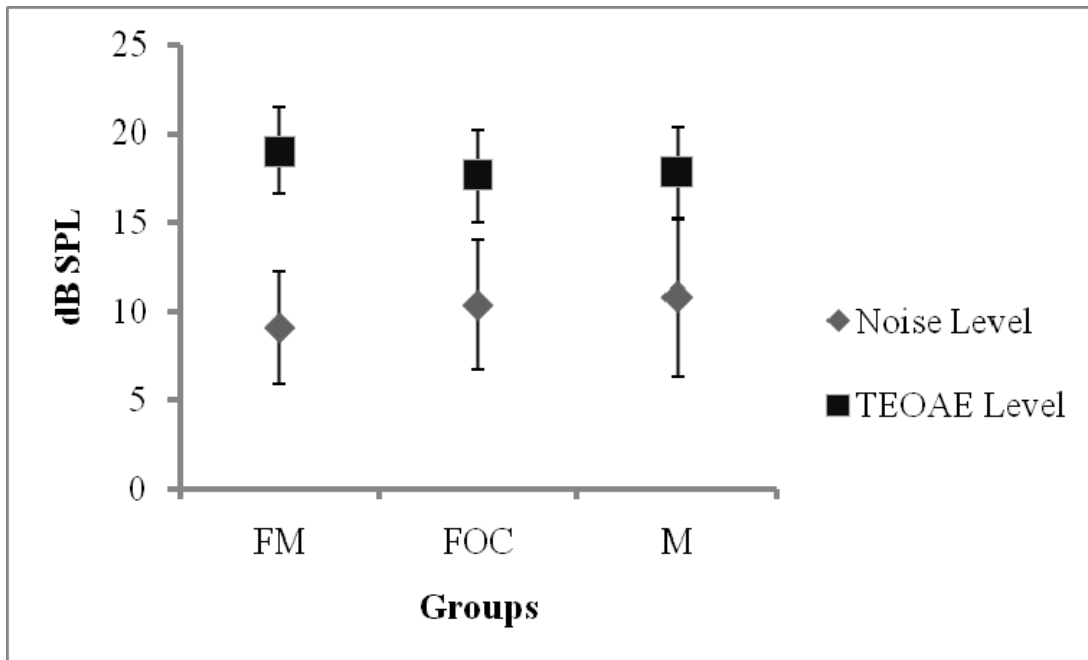


Figure 2. Mean unsuppressed broad-band TEOAE levels and noise levels collapsed across the three sessions for the three groups: females not on oral contraceptives (FM), females on oral contraceptives (FOC) and males (M). Error bars represent one standard error of the mean.

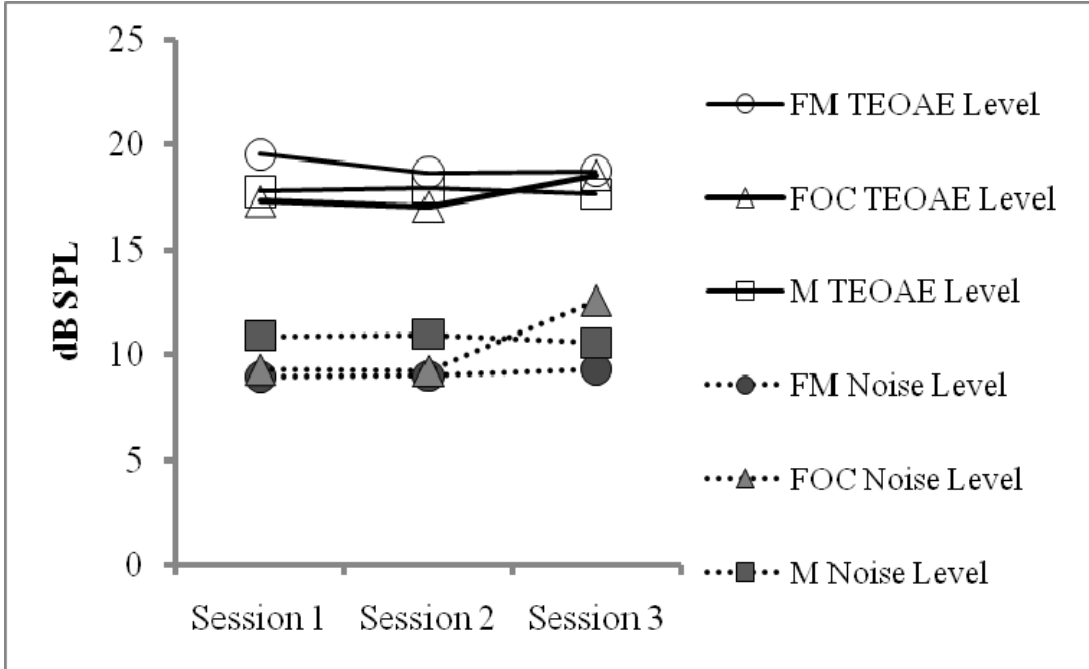


Figure 3. Mean unsuppressed broad-band TEOAE and noise levels for each group [females not on oral contraceptives (FM), females on oral contraceptives (FOC), and males (M)] across each of the three sessions.

Table 2. Means and standard deviations for unsuppressed broad-band TEOAE level and noise levels for each group and for each session.

Group		Session 1		Session 2		Session 3	
		<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>
FM	TEOAE Level	19.54	2.86	18.67	2.33	18.77	2.25
	Noise Level	8.92	2.94	8.98	2.8	9.3	3.81
FOC	TEOAE Level	17.29	1.89	17.03	2.08	18.52	3.5
	Noise Level	9.27	3.46	9.21	3.46	12.57	3.78
M	TEOAE Level	17.76	2.7	17.92	2.9	17.65	2.49
	Noise Level	10.91	4.74	10.96	4.54	10.54	4.54

(ANOVA) with a split-plot factorial design was used. For this analysis there was one within-subject factor, session (three levels: first session, second session, and third session), and one between-subject factor, group (three levels: FM group, FOC group and M group). The effect of group was not significant, $F(2, 27) = 1.196, p > .05$. The effect of session was not significant, $F(2, 54) = .500, p > .05$. The interaction between group and session was not significant, $F(4, 54) = 1.189, p > .05$.

A two-way ANOVA with a split-plot factorial design was used to determine if the broad-band level of noise for the unsuppressed TEOAE condition changed across the three sessions in any of the groups. The purpose of this analysis was to ensure that the broad-band noise level was stable between groups and across sessions. This analysis included one within-subject factor, session, with three levels (first session, second session, and third session) and one between-subject factor, group, with three levels (FM group, FOC group and M group). The effect of group was not significant, $F(1, 27) = 1.024, p > .05$. The effect of session was not significant, $F(2, 54) = 1.238, p > .05$. The interaction between group and session was not significant, $F(4, 54) = 1.318, p > .05$.

Unsuppressed TEOAE and Noise Levels at Specific Frequencies

Analyses were conducted to determine whether the unsuppressed TEOAE or noise levels at specific individual frequencies were different across sessions and/or across groups. The following specific individual frequencies were selected: 1562 Hz, 2031 Hz, 3125 Hz and 4062 Hz. These particular frequencies were selected because the IHS Smart TrOAE system band-pass filters for TEOAE responses are from 500 to 5000 Hz and

because noise levels below 1500 Hz are usually higher than at frequencies of 1500 Hz and above (e.g., Gorga et al. 1993). The data from the two test runs in the without-noise condition were averaged to obtain the unsuppressed TEOAE and noise levels at the specific individual frequencies.

Review of individual data for unsuppressed TEOAE levels at the four specific individual frequencies revealed no obvious trend across sessions or across groups. Unsuppressed TEOAE level varied from session to session for some participants, while other participants showed little to no change in unsuppressed TEOAE level across sessions. Within-subject test-retest variability for TEOAE level from normal hearing listeners has been reported to be approximately 4 dB (e.g., Robinette, 2003). Individual data were examined to see how many participants' unsuppressed TEOAE levels changed across sessions using a difference of 5 dB or greater at two or more frequencies as the criteria. Six out of 10 female participants not on oral contraceptives showed a change of 5 dB or more at two or more frequencies across sessions. The changes ranged from approximately 1 to 17 dB. Seven out of 10 female participants on oral contraceptives showed a change of 5 dB or more at two or more frequencies, with changes ranging from approximately 1 to 9 dB. Eight out of 10 male participants showed a change of 5 dB or more at two or more frequencies. The changes ranged from approximately 1 to 22 dB. The changes observed were not consistently in a specific direction. Figure 4 shows examples of data from individuals with little to no change in unsuppressed TEOAE levels across sessions. The top panel displays data for a female participant not on a oral contraceptive (FM5). The middle panel displays data for a female participant on an oral contraceptive (FOC9). The bottom panel displays data for a male participant (M3).

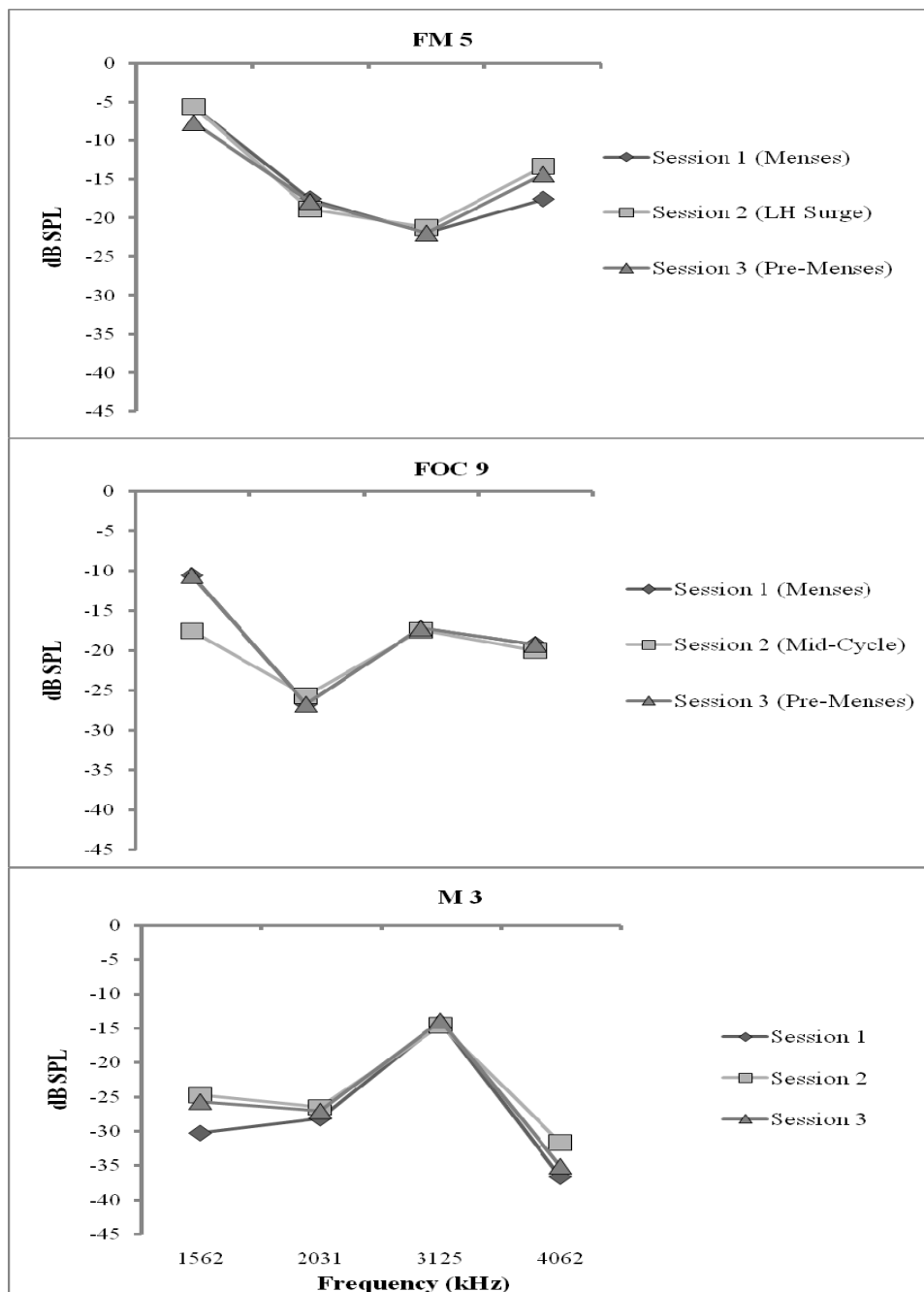


Figure 4. Examples of individuals whose unsuppressed TEOAE levels showed little-to-no change across the three sessions. The top panel displays data for a female participant not on a oral contraceptive (FM5). The middle panel displays data for a female participant on a oral contraceptive (FOC9). The bottom panel displays data for a male participant (M3).

Figure 5 shows examples of data for individuals whose unsuppressed TEOAE levels changed from session to session. The top panel displays data for a female participant not on a oral contraceptive (FM8). The middle panel displays data for a female participant on a oral contraceptive (FOC5). The bottom panel displays data for a male participant (M4).

Mean unsuppressed TEOAE and noise levels at the four specific individual frequencies for each session are shown in Figure 6. Standard error bars were not included in Figure 6 for clarity of presentation. The top panel illustrates data for females not on oral contraceptives, the middle panel illustrates data for females on oral contraceptives, and the bottom panel illustrates data for males. Means and standard deviations for unsuppressed TEOAE and noise levels at the four specific individual frequencies for each group in each session are listed in Table 3. Little change is observed in the mean unsuppressed TEOAE levels at the four frequencies across sessions for each group. Little difference is observed in the mean noise levels across all sessions for each group.

A three-way ANOVA with a split-plot factorial design was used to compare the level of unsuppressed TEOAEs at the four frequencies mentioned above across groups and to determine if there was an effect of session. For this analysis there were two within-subject factors, session (three levels: first session, second session, and third session) and frequency (four levels: 1562 Hz, 2031 Hz, 3125 Hz and 4062 Hz) and one between-subject factor, group (three levels: FM group, FOC group and male group). The effect of group was not significant, $F(2, 27) = 2.349, p > .05$.

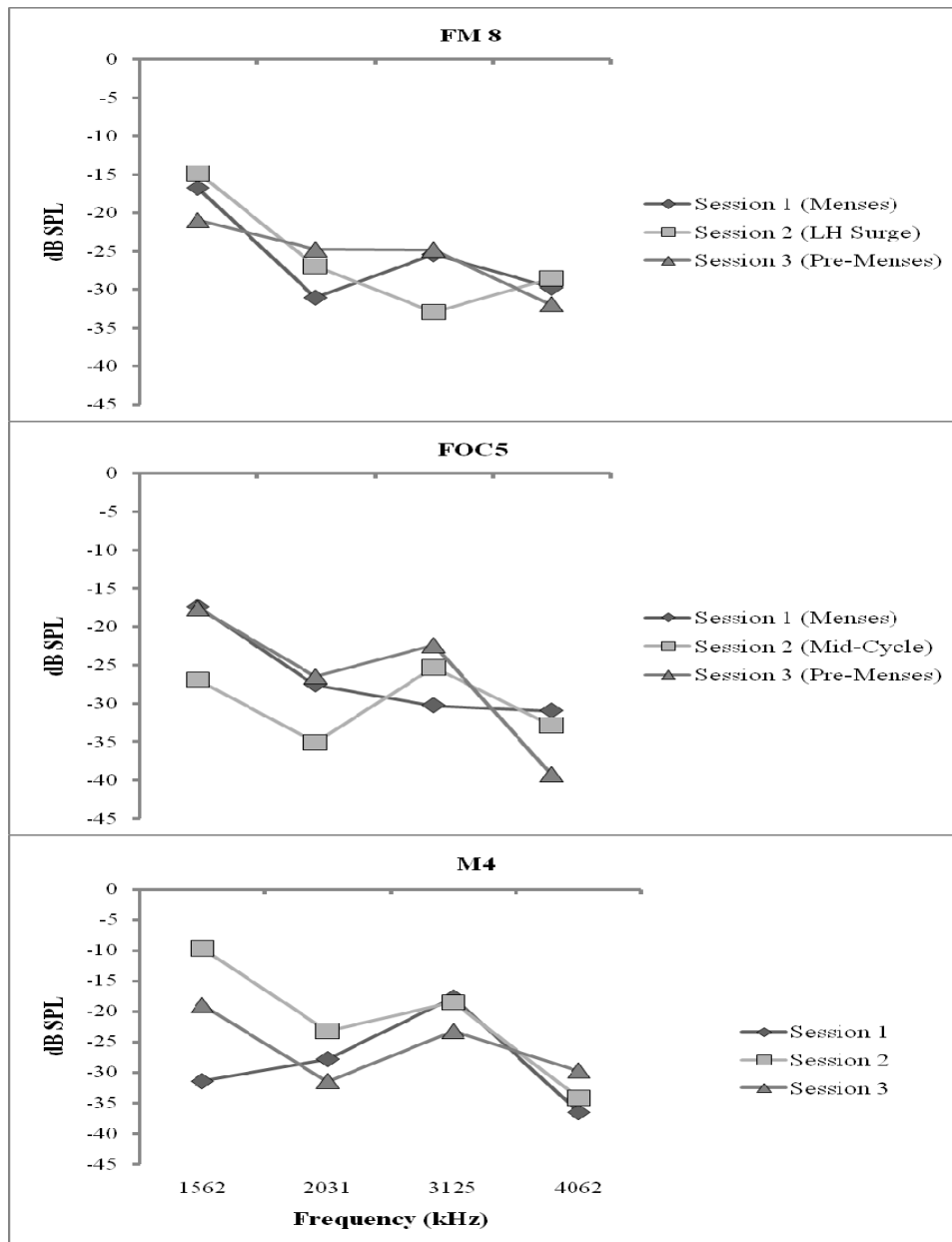


Figure 5. Examples of individuals whose unsuppressed TEOAE levels changed across the three sessions. Only TEOAE levels differing by 5 dB or more at two or more frequencies were considered to have changed across sessions. The top panel displays data for a female participant not on a oral contraceptive (FM8). The middle panel displays data for a female participant on an oral contraceptive (FOC5). The bottom panel displays data for a male participant (M4).

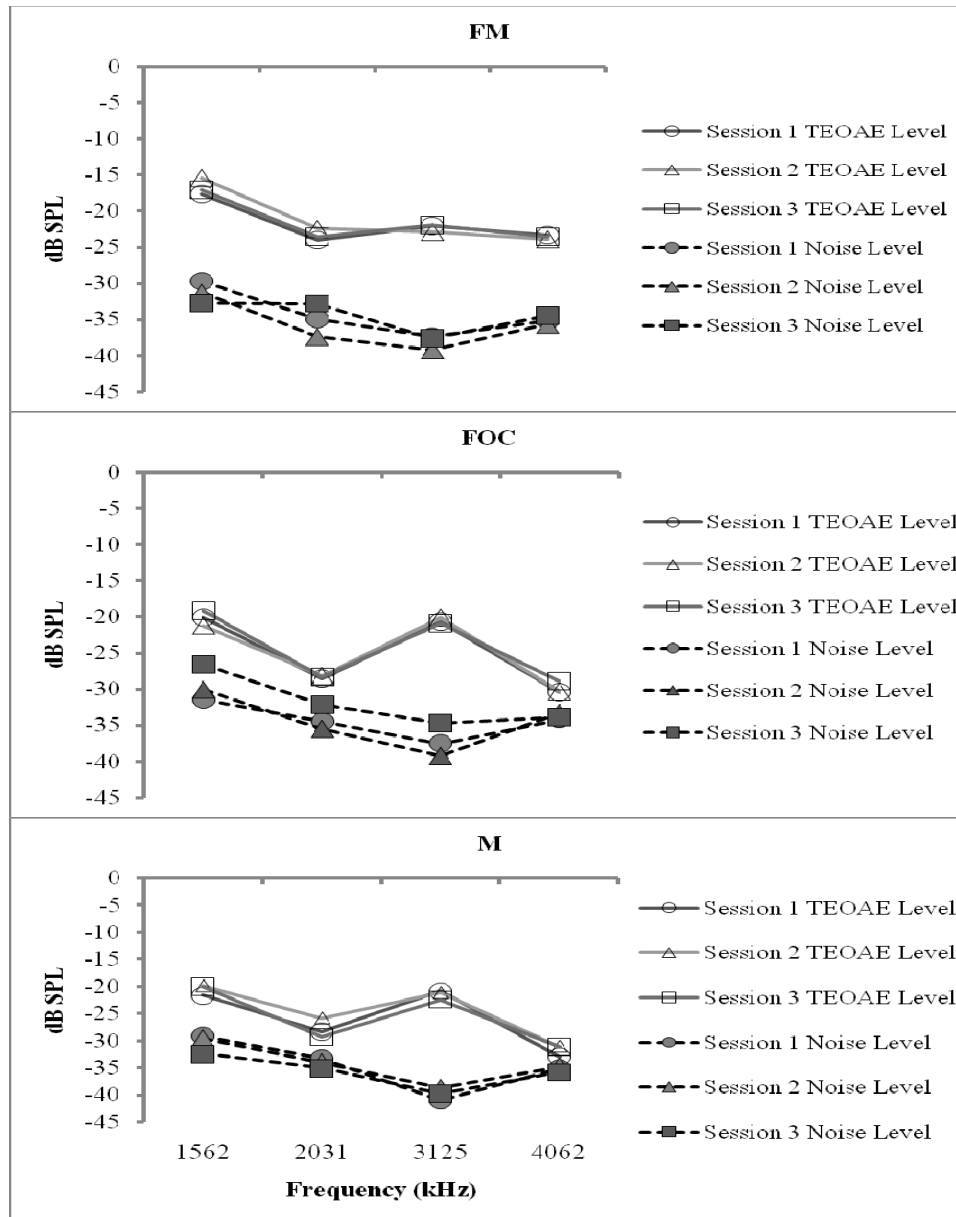


Figure 6. Mean unsuppressed TEOAE and noise levels at the four frequencies for each of the three sessions. The top panel displays data for the females not on oral contraceptives. The middle panel displays data for females on oral contraceptives. The bottom panel displays data for males.

Table 3. Means and standard deviations for unsuppressed TEOAE and noise levels at the four frequencies for each group and each session.

Group	Frequency (kHz)	1562		2031		3125		4062	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
FM	Session 1 TEOAE Level	-17.61	9.99	-23.97	9.94	-22.00	4.26	-23.28	8.87
	Session 1 Noise Level	-29.74	3.76	-34.93	4.15	-37.34	4.18	-35.19	6.01
	Session 2 TEOAE Level	-15.36	6.43	-22.45	6.63	-22.88	4.88	-23.92	9.56
	Session 2 Noise Level	-31.28	3.97	-37.45	3.02	-39.28	4.59	-35.73	5.70
	Session 3 TEOAE Level	-17.09	7.04	-23.57	8.60	-22.02	4.37	-23.60	10.04
	Session 3 Noise Level	-32.69	3.85	-32.75	4.35	-37.63	2.59	-34.45	4.92
FOC	Session 1 TEOAE Level	-20.11	6.12	-28.57	4.57	-20.69	4.96	-30.37	6.63
	Session 1 Noise Level	-31.49	4.92	-34.50	4.32	-37.56	3.23	-34.23	4.73
	Session 2 TEOAE Level	-21.14	5.04	-28.12	5.75	-20.01	4.30	-30.26	4.34
	Session 2 Noise Level	-30.05	6.66	-35.44	5.52	-39.19	5.69	-33.25	2.53
	Session 3 TEOAE Level	-19.19	5.34	-28.31	4.76	-20.98	3.42	-28.95	5.57
	Session 3 Noise Level	-26.60	6.39	-32.15	4.77	-34.73	5.51	-33.95	4.31
M	Session 1 TEOAE Level	-21.65	8.43	-28.33	7.30	-20.86	4.83	-33.00	8.12
	Session 1 Noise Level	-29.12	5.20	-33.26	5.05	-41.01	6.46	-35.08	4.25
	Session 2 TEOAE Level	-19.88	7.49	-25.86	7.79	-21.14	4.95	-31.05	6.21
	Session 2 Noise Level	-29.53	5.05	-33.93	3.61	-38.63	3.67	-34.70	4.10
	Session 3 TEOAE Level	-19.97	5.22	-29.38	8.30	-22.39	3.83	-31.19	4.28
	Session 3 Noise Level	-32.43	8.22	-35.11	4.07	-39.82	3.48	-35.80	4.27

The effect of session was not significant, $F(1.625, 43.866) = .913, p > .05$. The effect of frequency was significant, $F(2.196, 59.286) = 24.463, p < .001$. There was no significant interaction between session and group, $F(3.249, 43.866) = .569, p > .05$. There was no significant interaction between frequency and session, $F(4.843, 130.755) = .934, p > .05$. There was no significant interaction between frequency x session x group, $F(9.686, 130.755) = .636, p > .05$.

Mean unsuppressed TEOAE levels at the individual four frequencies collapsed across group and session are shown in Figure 7. Results of the post-hoc paired sample 2-tailed t-test analyses are listed in Table 4. TEOAE level was significantly larger at 1562 and at 3125 Hz than at 2031 and 4062 Hz.

A similar analysis was conducted to determine whether noise levels at the four frequencies differed across group or session. The effect of group was not significant, $F(2, 27) = 1.829, p > .05$. The effect of session was not significant, $F(2, 54) = .579, p > .05$. The effect of frequency was significant, $F(3, 81) = 47.136, p < .001$. The interaction between group and session was not significant, $F(4, 54) = 1.683, p > .05$. The interaction between frequency and session was not significant, $F(3.968, 107.124) = .815, p > .05$. The interaction between frequency x session x group was not significant, $F(7.935, 107.124) = 1.023, p > .05$. Mean noise levels at the four individual frequencies collapsed across group and session are shown in Figure 8. Results of the post-hoc paired sample 2-tailed t-test analyses are listed in Table 5. Noise levels for all pairs of frequencies were significantly different from one another with the exception of 2031 and 4062 Hz.

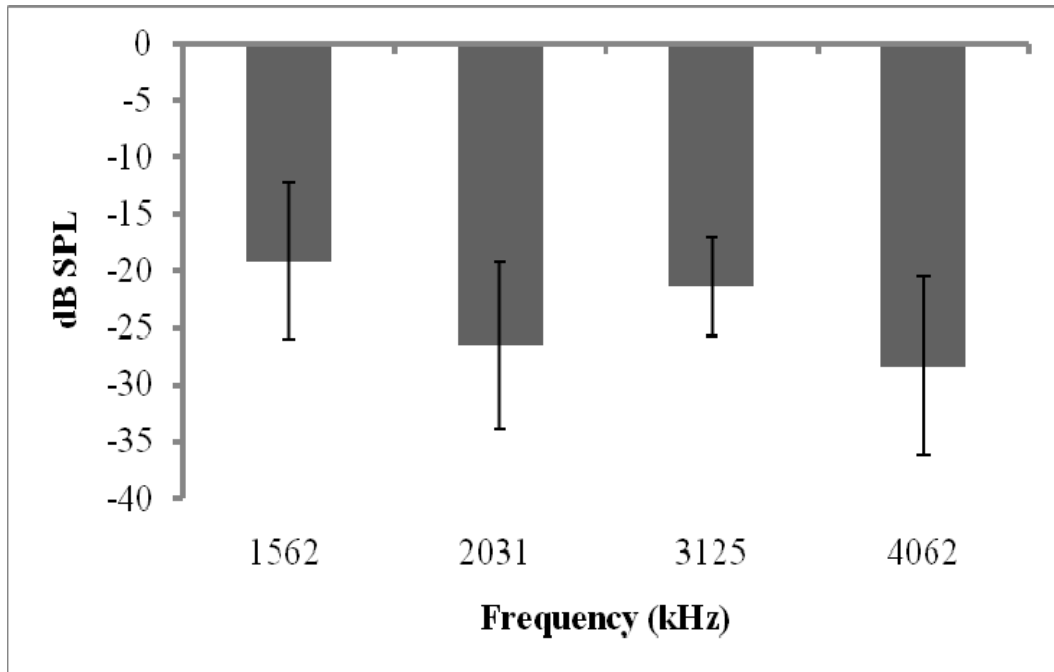


Figure 7. Mean unsuppressed TEOAE levels at the four frequencies collapsed across group and session. Error bars represent one standard error of the mean.

Table 4. Results of post-hoc paired sample t-tests for unsuppressed TEOAEs at the four frequencies.

Paired Frequencies	<i>t</i>	<i>df</i>	<i>p</i>
1562 Hz and 2031 Hz	10.62	89	.0001*
1562 Hz and 3125 Hz	2.55	89	0.012
1562 Hz and 4062 Hz	15.16	89	.0001*
2031 Hz and 3125 Hz	-5.28	89	.0001*
2031 Hz and 4062 Hz	2.55	89	0.012
3125 Hz and 4062 Hz	7.11	89	.0001*

Note. The alpha level of .05 was corrected using the Bonferroni adjustment by dividing the number of comparisons that were performed in the paired sample 2-tailed t-test, which resulted in $*p < .01$.

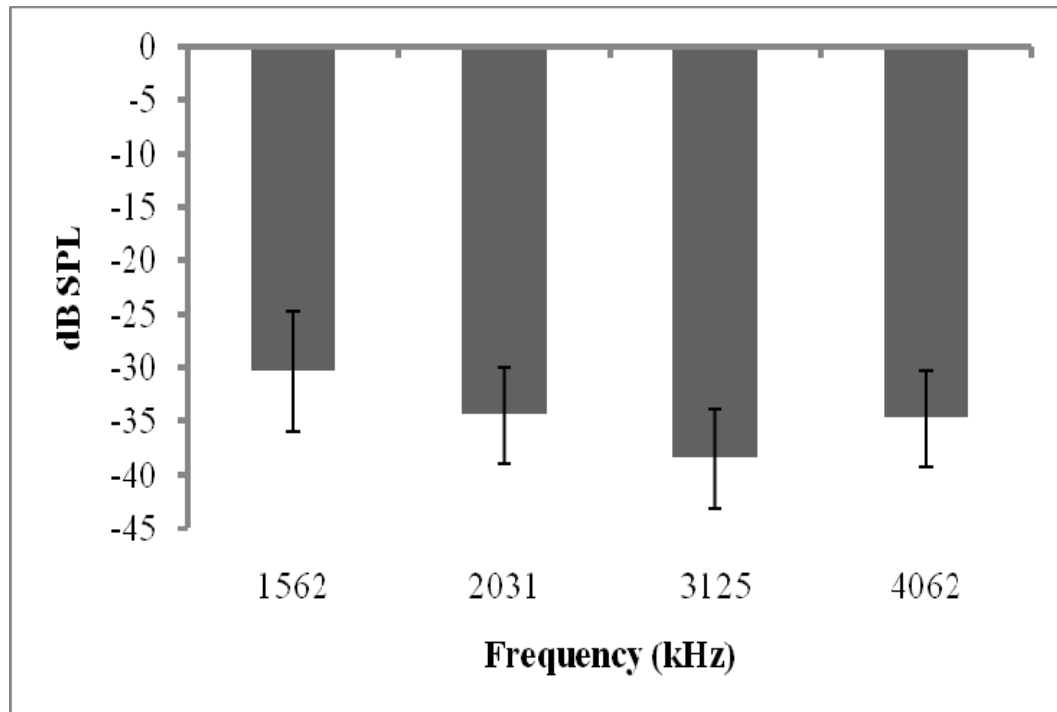


Figure 8. Mean noise levels for the without-noise condition at the four frequencies collapsed across group and session. Error bars represent one standard error of the mean.

Table 5. *Results of the post-hoc paired sample t-tests for noise levels at the four frequencies.*

Paired Frequencies	<i>t</i>	<i>df</i>	<i>p</i>
1562 Hz and 2031 Hz	7.5	89	.0001*
1562 Hz and 3125 Hz	13.17	89	.0001*
1562 Hz and 4062 Hz	5.96	89	.0001*
2031 Hz and 3125 Hz	6.83	89	.0001*
2031 Hz and 4062 Hz	0.54	89	0.590
3125 Hz and 4062 Hz	-5.19	89	.0001*

Note. The alpha level of .05 was corrected using the Bonferroni adjustment by dividing the number of comparisons that were performed in the paired sample 2-tailed t-test, which resulted in $*p < .01$.

Change in Broad-band TEOAE Level with the Presentation of Noise

To determine the change in broad-band TEOAE level following presentation of binaural noise, the mean TEOAE level obtained in the without-noise condition was subtracted from the mean TEOAE level obtained in the with-noise condition (with noise – without noise). Therefore, a negative result (decrease in TEOAE level when the noise is present) was defined as suppression, whereas a positive result (increase in TEOAE level when the noise is present) was defined as enhancement.

The data were analyzed to determine whether the change in broad-band TEOAE level in the presence of binaural noise differed across groups or across sessions. The change in broad-band TEOAE level ranged from -2.80 to +3.28 dB for females not on oral contraceptives, from -3.22 to +4.50 dB for females on oral contraceptives and from -2.80 to +2.87 dB for males. Mean change in broad-band TEOAE level for each session is shown in Figure 9. The top panel illustrates data for females not on oral contraceptives, the middle panel illustrates data for females on oral contraceptives, and the bottom panel illustrates data for males. The magnitude of change in TEOAE level appears to vary by session in females not on oral contraceptives; specifically, slightly greater suppression is noted during menstruation (session one) than during pre-menstruation (session three) and very little change in TEOAE level is noted following the presentation of binaural noise during the LH surge (session two). A very small amount of enhancement (.02 dB) for this group is noted in session two. Enhancement was noted in all sessions for females on oral contraceptives with the greatest enhancement in session three. However, the enhancement observed in all sessions for females on oral contraceptives was very small and ranged from .1 to .4 dB. The enhancement seen in this group may have

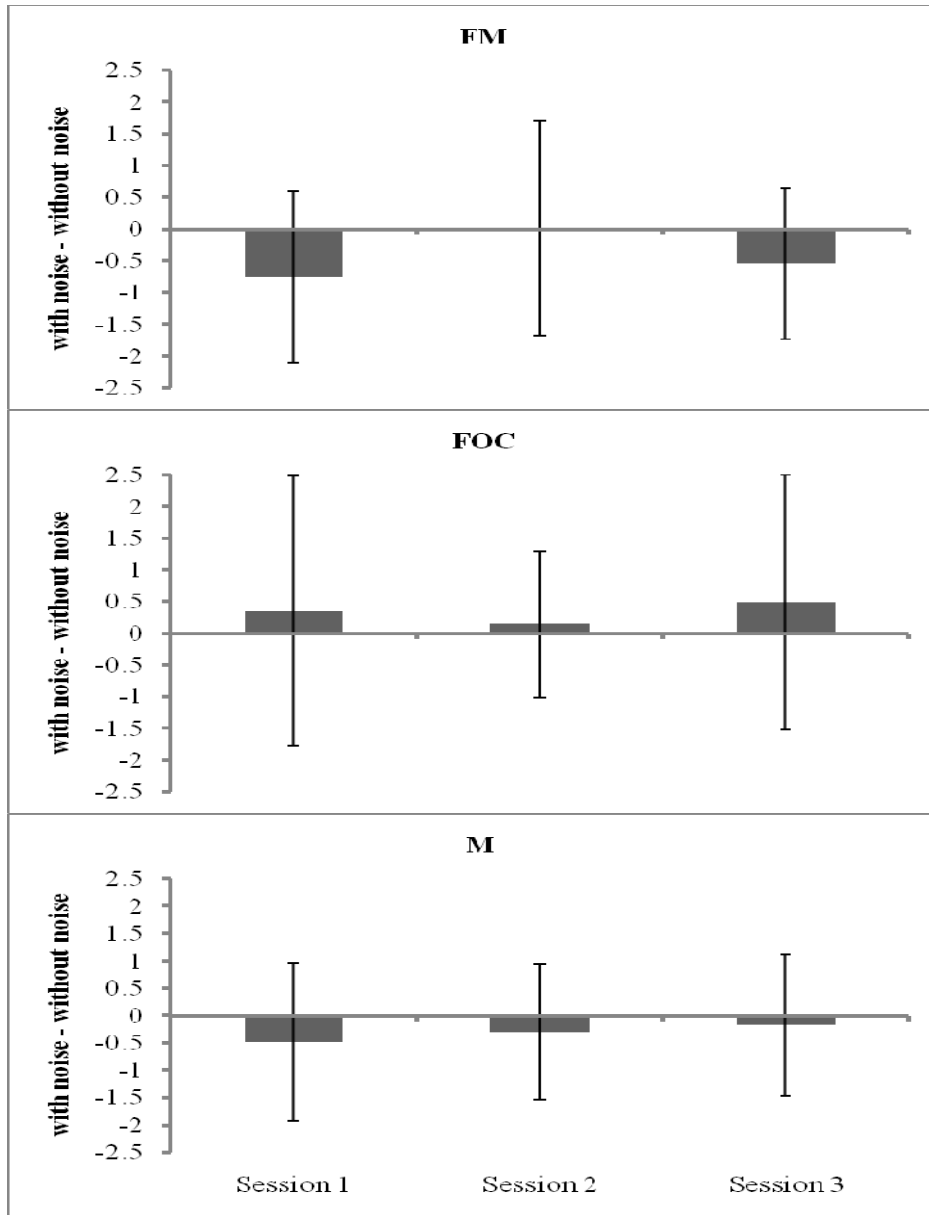


Figure 9. Mean change in broad-band TEOAE level at each of the three sessions. The magnitude of change was calculated by subtracting the mean TEOAE level recorded without noise from the mean TEOAE level recorded with noise. The top panel illustrates data for females not on oral contraceptives, the middle panel illustrates data for females on oral contraceptives, and the bottom panel illustrates data for males. Error bars represent one standard error of the mean.

been due to the considerable range of test-retest variability within each session. The magnitude of suppression appears to be similar across sessions in the male participants. It appears females not on oral contraceptives and males show the greatest amount of suppression in session one.

To determine if any of the observed trends in the change in TEOAE levels across groups or across the three were significant, a two-way analysis of variance (ANOVA) with a split-plot factorial design was used. For this analysis there was one within-subject factor, session (three levels: first session, second session, and third session), and one between-subject factor, group (three levels: FM group, FOC group and male group). The effect of group was not significant, $F(2, 27) = 1.196, p > .05$. The effect of session was not significant, $F(2, 54) = .312, p > .05$. The interaction between group and session was not significant, $F(4, 54) = .435, p > .05$.

Change in TEOAE Level Following Presentation of Binaural Noise for Specific Time Intervals

Changes in TEOAE levels following presentation of binaural noise were examined across both time and frequency for group and session effects using the Kresge Echomaster program. In the time domain, TEOAE level change was evaluated in the following six post-stimulus onset time intervals: 3.0-5.0 ms, 6.0-8.0 ms, 9.0-11.0 ms, 12.0-14.0 ms, 15.0-17.0 ms, and 18.0-20.0 ms. Review of individual data revealed that the majority of participants showed some amount of both suppression and enhancement in the various post-stimulus time intervals. All participants showed suppression in most time intervals, typically suppression was seen in the later time intervals (6.0-8.0 ms to

15.0-17.0 ms). No participants demonstrated a complete absence of suppression. For some participants, the amount of suppression or enhancement varied little from session to session while for other participants the amount of suppression or enhancement noticeably varied from session to session. However, no consistent trend was observed across groups or sessions. Examples of data from individuals for whom little change in TEOAE suppression or enhancement were noted are shown in Figure 10. The top panel displays data for a female participant not on an oral contraceptive (FM12). The middle panel displays data for a female participant on a oral contraceptive (FOC11). The bottom panel displays data for a male participant (M6). Examples from individuals whose TEOAE suppression or enhancement varied from session to session are displayed in Figure 11. The top panel displays data for a female participant not on an oral contraceptive (FM16). The middle panel displays data for a female participant on a oral contraceptive (FOC13). The bottom panel displays data for a male participant (M10). The change in TEOAE level following the presentation of binaural noise observed in the different post-stimulus time intervals ranged from -8.71 to +11.24 dB for females not on oral contraceptives, from -11.25 to +12.61 dB for females on oral contraceptives, and from -10.30 to +10.17 dB for males.

Mean change in TEOAE level during presentation of the binaural noise is shown for the three sessions in the six time intervals in Figure 12. The top panel displays data for females not on oral contraceptives (FM group). The middle panel displays data for females on oral contraceptives (FOC group). The bottom panel displays data for male participants (M group). Standard error bars were not included

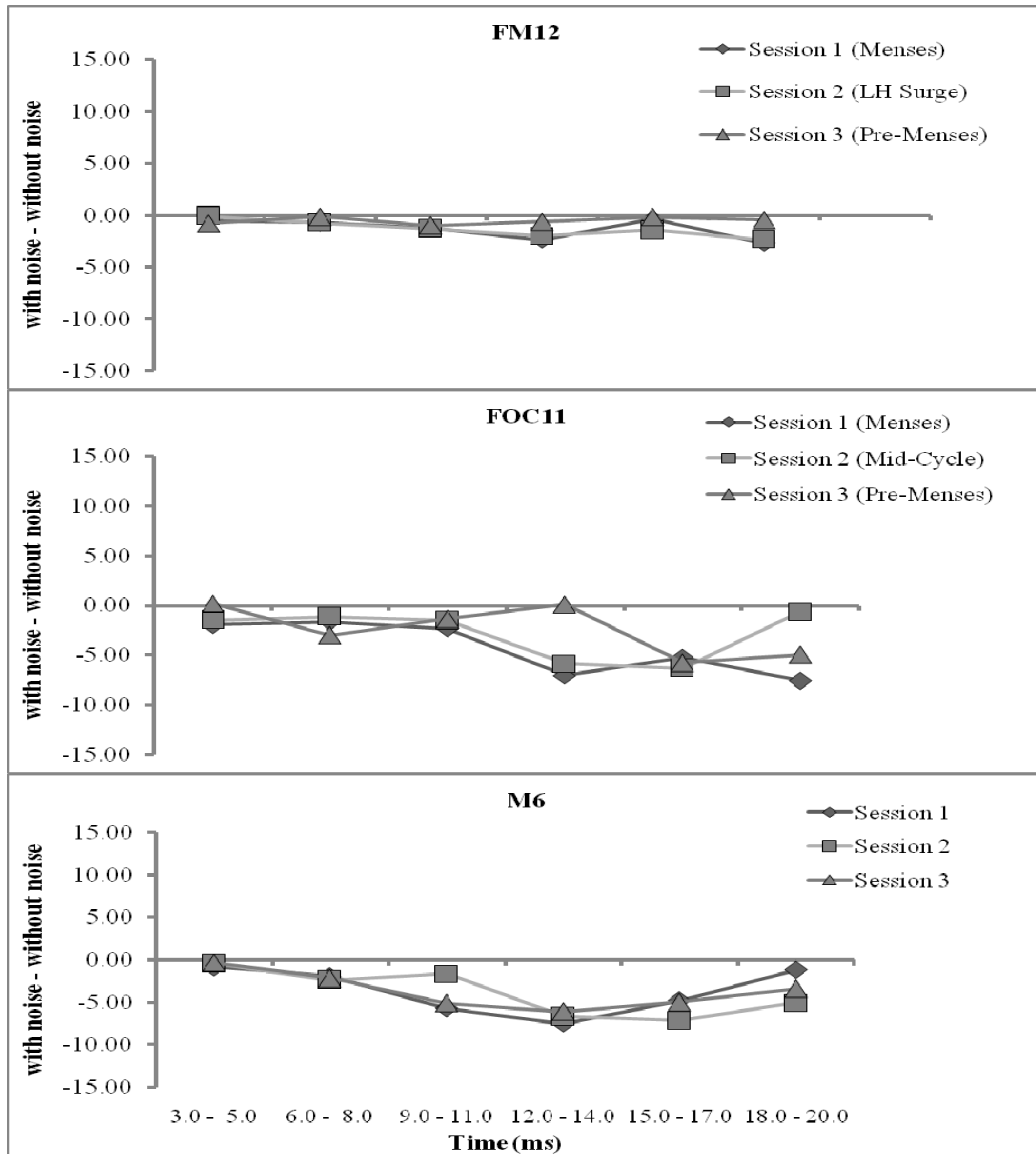


Figure 10. Examples of individual TEOAE suppression/enhancement in specific time intervals that changed little from session to session. The top panel displays data for a female participant not on a oral contraceptive (FM12). The middle panel displays data for a female participant on a oral contraceptive (FOC11). The bottom panel displays data for a male participant (M6).

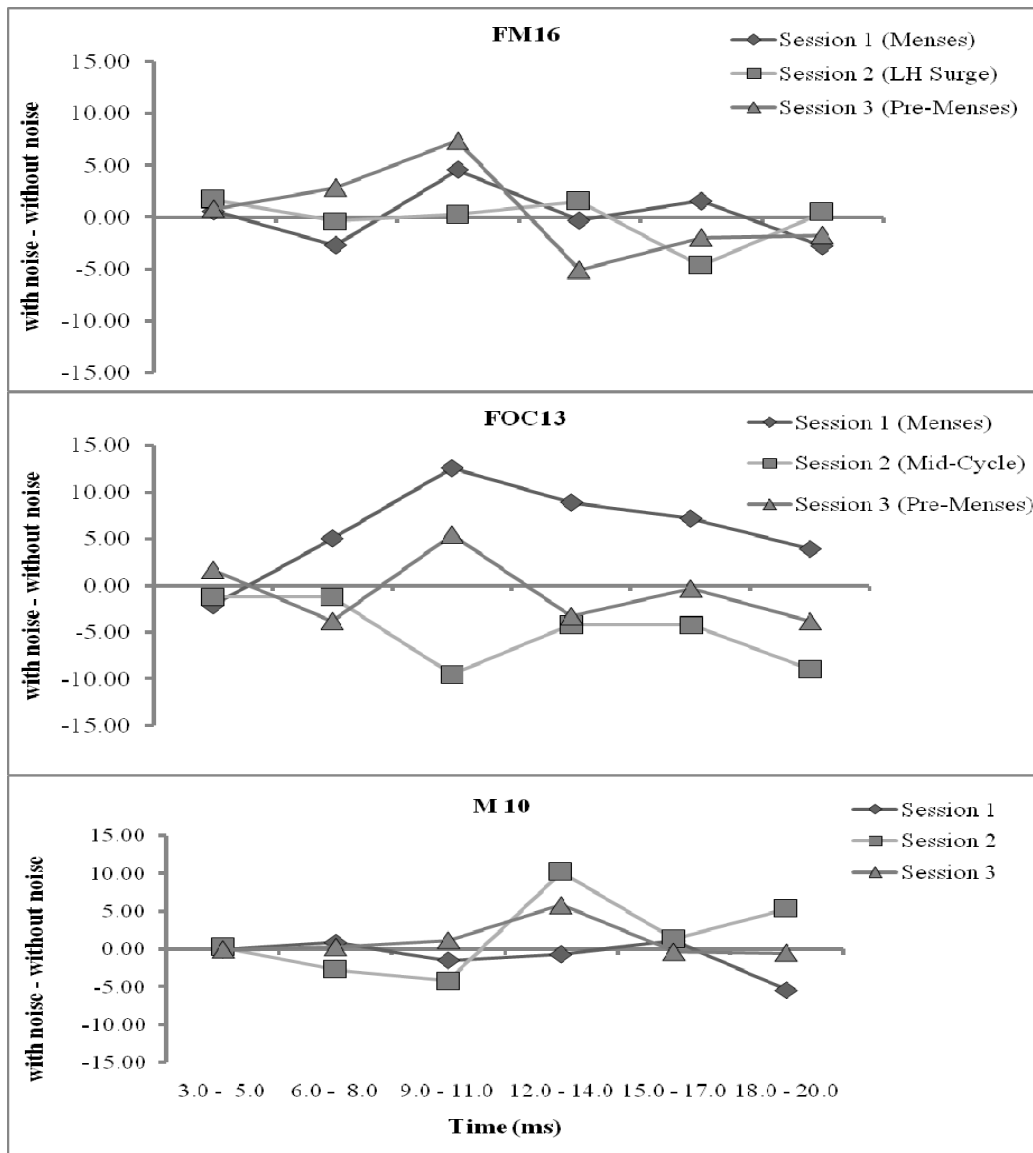


Figure 11. Examples of individual TEOAE suppression/enhancement in specific time intervals that changed from session to session. The top panel displays data for a female participant not on a oral contraceptive (FM16). The middle panel displays data for a female participant on a oral contraceptive (FOC13). The bottom panel displays data for a male participant (M10).

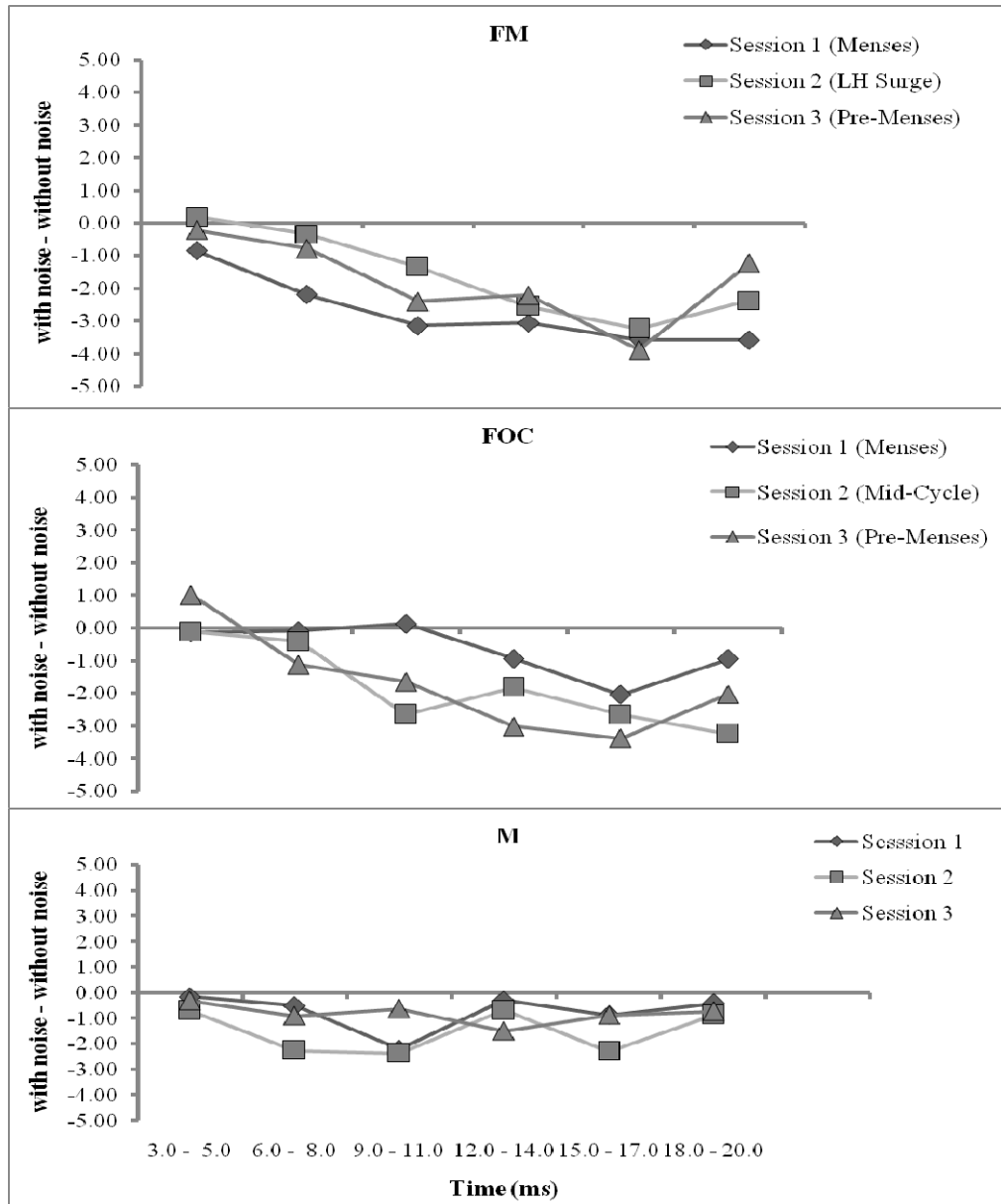


Figure 12. Mean change in TEOAE level following presentation of binaural noise in the six post-stimulus time intervals for the three sessions. The top panel displays data for females not on oral contraceptives (FM group). The middle panel displays data for females on oral contraceptives (FOC group) The bottom panel displays data for male participants (M group).

in Figure 12 for clarity of presentation. Mean changes in TEOAE level and standard deviations for each group in each session are listed in Table 6.

Mean data indicate that the presentation of the binaural noise resulted in a decrease in TEOAE levels for all groups in most time intervals with the exception of what appears to be a slight enhancement (1.01 dB) in the first time interval (3.0-5.0 ms) for the females taking oral contraceptive (FOC group, middle panel of Figure 12). For all groups, suppression appears to be greater in the later time intervals (from 6.0-8.0 to 18-20 ms). Changes in the magnitude of suppression across the three sessions differ in each group. In the FM group, suppression appears to be greatest during session one and least during session two. In contrast, suppression appears to be greatest during session three and least during session one for the FOC group. The magnitude of suppression appears to be relatively stable across sessions for the male group.

A three-way ANOVA with a split-plot factorial design was run to determine whether any of the observed trends were significant. For this analysis there were two within-subject factors, session (three levels: first session, second session, and third session) and time (six levels: 3.0-5.0 ms, 6.0-8.0 ms, 9.0-11.0 ms, 12.0-14.0 ms, 15.0-17.0 ms, and 18.0-20.0 ms), and one between-subject factor, group [three levels: females not taking oral contraceptives (FM group), females taking oral contraceptives (FOC group) and males (M group)]. The main effect of group was not significant, $F(2, 27) = .955, p > .05$. The main effect of session was not significant, $F(2, 54) = .258, p > .05$. The main effect of time was significant, $F(5, 135) = 5.942, p < .05$.

Table 6. Mean changes in TEOAE level and standard deviations in the specific post-stimulus time intervals for each group in each session.

Group	Time (ms)	3.0-5.0		6.0-8.0		9.0-11.0		12.0-14.0		15.0-17.0		18.0-20.0	
		<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>
FM	Session 1	-0.84	1.52	-2.2	1.12	-3.15	3.24	-3.06	2.91	-3.57	3.58	-3.58	3.54
	Session 2	0.18	1.1	-0.34	2.2	-1.35	1.95	-2.56	3.29	-3.24	2.56	-2.37	4.31
	Session 3	-0.21	0.87	-0.79	2.02	-2.4	4.38	-2.21	3.09	-3.88	3.55	-1.24	5.99
FOC	Session 1	-0.14	1.49	-0.09	3.27	0.13	5.15	-0.94	4.62	-2.04	4.01	-0.95	3.58
	Session 2	-0.12	1.16	-0.42	2.85	-2.65	3.83	-1.82	4.23	-2.66	2.84	-3.25	3.53
	Session 3	1.01	2.28	-1.13	2.05	-1.65	3.53	-3.02	2.25	-3.38	3.99	-2.02	3.34
M	Session 1	-0.16	0.86	-0.51	2.1	-2.21	2.66	-0.30	4.77	-0.87	3.87	-0.42	3.36
	Session 2	-0.7	0.71	-2.26	2.09	-2.36	4.2	-0.69	5.6	-2.29	4.82	-0.86	4.05
	Session 3	-0.31	2.18	-0.9	1.48	-0.62	2.89	-1.5	4.36	-0.87	3.68	-0.74	3.28

The interaction between group and session was not significant, $F(4, 54) = 1.855, p > .05$.

The interaction between time and session was not significant, $F(10, 270) = .429, p > .05$.

The interaction between time x session x group was not significant, $F(20, 270) = .736, p > .05$.

The mean change in TEOAE level in the six time intervals collapsed across group and session is shown in Figure 13. Results of the post-hoc paired sample 2-tailed t-tests are listed in Table 7. The magnitude of suppression was significantly greater in the later time intervals than in the earliest time interval (3.0-5.0 ms). The magnitude of suppression in other time intervals were not significantly different from one another with the exception of the 6.0-8.0 and 15.0-17.0 ms intervals.

Change in TEOAE Level Following Presentation of Binaural Noise at Specific Frequencies

Changes in TEOAE levels during presentation of binaural noise were examined at specific frequencies for group and session effects. Similar to the individual data for specific time intervals, all individual participants showed some amount of suppression and enhancement in the various frequencies. Participants showed suppression at most frequencies. No participants demonstrated a complete absence of suppression. For some participants, the amount of suppression or enhancement varied little from session to session while for other participants the amount of suppression or enhancement varied significantly from session to session; however, no consistent trend was noted. Examples from individuals for whom suppression/enhancement at specific individual frequencies

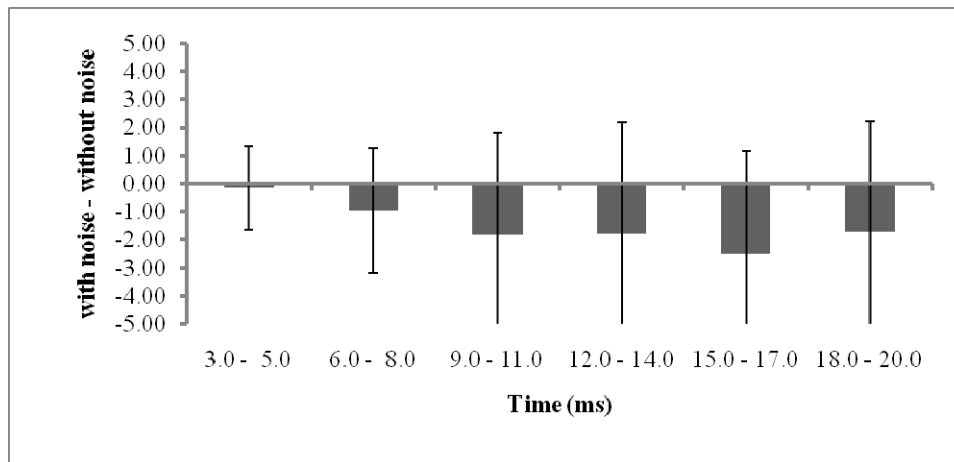


Figure 13. Mean change in TEOAE levels following presentation of binaural noise for the six time intervals collapsed across group and session. Error bars represent one standard error of the mean.

Table 7. Results of post-hoc paired sample t-tests for change in TEOAE level following presentation of binaural noise in the six time intervals.

Paired Time Intervals	<i>T</i>	<i>df</i>	<i>P</i>
3.0 – 5.0 and 6.0 – 8.0 ms	3.14	89	.002*
3.0 – 5.0 and 9.0 – 11.0 ms	4.18	89	0*
3.0 – 5.0 and 12 – 14.0 ms	3.9	89	0*
3.0 – 5.0 and 15.0 -17.0 ms	5.89	89	0*
3.0 – 5.0 and 18.0 – 20.0 ms	3.77	89	0*
6.0 – 8.0 and 9.0 – 11.0 ms	2.2	89	.03
6.0 – 8.0 and 12.0 – 14.0 ms	1.92	89	.05
6.0 – 8.0 and 15.0 – 17.0 ms	3.81	89	0*
6.0 – 8.0 and 18.0 – 20.0 ms	1.72	89	.08
9.0 – 11.0 and 12.0 – 14.0 ms	-.04	89	.96
9.0 – 11.0 and 15.0 – 17.0 ms	1.78	89	.07
9.0 – 11.0 and 18.0 – 20.0 ms	-.22	89	.82
12.0 – 14.0 and 15.0 – 17.0 ms	1.74	89	.08
12.0 – 14.0 and 18.0 – 20.0 ms	-.15	89	.87
15.0 – 17.0 and 18.0 – 20.0 ms	-1.89	89	.06

Note. The alpha level of .05 was corrected using the Bonferroni adjustment by dividing the number of comparisons that were performed in the paired sample 2-tailed t-test, which resulted in $*p < .003$.

changed little from session to session are shown in Figure 14. The top panel displays data for a female participant not on a oral contraceptive (FM12). The middle panel displays data for a female participant on a oral contraceptive (FOC2). The bottom panel displays data for a male participant (M10). Figure 15 displays example data from individuals for whom suppression/enhancement at specific individual frequencies changed from session to session. The top panel displays data for a female participant not on a oral contraceptive (FM6). The middle panel displays data for a female participant on an oral contraceptive (FOC9). The bottom panel displays data for a male participant (M6). The change in TEOAE level during presentation of binaural noise at the specific frequencies ranged from -7.41 to +2.93 dB for females not on oral contraceptives, from -6.09 to +3.83 dB for females on oral contraceptives and from -8.64 to +2.53 dB for males. For the majority of participants, suppression appeared to be greatest at 1562 Hz. Mean change in TEOAE level following presentation of binaural noise is shown for each session at the four frequencies in Figure 16. The top panel displays data for females not on oral contraceptives (FM group). The middle panel displays data for females on oral contraceptives (FOC group) The bottom panel displays data for male participants (M group). Standard error bars were not included in Figure 16 for clarity of presentation.

Mean changes in TEOAE level and standard deviations for each group in each session can be found in Table 8. Mean data for all groups indicated suppression of the TEOAE levels following presentation of binaural noise in all frequencies. No enhancement of TEOAE levels was noted. The magnitude of suppression appears to decrease slightly with increasing frequencies for all groups.

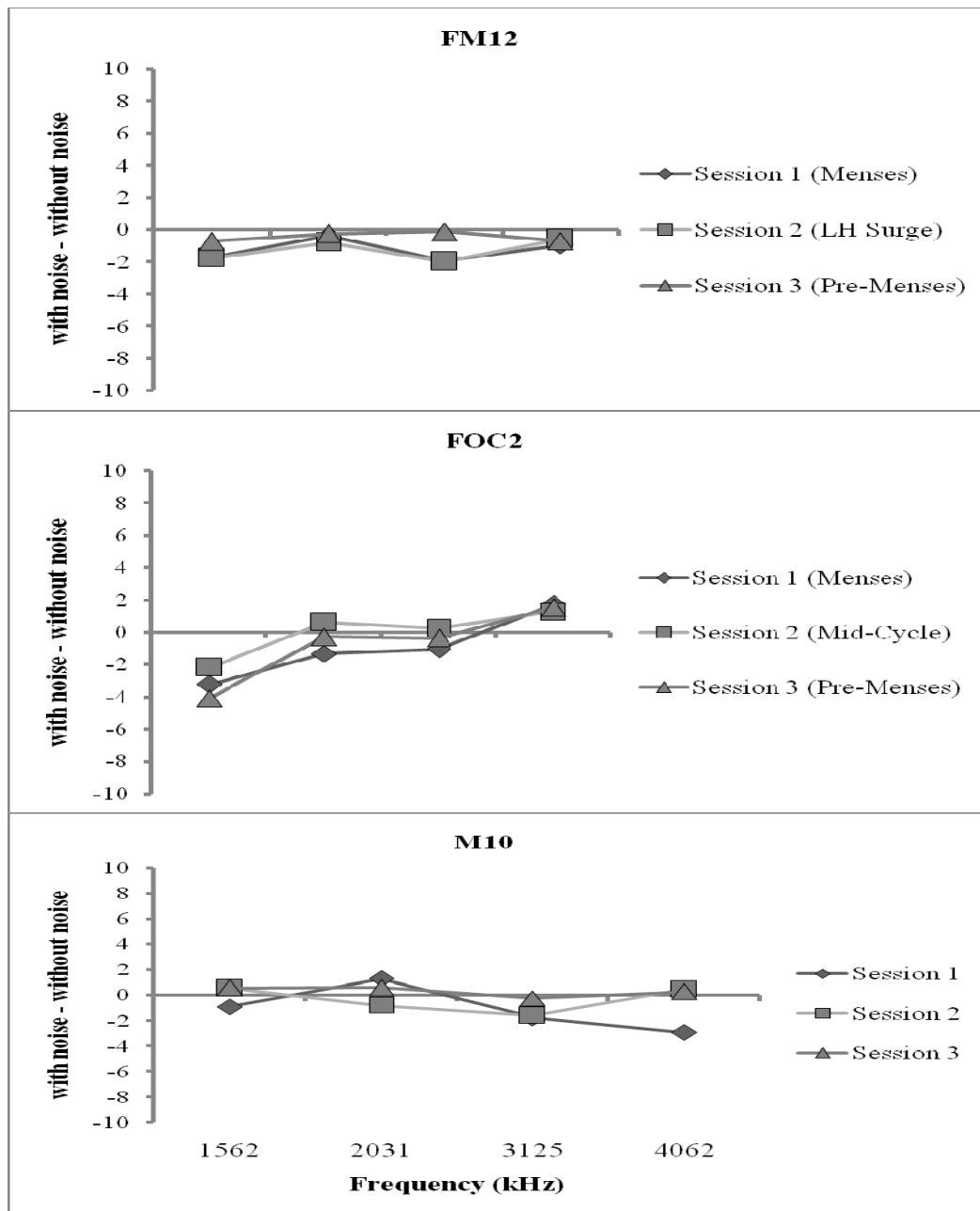


Figure 14. Example of data from individuals for whom suppression and/or enhancement at specific frequencies changed little from session to session. The top panel displays data for a female participant not on an oral contraceptive (FM12). The middle panel displays data for a female participant on an oral contraceptive (FOC2). The bottom panel displays data for a male participant (M10).

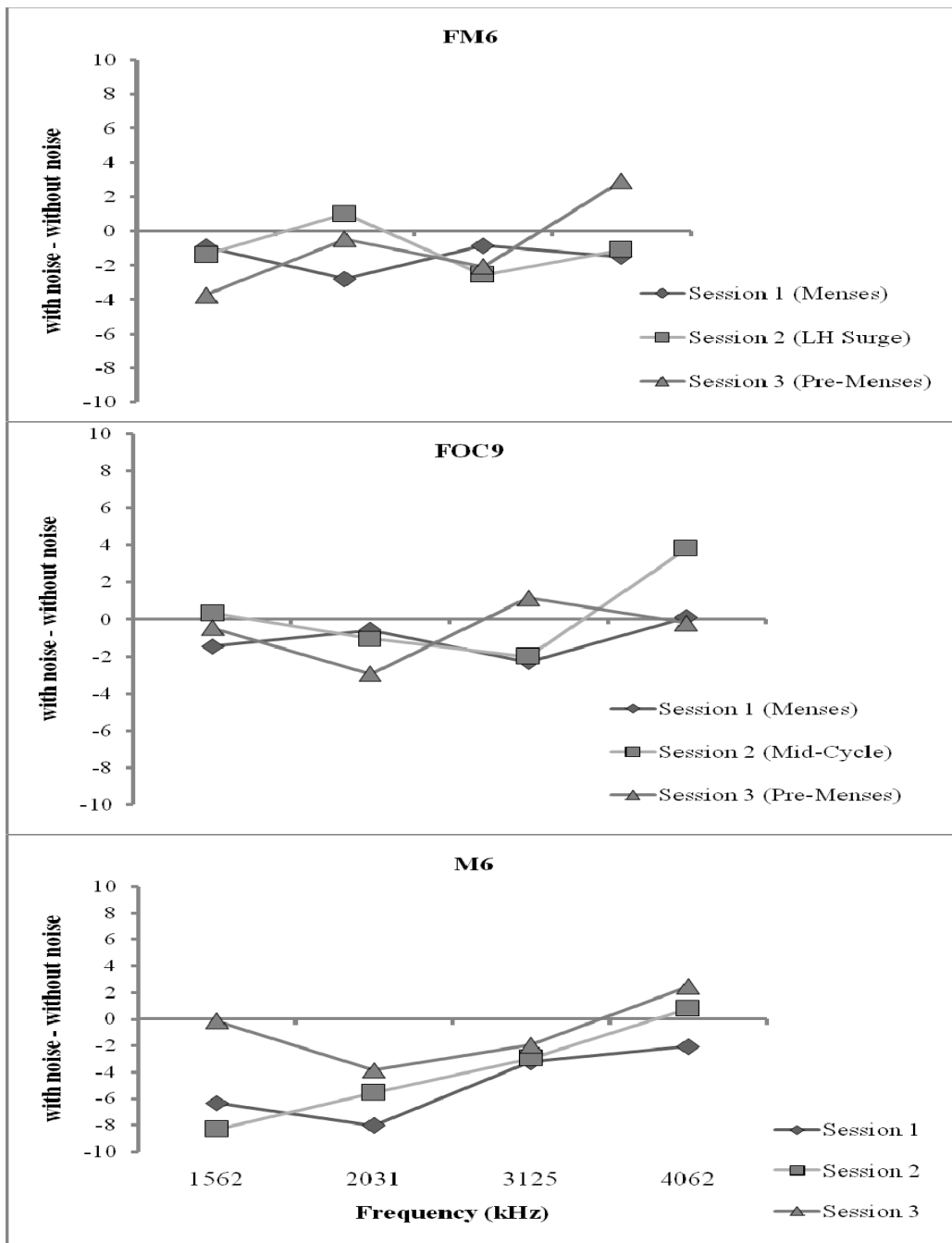


Figure 15. Examples of data from individuals for whom suppression/enhancement at specific frequencies changed from session to session. The top panel displays data for a female participant not on an oral contraceptive (FM6). The middle panel displays data for a female participant on an oral contraceptive (FOC9). The bottom panel displays data for a male participant (M6).

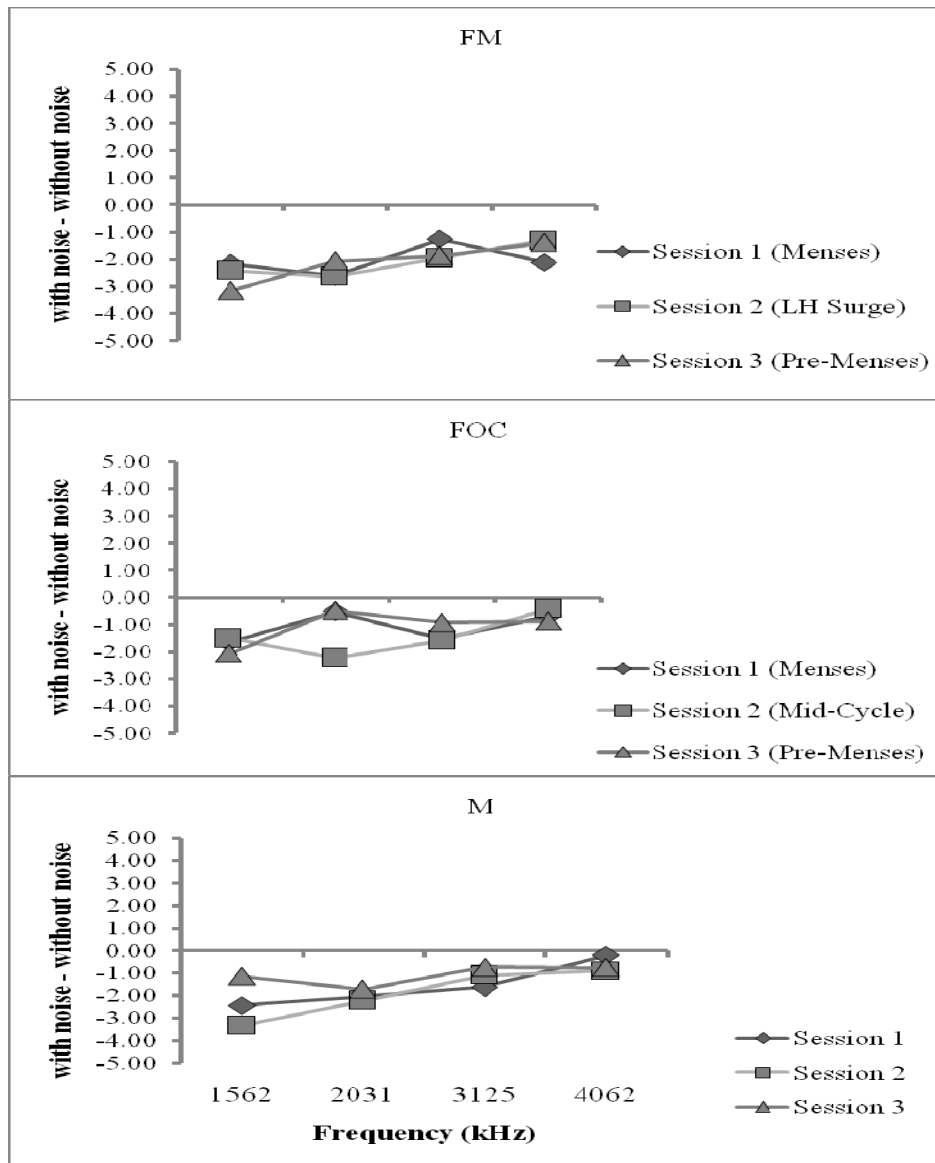


Figure 16. Mean change in TEOAE level following presentation of binaural noise at the four frequencies is shown for each session. The top panel displays data for females not on oral contraceptives (FM group). The middle panel displays data for females on oral contraceptives (FOC group). The bottom panel displays data for male participants (M group).

Table 8. Mean changes in TEOAE level and standard deviations at the four frequencies for each group in each session.

Group	Frequency (kHz)	1562		2031		3125		4062	
		<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>
FM	Session 1	-2.16	1.47	-2.63	1.79	-1.26	1.52	-2.1	1.42
	Session 2	-2.4	2.74	-2.63	2.66	-1.95	1.79	-1.31	1.34
	Session 3	-3.14	1.48	-2.06	1.73	-1.86	1.83	-1.39	2.2
FOC	Session 1	-1.64	1.94	-0.52	1.87	-1.51	0.54	-0.68	1.63
	Session 2	-1.5	2.17	-2.21	1.79	-1.58	1.11	-0.41	2.59
	Session 3	-2.06	3.06	-0.48	2.1	-0.92	0.97	-0.87	1.75
M	Session 1	-2.44	3.14	-2.04	2.93	-1.62	1.05	-0.21	2.15
	Session 2	-3.35	3.06	-2.21	3.13	-1.1	1.13	-0.88	1.61
	Session 3	-1.15	2.51	-1.72	2.21	-0.73	1.4	-0.76	2.73

The magnitude of suppression appears to be essentially stable across all sessions for the FM group. The magnitude of suppression also appears to be stable across sessions for the FOC group at all frequencies except 2031 Hz. At 2031 Hz, suppression appears to be greatest at mid-cycle (session 2). The magnitude of suppression remained stable across sessions in all frequencies except for 1562 Hz for the male group. The mean magnitude of suppression was largest in session two and smallest in session three.

A three-way ANOVA with a split-plot factorial design was used to determine whether any of the observed trends were significant. For this analysis there were two within-subject factors, session (three levels: first session, second session, and third session) and frequency (four levels: 1562 Hz, 2031 Hz, 3125 Hz, and 4062 Hz), and one between-subject factor, group (three levels: FM group, FOC group, and M group). The effect of group was not significant, $F(2, 27) = 1.199, p > .05$. The effect of session was not significant, $F(2, 54) = .1616, p > .05$. The effect of frequency was significant, $F(3, 81) = 6.069, p < .05$. The interaction between group and session was not significant, $F(4, 54) = .391, p > .05$. The interaction between frequency and session was not significant, $F(4.129, 111.476) = .653, p > .05$. The interaction between frequency x session x group was not statistically significant, $F(8.257, 111.476) = 1.721, p > .05$.

The mean change in TEOAE level at each frequency collapsed across group and session is shown in Figure 17. Suppression was noted at all frequencies with the greatest amount of suppression in the low to mid frequencies (1562 Hz and 2031 Hz). Results of the post-hoc paired sample 2-tailed t-tests are listed in Table 9. The magnitude of

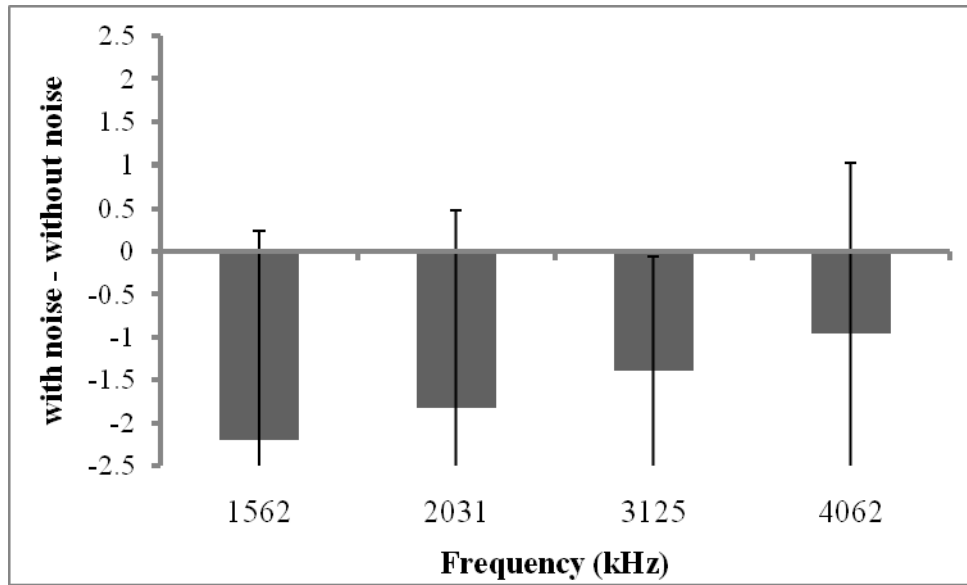


Figure 17. Mean change in TEOAE level following presentation of the binaural noise at each of the four frequencies collapsed across group and session. Error bars represent one standard error of the mean.

Table 9. Results of post-hoc paired sample t-tests for change in TEOAE Level at the four frequencies

Paired Frequencies	<i>T</i>	<i>Df</i>	<i>p</i>
1562 Hz and 2031 Hz	-1.27	89	0.2
1562 Hz and 3125 Hz	-3.57	89	.001*
1562 Hz and 4062 Hz	-4.38	89	.0001*
2031 Hz and 3125 Hz	-1.81	89	.073
2031 Hz and 4062 Hz	-3.07	89	.003*
3125 Hz and 4062 Hz	-2.01	89	.047

Note. The alpha level of .05 was corrected using the Bonferroni adjustment by dividing the number of comparisons that were performed in the paired sample 2-tailed t-test, which resulted in $*p < .008$.

suppression was greater at 1562 Hz than at 3125 and 4062 Hz. The magnitude of suppression at 2031 Hz was also significantly greater than at 4062 Hz.

Chapter 6: Discussion

The primary purpose of this study was to investigate the effects of the menstrual cycle on binaural TEOAE suppression. Changes in unsuppressed TEOAE levels over the course of one month (one menstrual cycle) were also examined. TEOAEs were measured both with and without the simultaneous presentation of a binaural noise in three different groups of participants: females with normal menstrual cycles not taking oral contraceptives, females with normal menstrual cycles taking oral contraceptives, and males.

Unsuppressed (without noise) Broad-band TEOAE Levels and Noise

It was hypothesized that the unsuppressed broad-band TEOAE level would vary across a period of one month (one menstrual cycle) in females with normal menstrual cycles not taking oral contraceptives but would be stable in females with normal menstrual cycles taking oral contraceptives and in males. Review of the individual data for unsuppressed broad-band TEOAE levels revealed no consistent trends for any group or across sessions. Statistical analysis confirmed no statistically significant differences between groups or across sessions.

Mean unsuppressed broad-band TEOAE levels ranged from 11 dB SPL to 24 dB SPL across participants using 60 dB pSPL linear clicks. The range of mean unsuppressed broad-band TEOAE levels reported in this study are higher than the range of mean broad-band TEOAE levels reported in the Hurley et al. (1996) study. The researchers reported mean unsuppressed TEOAE levels ranged from 4.927 to 13.121 dB SPL using 60 dB

pSPL linear clicks for their sample of nine female participants with normal hearing aged 24 to 39 years. It is well documented that there is considerable variation in the level of unsuppressed OAEs in normal-hearing individuals (e.g., Balatsouras et al. 2004; Prieve et al. 1993; Vedantam & Musiek, 1991). For example, Balatsouras et al. (2004) recorded TEOAEs using 80 dB pSPL non-linear clicks and reported levels ranging from 2.2 to 17.7 dB in their sample of 44 males and 63 females with mean ages of 34.8 and 31.3 years. Vedantam and Musiek (1991) also measured TEOAEs in a large sample. They measured TEOAEs using 83 +/- 2dB pSPL non-linear clicks and reported levels ranging from 4.4 to 25.3 dB in their sample of 100 ears of normal hearing participants aged 17 to 63 years.

The group mean for unsuppressed broad-band TEOAE levels of 18.12 dB SPL was also higher in this study compared to other studies. Hood et al. (1996) reported a group mean for unsuppressed TEOAE level of 9.05 dB SPL between 8 and 18 ms for 60 dB pSPL linear clicks for their sample of 48 participants with normal hearing aged 12 to 59 years. Age may be a factor in the low TEOAE level obtained in the Hood et al. (1996) study. Some studies have documented age effects on TEOAEs (e.g. O-Uchi et al. 1994). Prieve, Fitzgerald and Schulte (1997) studied TEOAEs (unsuppressed) using the ILO88 system in 223 participants aged four weeks to 29 years. Review of their input/output functions revealed a group mean for unsuppressed TEOAE level of approximately 2.5 dB SPL for 60 dB pSPL non-linear clicks for their adult participants. As mentioned previously there is considerable variation in the level of unsuppressed OAEs in normal hearing individuals. Berlin et al. (1993) reported a group mean for unsuppressed TEOAE level of 11 dB SPL for 80-82 dB pSPL non-linear clicks for their sample of 11 adults

with normal hearing aged 29 to 65 years. Similarly, Vedantam and Musiek (1991) reported a group mean for unsuppressed TEOAE level of 13 dB SPL for 83 +/- 2 dB pSPL non-linear clicks. Komazec et al. (2003) reported a group mean for unsuppressed TEOAE level as high as 17.89 dB SPL for 80 dB pSPL non-linear clicks in their sample of 28 ears of normal hearing participants with a mean age of 34.3 years.

The differences in the range and group mean levels of unsuppressed TEOAEs across studies may have been due to differences in procedure. One of the eligibility criteria for the current study was robust unsuppressed TEOAEs, defined as a signal-to-noise ratio (SNR) of 6 dB or greater in at least three out of four frequency bands tested. Hood et al. (1996) and Hurley et al. (1996) did not have a similar requirement. The differences in the mean unsuppressed TEOAE levels may be attributed to use of different equipment. This study used the Intelligent Hearing System (IHS) Smart TrOAE (version 2.60) system, while the Hurley et al. (1996) study used the Otodynamics ILO88 system version 4.2C software. Berlin et al. (1993), Hood et al. (1996), Prieve et al. (1997), and Vedantam and Musiek (1991) also used the Otodynamics ILO88 system but the version of the software was not specified in their studies. Komazec et al. (2003) used the Capella Madsen software and hardware. Balatsouras et al. (2004) used the DP Echoport ILO 292 Otodynamics analyzer. It would be helpful if normative data were available for the IHS Smart TrOAE system for comparison.

The results in the present study are consistent with those reported by Yellin and Stillman (1999). They noted no statistically significant change in unsuppressed TEOAE levels across three menstrual cycles in a group of 13 females not taking oral contraceptives aged 25 to 49 years. However, the results in the present study conflict

with those reported by Hurley et al. (1996). Those researchers found unsuppressed TEOAE levels changed over the course of two menstrual cycles in their sample of six female subjects not taking oral contraceptives and three female subjects taking oral contraceptives. The changes observed in the Hurley et al. (1996) pilot study might be due to uncontrolled variables, such as middle ear function, particularly middle ear pressure, and noise exposure. Hurley et al. (1996) performed tympanometry only once at the beginning of the experiment. In contrast, normal middle ear function and normal middle ear pressure were confirmed prior to every session in the current study. Hurley et al. (1996) did not monitor for possible noise exposure prior to testing. In the present study, participants were questioned regarding noise exposure in the previous 48 hours and hearing sensitivity was re-assessed at 4000 Hz prior to OAE testing to rule out noise exposure. In addition, Hurley et al. (1996) did not discuss a method of monitoring the menstrual cycle. In the present study, the menstrual cycle was monitored via a menstrual calendar and an ovulation prediction kit for females not on oral contraceptives. The menstrual cycle for females on oral contraceptives was monitored by a menstrual calendar.

The results of the present study revealed a lack of significant differences in unsuppressed TEOAE levels between the two female participant groups. Hurley et al. (1996) study also revealed a lack of significant differences in unsuppressed TEOAE levels between females not taking oral contraceptives and females taking oral contraceptives. However, unsuppressed TEOAE levels were expected to differ between genders in the present study; specifically, unsuppressed TEOAE levels were expected to be larger in females than males. Higher unsuppressed TEOAE levels in females

compared to males have been documented in previous studies (e.g., Kulawiec & Orlando, 1995). In addition, unsuppressed TEOAE levels are larger in individuals with SOAEs compared to individuals without SOAEs (e.g., Moulin, Collet, Veuillet, & Morgan, 1993) and females tend to have SOAEs more often than males (Penner et al. 1997). In the current sample, SOAEs were present in six females but only one male. It is possible that statistically significant differences in unsuppressed TEOAE levels between groups were not found because of the small sample size.

Although differences in unsuppressed TEOAE levels were expected at the outset of the study, differences in corresponding noise levels were not expected across groups or sessions. Mean noise levels were 9.06 dB SPL for females not on oral contraceptives, 10.35 dB SPL for females on oral contraceptives, and 10.80 dB SPL for males. Statistical analysis for noise level for broad-band unsuppressed TEOAE levels confirmed that noise levels did not differ significantly across groups or sessions.

Noise levels recorded in the present study were high compared to previous reports (e.g., Prieve et al. 1993; Vedantam & Musiek, 1991). Prieve et al. (1993) reported a mean noise level of 3.43 dB (reference not specified) in their sample of 11 participants aged 4-81 years tested using the ILO88 system and 80 dB pSPL nonlinear clicks. Vedantam and Musiek (1991) measured TEOAEs using the ILO88 system, 83 +/- 2 dB pSPL clicks and reported a mean noise level of 0.88 dB (reference not specified) for their sample of adults. Researchers who measured unsuppressed TEOAEs using lower click levels and the ILO88 system did not report on mean noise levels (e.g., Berlin et al. 1995; Hood et al. 1996; Hurley et al. 1996). The higher noise levels were noted despite the fact

that the linear mode was used. Fitzgerald and Prieve (1997) reported lower noise floor for the linear click presentation mode compared to the nonlinear mode.

The differences in noise levels are most likely attributable to differences in equipment used. The majority of previous studies have used the Otodynamics ILO system, whereas the Intelligent Hearing Systems Smart TrOAE was employed in the present study. The filter setting on the IHS Smart TrOAE system may be set wider than the filter settings for Otodynamics ILO system. Fitzgerald and Prieve (1997) used a filter setting from 976 to 4886 Hz for the Otodynamic ILO system. As mentioned previously, the default setting for the filter on the IHS system is from 500-5000 Hz. This may have resulted in higher noise levels due to the inclusion of more low frequency energy.

The majority of participants in the study showed changes in TEOAE levels across each session. As a result, the range of variability test-retest within each session for each group for broad-band TEOAE level in the without-noise and with-noise were examined for comparisons. For broad-band TEOAE level measured without noise the mean variability for the females not on oral contraceptives ranged from +.19 to +.28 dB. The mean variability ranged from +.02 to +.25 dB for females on oral contraceptives and the mean variability ranged from was -.22 to +0.59 dB for males. For broad-band TEOAE levels measured in the with-noise condition the mean variability ranged from -.04 to -.4 dB for females not on oral contraceptives. The mean variability ranged from -.07 to +.06 dB for females on oral contraceptives and ranged from -.45 to +1.3 dB for males. It is well documented that there is considerable variability in suppression within and between participants, which may be due to the fact that the suppression effect is very small (Graham & Hazell, 1994). Graham and Hazell (1994) studied the individual variability

for contralateral suppression in normal hearing participants and participants with tinnitus for six weeks. The researchers not only found significant variability between tests for each session for participants with tinnitus but also found significant variability between tests for each session for participants with normal hearing. The standard deviation for the normal hearing participants ranged from +.10 to +.25 dB. Hood et al. (1996) also examined the variability for contralateral suppression across participants and found the standard deviation for variability ranged from +.07 to +.36 dB. A direct comparison of these studies cannot be made to the present study as this study examined the mean variability for broad-band TEOAE level in the without-noise and with-noise conditions while the other studies examined the standard deviations for contralateral suppression. The variability within each session in this study was minimized, because in most cases the OAE probe was not removed and reinserted between test runs. However, occasional repositioning of the ear probe or insert earphone was required. The size of the tip used on the OAE probe was recorded for each participant and as a result, the same size ear tip was used for each session for that particular participant.

Unsuppressed TEOAE and Noise Levels at Specific Frequencies

Unsuppressed TEOAE levels at specific frequencies were examined for differences across groups or sessions. Inspection of individual data indicated that a change in TEOAE level of 5 dB or more at two or more frequencies was noted between sessions for a majority of the participants (21 of 30); however, a consistent pattern of change was not apparent within a given participant group or across test sessions/ phases of the menstrual cycle. Statistical analysis confirmed that there was no significant

difference in unsuppressed TEOAE levels between groups or across sessions at specific frequencies. A significant effect of frequency was noted, consistent with previous reports in the literature. Unsuppressed TEOAEs are larger in the 1000 and 2000 Hz frequency bands in normal hearing adults (e.g., Bonfils & Uziel, 1989; Vedantam & Musiek, 1991). In the present study, unsuppressed TEOAE levels were significantly larger at 1562 and 3125 Hz compared to 2031 and 4062 Hz. A direct comparison cannot be made to the Bonfils and Uziel (1989) or Vedantam and Musiek (1991) studies as those researchers reported on a range of frequencies and the band-widths of the frequency bands were not specified. In contrast, the present study examined TEOAE levels at individual specific frequencies. However, the patterns observed in the present study are consistent with the Bonfils and Uziel (1989) study.

Noise levels at specific frequencies were also examined to determine if the levels were significantly different across groups or sessions. The purpose of analyzing noise levels at specific frequencies was to ensure the noise levels were stable for each group and from session to session. Statistical analysis confirmed that there were no significant differences in noise levels between groups or across sessions. However, there was a significant effect of frequency, consistent with previous literature. It is well documented that noise levels at frequencies below 1500 Hz are higher than at frequencies of 1500 Hz and above (e.g., Gorga et al. 1993). Mean noise levels for unsuppressed TEOAEs were largest at 1562 Hz and noise levels at different frequencies were significantly different from one another with the exception of 2031 and 4062 Hz. In most previous work, TEOAE and noise levels were examined across a range of frequencies, typically octave, half-octave, or 1/3 octave bands (e.g., Gorga et al. 1993). In the present study TEOAE

and noise levels were examined at specific individual frequencies and as a result a direct comparison cannot be made but the patterns observed in the present study are consistent with earlier work.

Change in Broad-band TEOAE Level with the Presentation of Noise

Broad-band TEOAE levels measured following presentation of binaural noise were expected to change across the period of one month (one menstrual cycle) in females with normal menstrual cycles not taking oral contraceptives but to remain stable across the period of one month (one menstrual cycle) in females with normal menstrual cycles taking oral contraceptives and in males. Changes in broad-band TEOAE level following presentation of binaural broad-band noise ranged from -2.80 to +3.28 dB for females not on oral contraceptives, from -3.22 to +4.50 dB for females on oral contraceptives and from -2.80 to +2.87 dB for males. Both suppression and enhancement were seen. The magnitude of change was consistent with that reported in previous literature (e.g., Vuillet et al. 1991; Vuillet, Duvercy-Bertholon & Collet, 1996). For example, Berlin et al. (1995) reported a change -2.5 to -4 dB between 8-18 msec for binaural TEOAE suppression using the ILO88 system.

The mean data seem to indicate several trends as shown in Figure 9. The mean data for females not on oral contraceptives indicated suppression at the first and third sessions (menstruation and pre-menstruation) but little change at the second session (during the LH surge). Data for males indicated mainly suppression that appeared to remain relatively stable across sessions. However, the magnitude of suppression was small in these two groups and ranged from -.16 to -.75 dB. Mean data for females on oral

contraceptives seem to indicate enhancement at all sessions. Enhancement of TEOAEs has been reported in isolated cases of individuals with tinnitus and hyperacusis (Collet, Veuillet, Bene & Morgan, 1992) or acoustic neuromas (Quaranta, Gandolfi, Fava, Quaranta, & Zini, 2000). Enhancement has most commonly been reported for DPOAEs (e.g., Brown & Norton, 1990). However, the enhancement observed in this group also was small, ranging from .1 to .4 dB, and similar in magnitude to the range of test-retest variability. It seems likely that the small mean values for the group can be attributed to the variability in suppression/enhancement magnitudes across individuals. The individual values ranged from -3.22 dB of suppression up to +4.5 dB of enhancement and likely cancelled one another out to a great extent when the means were calculated.

Statistical analyses indicated no significant group or session effects. The small number of participants in each group may have contributed to the lack of statistical significance. Perhaps the trends seen in the female groups would have been more apparent and reached significance in a larger sample. The trend of enhancement for the females on oral contraceptives would be notable if it is genuine. As mentioned previously, enhancement of TEOAEs has been reported in isolated and rare cases of individuals with tinnitus and hyperacusis (Collet, Veuillet, Bene & Morgan, 1992) or acoustic neuromas (Quaranta, Gandolfi, Fava, Quaranta, & Zini, 2000). Enhancement has most commonly been reported for DPOAEs (e.g., Brown & Norton, 1990). Several researchers propose that the enhancement seen in DPOAEs may be a result of the combination of the energy from the two DPOAE mechanisms/sources (e.g., Martin et al. 2005; Meinke et al. 2005). It may be possible that the synthetic hormones used by the females on oral contraceptives may have affected the efferent system which then may

have impacted the function of the outer hair cells. It is also possible that the trend seen in this group may simply be an artifact and may have not existed if a larger sample was tested.

Change in TEOAE Level Following Presentation of Binaural Noise for Specific Time Intervals

All participants in this study showed suppression or enhancement following presentation of binaural noise in at least some post-stimulus time intervals. Both suppression and enhancement were noted, sometimes within the same individual in different time intervals. Changes in TEOAE levels ranged from -8.71 to +11.24 dB for females not on oral contraceptives, from -11.25 to +12.61 dB for females on oral contraceptives, and from -10.30 to +10.17 dB for males. The changes in TEOAE levels reported in this study are greater than those reported by Hurley et al. (1996). Hurley et al. (1996) reported magnitudes of suppression ranging from -0.425 to -4.436 dB SPL.

The change in TEOAE levels reported in this study also is greater than the range of suppression reported by Berlin et al. (1995) study. These researchers reported that the amount of binaural TEOAE suppression ranged from -2.5 to -4 dB between 8 and 18 ms post-stimulus. Several factors may have contributed to the differences. Berlin et al. (1995) tested using clicks and binaural white noise presented at 65 dB p SPL. In this study the click level was set at 60 dB pSPL and the noise level was presented binaurally at 65 dB pSPL. Both Berlin et al. (1995) and Hurley et al. (1996) used the ILO88 system, while this study used the IHS system.

Review of the individual data revealed no consistent trend of TEOAE level change in the various post-stimulus time intervals. Some participants showed suppression or enhancement that varied little from session to session, while for other participants the amount of suppression or enhancement varied more notably from session to session. Hood (2002) reports that normal hearing individuals show suppression at most time intervals. In the literature, mainly mean TEOAE suppression data have been reported. In the current study, mean data for TEOAEs measured following presentation of binaural noise revealed primarily suppression in the time domain. As shown in Figure 12, changes in the magnitude of suppression across the three sessions appeared to differ for each group. In the FM group, suppression appeared to be greatest during menses (session one) and least during the LH surge (session two). In contrast, suppression appeared to be greatest during pre-menstruation (session three) and least during menses (session one) for the FOC group. The FOC group showed a slight enhancement of 1.01 dB in the first time interval (3.0-5.0 ms) in the third session (pre-menses). The magnitude of suppression appeared to be smaller and stable across sessions for the male group. However, statistical analysis of group data indicated no significant effects of group or session.

Results from the present study are consistent with those reported by Hurley et al. (1996). Hurley et al. (1996) found TEOAE suppression to be stable across the menstrual cycle in females not taking oral contraceptives and females taking oral contraceptives and noted no differences in the magnitude of suppression between the two groups. On the other hand, the results in the current study differ from those reported by Barham et al. (1995). Barham et al. (1995) reported that the absolute amount of suppression in three

noise conditions (binaural, ipsilateral and contralateral) for TEOAE suppression was greater in females than in males. Barham et al. (1995) did not specify the difference in the magnitude of suppression for females versus males. As stated previously, a difference in the magnitude of suppression between females and males could have been expected based on the trends observed in Figure 12; however, it is possible that the difference between groups did not reach statistical significance in this study because of the small sample size.

As shown in Figure 13, mean suppression was significantly greater in the later time intervals, specifically from 6.0-8.0 ms to 18.0-20.0 ms. This pattern for suppression has been well documented (e.g., Hood et al. 1996; Velenovsky & Glatke, 2002). Berlin et al. (1993b) proposes that suppression may be seen in the later time intervals as it may take at least 4 ms for the information to travel to and back from the olivocochlear neurons.

Change in TEOAE Level Following Presentation of Binaural Noise at Specific Frequencies

Similar to the individual data for the post-stimulus time intervals, some amount of suppression and enhancement was noted in at least some frequencies for all participants. For some participants, the magnitude of suppression or enhancement varied little from session to session while for other participants the amount of suppression or enhancement varied more notably from session to session. The change in TEOAE level at specific frequencies during presentation of binaural noise ranged from -7.41 to +2.93 dB for females not on oral contraceptives, -6.09 to +3.83 dB for females on oral contraceptives,

and -8.64 to +2.53 dB for males. No enhancement was observed in the mean data for the different groups. Unfortunately, the ability to compare the present results to other studies is limited, because other researchers have most often describe suppression as an absolute overall amplitude in dB (e.g. Collet et al. 1990) or describe suppression in only post-stimulus time intervals (e.g. Berlin et al. 1995; Berlin et al. 1996; Hood et al. 1996) and not at specific frequencies or frequency bands. Brashears et al. (2003) used binaural noise and reported suppression of approximately -1 to -2 dB SPL for non-musicians and -1 to -4 dB SPL for musicians across 32 frequency bands from .195 to 6.25 kHz. The smaller magnitude of change in TEOAE levels reported by Brashears et al. (2003) study compared to this study may be due to age differences between the populations tested. Brashears et al. (2003) tested 28 participants aged 25.4 to 62.8 years. The 30 participants in the present study ranged in age from 18 to 35 years. There were also differences in stimuli parameters and equipment between the two studies. The click level was set at 65 dB pSPL and the noise level was set at 70 dB pSPL for the Brashears et al. (2003) study. For this study, the click level was set at 60 dB pSPL and the noise level was set at 65 dB pSPL. The ILO88 system was used in the Brashears et al. (2003) study whereas the IHS system was used in this study.

Morand et al. (2000) also studied change in TEOAE level as a function of frequency in 59 participants with a mean age of 24 years but used only contralateral noise. They reported mean suppression of approximately .5 to 1 dB for their sample across 11 frequency bands from 500 to 6000 Hz. The smaller magnitude of change in TEOAE levels reported by Morand et al. (2000) compared to this study is likely due to differences in stimulus parameters and the suppression paradigm. Morand et al. (2000)

recorded TEOAEs using linear clicks presented between 60 and 72 dB pSPL and broadband noise presented contralaterally at 30 dB sensation level through an audiometer. It is well documented that contralateral and ipsilateral stimulation produces the least amount of suppression and the greatest amount of suppression is seen with binaural stimulation (Berlin et al. 1995).

Morand et al. (2000) found suppression to be greater in the low frequencies, specifically greater suppression was observed in the 750-1750 Hz frequency band. Brashears et al. (2003) found greater suppression in the 1000-2000 Hz frequency band. These results are similar to the present study in that suppression was found to be greater in the lower frequencies, specifically 1562 Hz and 2031 Hz, even though the present study examined suppression in individual specific frequencies and not in frequency bands. Morand et al. (2000) propose that the spectrum of the suppressor or the spectrum of the stimulus may cause suppression to be greater in the lower frequencies. Similarly, the spectrum of a TEOAE depends on the spectrum of the stimulus used to evoke it (Probst et al. 1991) and the cochlea is tonotopically organized (e.g., Kemp, 1978).

SOAEs

SOAEs were present in five females not on oral contraceptives, one female on a oral contraceptive, and one male. It was expected that more females than males would have SOAEs and more participants in general would have SOAEs based on previous reports. Penner and Zhang (1997) estimated the prevalence of SOAEs in females to be from 64 to 81% and the prevalence of SOAEs in males is estimated to be from 39 to 55%. We had intended to examine whether SOAE frequencies changed across a period

of one month (one menstrual cycle); the SOAE data could not be interpreted with confidence, because the noise floor varied from session to session. There were multiple cases where an SOAE was present at a particular frequency in one session but was absent at that particular frequency in another session. It was difficult to determine if this change in SOAEs was actually due to the phase of the menstrual cycle or due to an increase or decrease in the noise floor from session to session. SOAEs were assessed only once during each session and the stability and reliability of the SOAE, as well as the noise floor within a session could not be verified. As a result, the changes in SOAEs across the menstrual cycle were not analyzed in this study.

Limitations of the Present Study

There are several limitations to this study. The study consisted of a small sample size with only 10 individuals per group. Trends observed in the present study might have been statistically significant if a larger sample size were obtained. The sample also lacked diversity. The participants consisted of 23 Caucasians, three African Americans and four Asians. Previous work has indicated that race may have an effect on incidence of hearing loss (Helzner et al. 2005), susceptibility to noise damage (Jerger, Jerger, Pepe & Miller, 1986), and middle ear problems (Hunter, Davey, Kohtz, & Daly, 2007); therefore, it is possible that differences in OAE suppression might be found between members of different races. Future studies should examine the influence of race on the efferent system.

Another limitation to the study is that regularity of the menstrual cycle was based on self-report and marking of the calendar for only one cycle. Yellin and Stillman (1999)

monitored the menstrual cycle for three cycles and Hurley et al. (1996) monitored the cycle for two cycles. The menstrual cycle should be monitored for at least three cycles to ensure the menstrual cycle did not vary more than three days (personal communication with practicing Gynecologist, Dr. Taleb, M.D.). SOAEs were not assessed more than once during each session, which made interpretation of the data challenging. Testing of SOAEs twice during each session would have ensured the results were more reliable. Insertion depth of the OAE probe and insert earphone should be monitored. Secondary, independent verification of the level of the stimuli in the ear canal was not obtained using a probe microphone. In addition, secondary, independent verification of the duration of the suppressor and the interval between the suppressor and the stimulus were not obtained using a spectrum analyzer. Finally, no normative data were available for the IHS Smart TrOAE system. As a result, direct comparisons and generalizations of the results obtained in this study were difficult to make as previous studies have most often used the ILO Otodynamic system.

Conclusion

Although, measurements of TEOAE suppression are not performed routinely by clinicians at this time, clinical applications of TEOAE suppression are currently under investigation. Before any measure can be used effectively, normal variation must be defined. Multiple studies have shown an influence of female sex hormones on different hearing measurements (e.g., Baker & Weiler, 1977; Davis & Ahroon, 1982; Elkind-Hirsh et al. 1992); therefore, the menstrual cycle presented one potential source of variability. Results of the present study do not indicate any significant changes in unsuppressed

TEOAE level or in TEOAE suppression/enhancement associated with the menstrual cycle. From a clinical standpoint, these negative results could be considered fortuitous in that the phases of the menstrual cycle would not need to be taken into account when interpreting unsuppressed TEOAE levels or TEOAE suppression/enhancement results. However, it is possible that the small sample size contributed to the negative findings and that several trends noted in the data might be significant were a larger sample examined.

This may be the first study to report unsuppressed TEOAE levels and TEOAE levels obtained following presentation of binaural noise for young normal hearing adults using the IHS system. Furthermore, this study may be the first study to report mean noise levels for unsuppressed TEOAEs using the IHS system. When compared to levels reported in the literature, the present study found higher levels for unsuppressed TEOAEs, for TEOAEs recorded with binaural noise, and for noise. However, the patterns observed for these measurements, such as greater TEOAE suppression in later time intervals and at lower frequencies, were all consistent with the literature.

Appendix A

CONSENT FORM

<p>Project Title</p>	<p><i>The effect of the menstrual cycle on evoked otoacoustic emission suppression.</i></p>
<p>Why is this research being done?</p>	<p><i>This is a research project being conducted by Dr. Tracy Fitzgerald and Sally Mahmood in the Department of Hearing & Speech Sciences at the University of Maryland, College Park. We are inviting you to participate in this research project because you are over 18 years of age and in good physical health. The purpose of this research project is to study the effect of the menstrual cycle on the auditory system, specifically on sounds that can be recorded from the inner ear.</i></p>
<p>What will I be asked to do?</p>	<p><i>Full participation in this study and involves three to four sessions of 1-2 hours duration. Testing will take place in Lefrak Hall in the Hearing Clinic and in room number 0147D.</i></p> <p><i>During the initial session, you will be asked to complete a case history form on general and ear health. Female participants will also be asked to complete a questionnaire on regularity of the menstrual cycle and method of contraception. You will be weighed so that Body Mass Index (BMI) can be calculated. BMI is a measurement of your height/weight ratio. You will be informed as to whether you meet the criteria to continue participation in the study.</i></p> <p><i>You will then undergo a hearing test. You will listen to tones and be instructed to raise your hand or push a button. You will be asked to repeat back words heard through the earphones. Your ear canal and ear drum will be inspected. During this test, a small scope much like a flashlight with a plastic tip will be placed in the opening of the ear so that the investigator can look down the ear canal. You will then undergo tests to assess the health of the middle ear (ear drum, bones of ear). During this a small plug with a soft rubber tip will be placed into the opening of one ear and an earphone will be placed on the other ear. You will be asked to sit quietly and no response will be required. You will hear a buzzing tone coming from the plug and will feel a slight change in pressure while the machine checks eardrum mobility. You will then hear a series of short tones coming from the plug and the earphone. The middle ear testing will be followed by a measure of soft sounds that can be recorded in the ear canal, which will test the function of the inner ear. During this test, you will be asked to sit quietly and no response will be required. A small plug with a soft rubber or foam tip will be placed in the opening of the ear. You will hear a clicking sound and/or noise coming from the plug. The results of the hearing test will be explained to you and you will be informed if you meet the criteria for further participation in the study.</i></p> <p style="text-align: center;"><i>-continued on next page-</i></p>

Project Title	<i>The effect of the menstrual cycle on evoked otoacoustic emission suppression.</i>
	<p><i>The remaining sessions (two-four) will involve repeated testing to check the outer and middle ear and measurements of the sounds in the ear canal, as well as repeat testing of hearing to ensure hearing is stable during each session. We will be checking how the sounds in the ear canal change in the presence of a noise. During these measurements, you will be asked to sit quietly and no response will be required. A small plug with a soft rubber or foam tip placed in the opening of one ear and an earphone in the other ear. You will hear clicks or noise coming from the plug and the earphone. Please note that if normal results are not obtained for the outer or middle ear tests on a particular day or if hearing changes significantly during the hearing test, then testing will have to be re-scheduled for a different day. You will be informed of your outer and middle ear test and hearing results at each session.</i></p> <p><i>If you are male participant, you will be tested in three sessions. The second session will be scheduled approximately 2 weeks after the first session and the third session will be scheduled 7-9 days after the third session.</i></p> <p><i>If you are a female participant, you will be tested over four sessions. The second session will be within the first three days of your menstrual period, the third session will be scheduled approximately 2 weeks later, and the fourth session will be scheduled 7-9 days after the third session. Female participants who are not taking oral contraceptives will also be provided with an ovulation prediction kit and will be asked to monitor the lutenizing hormone (LH) for approximately 7 days to assist the experimenter in determining the time of ovulation. LH is one of the hormones that is characteristic of the menstrual cycle.</i></p> <p><i>If you complete all test sessions you will be reimbursed \$10.00 an hour for your time, which will be given to you at the end of the last session.</i></p>
What about confidentiality?	<p><i>We will do our best to keep your personal information confidential. To help protect your confidentiality, your name will not be included on the collected data; all data will be coded using a number and not with any identifying information. Your data will be grouped with data from other participants for reporting and presentation; participants' names will not be used.</i></p> <p><i>Your information may be shared with representatives of the University of Maryland, College Park or governmental authorities if you or someone else is in danger or if we are required to do so by law. In accordance with legal requirements and/or professional standards, we will disclose to the appropriate individuals and/or authorities information that comes to our attention concerning child abuse or neglect or potential harm to you or others</i></p>

<p>What are the risks of this research?</p>	<p><i>There are no known risks associated with your participation in this research. The hearing, middle ear, and inner ear tests used in this study are used in audiometry clinics during routine evaluations of hearing.</i></p>
<p>Project Title</p>	<p><i>The effect of the menstrual cycle on evoked otoacoustic emission suppression.</i></p>
<p>What are the benefits of this research?</p>	<p><i>This research is not designed to help you personally, but the results may help the investigator learn more about the effects of the menstrual cycle on the inner ear measures. We hope that, in the future, other people might benefit from this study through improved understanding of how female sex hormones affect the functioning of the central auditory system. You will receive a free hearing test and you will be provided with a copy of your hearing results.</i></p>
<p>Do I have to be in this research? May I stop participating at any time?</p>	<p><i>Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time. If you decide not to participate in this study or if you stop participating at any time, you will not be penalized or lose any benefits to which you otherwise qualify.</i></p>
<p>What if I have questions?</p>	<p><i>This research is being conducted by Sally Mahmood and Tracy Fitzgerald, Ph.D. in the Department of Hearing and Speech Sciences at the University of Maryland, College Park. If you have any questions about the research study itself, please contact:</i></p> <p>Tracy Fitzgerald, Ph.D., Department of Hearing and Speech Sciences, University of Maryland, College Park, MD 20742, (301)405-4224, tfitzgerald@hesp.umd.edu</p> <p><i>If you have questions about your rights as a research subject or wish to report a research-related injury, please contact:</i></p> <p>Institutional Review Board Office, University of Maryland, College Park, Maryland, 20742; (e-mail) irb@deans.umd.edu; (telephone) 301-405-0678</p> <p><i>This research has been reviewed according to the University of Maryland, College Park IRB procedures for research involving human subjects.</i></p>
<p>Statement of Age of Subject and Consent</p>	<p><i>Your signature indicates that:</i> <i>you are at least 18 years of age,;</i> <i>the research has been explained to you;</i></p>

	<i>your questions have been fully answered; and you freely and voluntarily choose to participate in this research project.</i>	
Signature and Date	NAME OF SUBJECT	
	SIGNATURE OF SUBJECT	
	DATE	

To facilitate scheduling of later sessions, please provide the following contact information:

PHONE _____

E-MAIL _____

____ Please check here if you are interested in being contact for future studies, yet you are not obligated to do so.

Subject # _____

Date _____

Audiological and General Health History

The following questions are intended to help us determine your eligibility for the study. In particular we need to rule out problems related to hearing and hormones. If you are uncomfortable answering these questions, you are free to withdraw from the study without penalty.

Gender _____

Height _____

DOB _____

Age _____

examiner use only:

Weight _____

BMI: _____

Audiological History:

1. Do you have a hearing loss or do you suspect you have trouble with your hearing? If yes, please describe:

2. Is there a history of hearing loss in your family? If yes, please describe.

3. Have you been exposed to loud noise at work or in recreational situations? If yes, please describe.

4. Have you experienced any head trauma? If yes, please describe:

5. Do you experience tinnitus (ringing or sounds in the ears)? If yes, please describe:

6. Do you experience problems with dizziness or balance? If yes, please describe:

7. Do you have a medical problem that involves your ears? If yes, please describe:

8. Have you ever had any ear infections? If yes, when, how many and how were they treated?

History of Disease: Please circle any of the following that apply to you.

Cushing's Syndrome / Hypercortisolism (body is exposed to too much of the hormone cortisol).

Thyroid Disorder

Pituitary Gland Disorder

Pituitary Tumor

Hyperprolactinemia (body is exposed to too much of the hormone prolactin)

Hypogonadotropin (brain does not make enough gonadotropin releasing hormones)

Lupus (autoimmune disease)

Adrenal Disorder

Blood Disorder

Diabetes

Liver Disease

Kidney Disease

Premenstrual Dysphoric Disorder (PMDD) (severe PMS that is distressing and disabling and requires treatment)

Polycystic Ovary Disease (benign cysts that form on the ovaries)

Uterine Fibroids (benign tumors in the uterus)

Cervical Polyps (growths originating from the mucosal surface of the cervix or endocervical canal)

Endometrial Polyps (localized overgrowths of the innermost uterine layer)

Pelvic Inflammatory Disease (infection of the upper genital tract)

Adenomyosis (presence of endometrial glands and supporting tissues in the muscle of the uterus where it would not occur normally)

Endometriosis (endometrial tissue that grows outside of the uterus and attaches to other organs)

Endometrial Hyperplasia (thickening and overgrowth of the endometrium)

Cancer

Turner Syndrome (syndrome associated w/ heart defects, short stature and loss of ovarian function)

Hermaphroditism (referring to being of both sexes (intersexual))

Subject # _____

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Testicular feminization / Androgen Insensitivity Syndrome (AIS) (a person has one X and one Y sex chromosome (making them genetically male), but is resistant to male hormones)

Depression

Epilepsy

History of Treatment / Medication:

1. Have you ever had chemotherapy or radiation therapy?

2. Are you currently on or have you been on any hormone replacement therapy?

3. Do you take medications for depression?

4. Do you take medications for epilepsy?

5. Please circle any of the following medications that apply to you?
Gonadotropin-releasing hormone (GnRH)
Nafarelin (Synarel)
Leuprolide (Lupron)
Goserelin (Zoladex)
Danazol (Danocrine)

6. Please list your current medications.

Race & Ethnicity

The following questions will in no way affect your eligibility to participate in the study, but may be used in data analysis. If you are uncomfortable answering these questions, you are free to withdraw from the study without penalty or check the box at the bottom of the list.

Ethnicity

Do you consider yourself Hispanic or Latino? (See definition below). Select one.

Hispanic or Latino: A person of Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race. The term “Spanish origin” can be used in addition to “Hispanic or Latino”.

Hispanic or Latino

Not Hispanic or Latino

Race

What race do you consider yourself to be? Select one or more of the following:

- American Indian or Alaska Native.*** A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.
- Asian.*** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies).
- Black or African American.*** A person having origins in any of the black racial groups of Africa. Terms such as “Haitian” or “Negro” can be used in addition to “Black” or “African American”.
- Native Hawaiian or Other Pacific Islander.*** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
- White.*** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
- More than one race or other subpopulation.

Check here if you do not wish to provide some or all of the above information

Subject # _____

Date _____

Questionnaire For Female Subjects

The answers to the following questions will help us determine your eligibility for this study. We need to know more about your periods, menstrual cycle history and contraceptive use, because we are interested in how the menstrual cycle effects our measurements. If you are not comfortable answering these questions, you may withdraw from the study at any time without penalty.

History of Menstrual Period:

1. Do you have a regular menstrual period?
2. How many days does your period last?
3. How many days long is your menstrual cycle? (time from the start of you period to the start of your next period)
4. When was the first day of your last period?
5. Do you experience a feeling or physical symptom(s) that indicate you are going to have your period (e.g., bloating, breast tenderness)? If yes, please describe.
6. Has your menstrual period ever stopped for more than 6 months?
7. Do your menstrual periods occur 6 weeks or more apart?
8. Does your menstrual period occur more frequently than every 25 days?
9. Do you experience bleeding between your periods?
10. Do you have heavy periods where your sanitary napkin or tampon is soaked every hour?
11. Do you experience short or light periods (streaks of blood)?

History of Pregnancy:

1. Have you been pregnant in the last 2-3 months?
2. Are you currently breast-feeding?
3. Are you currently trying to get pregnant?

Appendix C

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Subject # _____

General Health:

1. Do you exercise regularly?
2. If yes, how many hours a week do you exercise?
3. If yes, are you an athlete? Please describe:

4. Does your weight fluctuate frequently? Please describe:

Method of Contraception:

1. Do you take an oral contraceptive (“the pill”)? **If yes, please answer Questions 2 –6; if no skip to Question 7.**
2. What is the name of the oral contraceptive you are taking?
3. How long have you been taking the oral contraceptive?
4. Do you take the pill to prevent pregnancy or to regulate your cycle?
5. How many times in the last year have you missed a pill?
6. When was the last time you missed a pill?
7. If you do not take an oral contraceptive, but have taken one in the past, how long have you been off the pill?
8. Please circle any of the following birth control methods that you are currently using or have used within the past three months:

Transdermal patch such as Ortho Evra

Injectable contraceptive such as Depo Provera

Norplant sub-dermal implant

Intrauterine system such as Mirena

Vaginal ring such as Nova Ring

Plan B

Seasonale

Appendix D

MENSTRUAL CYCLE CALENDAR

Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	No. of days from start of period to beginning of next			
January																																			
February																																			
March																																			
April																																			
May																																			
June																																			
July																																			
August																																			
September																																			
October																																			
November																																			
December																																			

Instructions:

Please mark an X for every day you have your period (first day of bleeding to the last day of bleeding).

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