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Measures of Auditory Inhibition in Female Smokers and Non-Smokers

Christopher Gray Clinard
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To the Graduate Council:

I am submitting herewith a thesis written by Christopher Gray Clinard entitled "Measures of Auditory Inhibition in Female Smokers and Non-Smokers." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Arts, with a major in Speech and Hearing Science.

Ashley W. Harkrider, Major Professor

We have read this thesis and recommend its acceptance:

James Thelin, Mark Hedrick

Accepted for the Council:
Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

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Vice Chancellor and Dean of Graduate Studies

MEASURES OF AUDITORY INHIBITION IN FEMALE SMOKERS AND NON-SMOKERS

A Thesis Presented for the

Master of Arts Degree

The University of Tennessee, Knoxville

Christopher Gray Clinard

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ABSTRACT

This study examined the chronic effects of cigarette smoking on auditory inhibition in normal-hearing female smokers and non-smokers. Nicotine is an acetylcholinomimetic drug that affects the central auditory nervous system. Physiologic measures were acoustic reflex threshold, click-evoked otoacoustic emission (CEOAE) amplitude, contralateral CEOAE suppression, and the auditory late latency response (LLR). The behavioral measure recorded was word recognition in the presence of a broadband masker at two signal-to-noise ratios (-5 and 0dB). Auditory responses were obtained from 13 smokers and 10 non-smokers. Results indicated that smoking does not have a significant effect on these auditory measures. However, tendencies observed for the P2 and N2 latencies to increase in the direction of non-smokers' latencies and for word recognition in noise to improve with increasing number of cigarettes smoked on the day of the test session are consistent with the theory that nicotine helps to normalize some parts of the auditory system.

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CHAPTER I

Introduction

This study examined the effects of smoking on auditory inhibition by comparing physiological and behavioral measures in female smokers and non-smokers. Nicotine is an acetylcholinomimetic drug that may affect auditory inhibition by acting on nicotinic cholinergic receptors (nAChRs) present throughout the ascending and descending central auditory nervous system. Several measures of auditory inhibition, including late latency responses (LLR), word recognition in noise, suppression of click-evoked otoacoustic emissions (CEOAEs), and acoustic reflexes to broadband noise in smokers versus non-smokers were examined. There are no reports of these measures being compared previously in this population.

CHAPTER II

Review of Literature

Smoking & Nicotine

Smoking and Nicotine Control

The majority of research focusing on the acute effects of nicotine is confounded by the lack of an ideal method of steady administration. Due to the many chemicals present in cigarettes, studies that have used cigarettes as the means of nicotine administration cannot rule out the effects of these other chemicals. In addition, smokers do not inhale the same amount of smoke, nor do all brands of cigarettes have the same amount of nicotine in them. Various studies have attempted to control for nicotine administration by using tablets (Wesnes and Warburton, 1983), nicotine chewing gum (Adler et al, 2001), subcutaneous injection (Kumari, Cotter, Checkley, and Gray, 1997), cigarettes (Dengerink, Lindgren, and Axelsson, 1992), and by transdermal nicotine patch (Harkrider, Champlin, and McFadden, 2001; Harkrider and Champlin, 2001a; Harkrider and Champlin, 2001b). In studies where nicotine was administered by cigarettes, there have been attempts to control nicotine intake by setting an amount of cigarette puffs, seconds inhalations are held, and volume of cigarettes smoked.

Nicotine reaches the brain within ten seconds of inhaling cigarette smoke, and over 90% of the nicotine that reaches the brain is absorbed. Nicotine has a half-life of twenty minutes. Following smoking, nicotine levels may drop to less than 50% of peak value within ten minutes (Wesnes and Warburton, 1983).

In order to avoid the complications of controlling for additive effects of pre-test cigarettes in smokers, one can measure chronic (versus acute) effects of cigarette smoking on experimental measures. Studies of the chronic effects of smoking have varied in the way they have controlled for residual levels of nicotine. Some examples include abstaining overnight from smoking (Wesnes and Warburton, 1983; Tong, Booker, and Knott, 1978), abstaining for specific hours before testing (Tong, Henderson, and Chipperfield, 1980), following normal smoking patterns pre-testing (Della Casa, Hofer, and Feldon, 1999; Friedman, Goldberg, Horvath, and Meares, 1974), and requiring all subjects to smoke immediately before testing (Knott, 1985; Knott, 1986; Knott and Venables, 1978; Friedman, Goldberg, Horvath, and Meares, 1974). This study had smokers follow their normal smoking patterns on the day of the experimental session.

Pharmacological Effects of Nicotine in the CANS

Nicotine is an acetylcholinomimetic drug (Ginzel, 1967; Clarke, Schwartz, Paul, Pert, and Pert, 1985). Nicotinic cholinergic receptors (nAChRs) are found in both the ascending and efferent pathways of the central auditory nervous system. Specifically these receptors are located in the brainstem (Kumar and Tandon, 1996), the thalamus (Clarke et al, 1985), the hippocampus (Ehlers, Somes, Thomas, Riley, 1997; Koylu, 1997), and cortical regions (Bhargava, Salamy, and McKean, 1978). When nicotine is introduced systemically, it is rapidly transmitted from the bloodstream to the brain. Resulting acute effects include upregulation of nAChRs resulting in both excitatory and inhibitory central nervous system (CNS) effects. Previous investigators have interpreted

this as an enhancement of central nervous system responsiveness to stimulus type and stimulus intensity with an accompanying increase in the rate of habituation to those same repetitive stimuli.

Physiological Effects on the CANS

Smoking and nicotine have been shown to have acute effects on various auditory evoked potentials. In general, studies examining the effect of smoking on auditory evoked potentials have found an excitatory influence on some electrical brain activity and suppressive influence on others (Bhargava, 1978; Kumar and Tandon, 1996; Knott, 1987; Bickford and Wear, 1995; Crawford, McClain-Furmanski, Castagnoli Jr, and Castagnoli, 2002). Differences in methodology for smokers and cigarette/nicotine administration (discussed above) may partially explain these inconsistencies. It may also be the case that nicotine is excitatory in some brain regions and inhibitory in others.

Kumar and Tandon (1996) examined the auditory brainstem response (ABR) in ten smokers and twenty-eight age-matched non-smokers. They found that peak latencies of waves I and III were significantly prolonged in smokers as compared to non-smokers, indicating a disruption in neural firing of the auditory nerve and neurons in the lower brainstem. Contrary to the Kumar and Tandon study, Knott (1987) found no significant latency effects on the ABR, but did find a significant increase in wave V amplitude in smoking sessions relative to baseline recordings in which the same smokers had abstained from tobacco overnight.

To avoid many of the methodological confounds mentioned above, Harkrider et al (2001) investigated the acute effects of transdermal nicotine in non-smokers. They found that administration of a transdermal nicotine patch to non-smokers had the effect of increasing the latency and decreasing the amplitude of wave I of the ABR. ABR waves III and V were not significantly changed. This latency increase in wave I could have been due to an increase of efferent, inhibitory activity and/or changes in cochlear blood flow caused by nicotine administration. This amplitude reduction of wave I may also reflect inhibitory action at the level of the VIII nerve. No significant effects were seen in spontaneous or click-evoked otoacoustic emissions (OAEs), indicating the lack of a cochlear effect from nicotine administration.

Harkrider and Champlin (2001a) also examined the middle latency response (MLR) and 40-Hz response. In the MLR, an acute increase in both the amplitude of Na – Pa and the latency of wave Nb was found, suggesting that the excitability of neural generators responsible for these waves increased with nicotine administration. The absolute and inter-peak latencies of the 40-Hz response were also found to decrease, indicating an increased excitability of central generators responsible for the 40-Hz response, including the reticular activating system. These results indicate an effect of faster neural processing/transmission through the afferent central auditory nervous system (CANS).

Freidman, Goldberg, Horvath, and Meares (1974) found that the N1-P2 peak-to-peak amplitude of the late latency response (LLR) was significantly greater in smokers after twelve hours of abstaining from tobacco when compared to amplitudes obtained

when the smokers had followed their normal smoking patterns. Knott (1985a, 1985b, 1986) examined the effects of smoking in groups of female smokers and found that smoking significantly increased P1, N1, and P1-N1 peak-to-peak amplitudes during a non-task condition, but not during a task condition. Knott also found significantly larger P2-N2 amplitudes in non-smoking sessions.

Harkrider and Champlin (2001b) examined the LLR and transdermal nicotine in non-smokers. The amplitude of P1 – N1 increased in the right hemisphere and the latency of N2 decreased, suggesting nicotine increased the excitability of the primary auditory pathways responsible for the LLR. N1-P2 and P2-N2 amplitudes were reduced with nicotine, suggesting simultaneous enhanced inhibitory activity.

Harkrider and colleagues concluded: (1) effects seen in non-smokers with transdermal nicotine patches were similar to those reported in smokers, and (2) overall, the transdermal administration of nicotine to non-smokers acutely affected nuclei involved in afferent and efferent transmission with the paradoxical result of improving primary signal transmission, while at the same time increasing inhibitory modulation of the signal. These findings are consistent with the suggestion that nicotine enhances stimulus filtering or gating reflected by auditory startle (Duncan et al, 2001) and P50 responses (Adler et al, 1993; Crawford et al, 2002), which measure inhibition in the auditory system.

Measures of Inhibition in the Auditory System

Acoustic Reflex Pathway

The acoustic reflex is a contraction of the middle ear muscles elicited by an acoustic stimulus (see Møller, 1984 and Gelfand, 2002 for a detailed review). The stapedius muscle is innervated by the seventh (facial) cranial nerve, while the tensor tympani is innervated by the fifth (trigeminal) cranial nerve. The stapedius tendon projects anteriorly from the posterior wall of the tympanic cavity, where it attaches to the posterior of the neck of the stapes. When the stapedius muscle is activated, the neck of the stapes is pulled in a posterior direction. The tensor tympani resides in the anterior wall of the tympanic cavity, and its tendon articulates with the manubrium of the malleus. Upon contraction of the tensor tympani, the malleus is pulled anteriorly and medially.

When both of these muscles contract, they pull the ossicular chain in directions perpendicular to its normal rotation. This serves to stiffen the chain and reduces its efficacy in transmitting energy to the oval window of the cochlea. The acoustic reflex arc is well established and can be activated bilaterally by monaural (ipsilateral or contralateral) or binaural stimulation (for review, see Gelfand 2002). Thus, measurement of the acoustic reflex evaluates a component of the efferent auditory system. Normal acoustic reflex thresholds range from 85 - 100dB SPL for tonal stimuli and about 20dB lower for broadband stimuli (for review see Gelfand 1984). Test-retest variability has been shown to be low (Forquer, 1979). The acoustic reflex in humans is a contraction of the stapedius muscle (Moller, 1984).

There are several theories as to the purpose of the acoustic reflex. It has long been thought that the acoustic reflex may serve to protect the cochlea from damage. However, the exact purpose of the acoustic reflex is still a matter of debate. Simmons (1964) proposed his perceptual theory which included three ways the middle ear muscles improve perception: (a) the muscles smooth the frequency response of the middle ear (b) modulation of the muscles serves to modulate the frequency and intensity characteristics of environmental sounds and improve attention to acoustic environment and (c) internal low-frequency sounds may be attenuated while not attenuating higher-frequency environmental sounds (Simmons, 1964).

Borg, Counter, and Rösler (1984) reviewed previous theories of middle ear function and proposed its purpose to be an aid in auditory communication by preventing desensitization, interference, and injury to the auditory system. Prevention of desensitization is explained as preventing cochlear receptors from being overloaded and maintaining a semi-constant level of sensitivity. Prevention of interference is explained as the attenuation of low-frequency energy present in human vocalization, which reaches the cochlea by air and bone conduction. The contraction of the muscles to intense levels of sound is hypothesized to protect the inner ear from injury.

The acoustic reflex may be elicited by pure tones, filtered bands of noise, or broadband noise (BBN) presented ipsilateral or contralateral to the probe-ear. An immitance probe placed in the external ear canal indirectly measures the acoustic reflex. This probe contains a microphone, manometer, and small loudspeaker. Immitance is monitored by the probe and stimulus levels are adjusted until a reliable and repeatable

reflex is recorded. A transient increase in the sound level detected by the microphone represents increased impedance of the middle ear system caused by the stapedius muscle. The lowest level at which this response can be recorded is referred to as the acoustic reflex threshold. A hermetic seal must be maintained for acoustic reflex measurement. When possible, the acoustic reflex should be recorded while the air pressure is equal in the ear canal and middle ear.

Acoustic reflexes to BBN in smokers were measured in this study. There are no reports in the literature comparing the BBN acoustic reflex in smokers vs. non-smokers. The acoustic reflex is inhibitory and may be affected in a manner similar to that of the auditory startle response in smokers.

Auditory Startle Response

The auditory startle response (also known as the acoustic startle reflex) is an involuntary reflex of skeletal muscles in reaction to an intense and abrupt stimulus (Duncan et al, 2001; Kumari et al, 1997). The stimulus typically used in studying this response is a click-pair consisting of one low-intensity, non-startling click that may be immediately followed by a more intense startling click, or a startling click alone may be presented. In humans, electromyographic (EMG) recordings are typically made from electrodes placed below the pupil and at the lateral canthus of an eye to record the eyeblink component. Pulses may be pure tones or bands of noise. When the amplitude of the auditory startle response is altered by the less intense non-startling stimulus, this is

known as pre-pulse inhibition and is reflected by a lower amplitude response to the startle stimulus. This response is believed to be related, but not identical, to sensory gating.

Rasmussen, Kallman, and Helton (1997) examined the auditory startle response in rats and found it to be significantly greater when they were in withdrawal from nicotine, suggesting less effective sensory gating. Duncan et al. (2001) found that smokers who abstained from smoking overnight, but smoked as they normally would prior to testing had significantly greater pre-pulse inhibition when compared to their sessions without smoking and to sessions of non-smokers, indicating more efficient sensory gating.

Olivocochlear Bundle Pathway

The olivocochlear bundle (OCB) originates in the superior olivary complex (SOC) of the brainstem. The efferent auditory system has its origins in the auditory cortex. From the cortex it synapses with neurons in the inferior colliculus, lateral lemniscus, superior olivary complex, and the cochlear nuclei. Each cochlea receives bilateral input from the OCB. The primary neurotransmitter of the OCB is acetylcholine. GABA and other neurotransmitters also contribute to neural activation (for a complete review of the OCB, see Sahley, Nodar, and Musiek, 1997).

There are approximately 1800 nerve fibers in the rabbit OCB. Cell bodies of OCB neurons are located in the paracentral nuclei of the SOC, as opposed to the afferent cell bodies in the lateral and medial nuclei. The majority of these fibers (1200) do not cross the brain stem and terminates in the ipsilateral cochlea. These uncrossed fibers are

unmyelinated and primarily innervate ipsilateral inner hair cells (IHCs) by axodendritic synapses with their afferent fibers.

The remaining 600 fibers are myelinated and cross the brainstem near the floor of the fourth ventricle. Some of these crossed fibers have synapses which envelope the base of an outer hair cell (OHC). Stimulation of the medial OCB (MOCB) has several known effects: thresholds of IHCs increase (Brown and Nuttall, 1984), tuning curves of affected auditory nerve fibers are raised, and tuning curves of corresponding fibers are broadened. Efferent fibers have their greatest density at the basal end of the cochlea.

Activation of the MOCB fibers, which synapse with OHCs suppresses OAEs, changes IHC electrical potentials, alters tuning curves of OHCs, IHCs, and auditory nerve fibers, decreases the amplitude of the summating potential, and suppresses the discharge of afferent neurons (Brown and Nuttall, 1984;Galambos, 1956). Pickles (1988) proposed four groups of hypothetical MOCB functions in auditory performance: (1) improvement of signal detection in noise (2) protection of the cochlea from acoustic trauma (3) modulating the mechanical state of the cochlea (4) and a possible role in attention.

The MOCB can be non-invasively activated by contralateral acoustic stimulation (Berlin et al, 1993). It has been shown that stimulation of the medial efferent tract by contralateral acoustic stimulation can decrease the amplitude of OAEs, indicating suppression of OHC motility and basilar membrane motion (Kim, Frisina, and Frisina, 2002; Williams and Brown, 1997). Kujawa, Glattke, Fallon, and Bobbin (1994) suggest

that the pharmacologic properties of the medial efferent inhibition of distortion product OAEs (DPOAEs) are mediated by a nicotinic-like cholinergic receptor.

Measurement of MOCB Activation

There are two categories of OAEs: spontaneous and evoked. Spontaneous OAEs (SOAEs) are generated in the cochlea and are present at one or more frequencies in the absence of external stimulation. Evoked OAEs (EOAEs) have three subtypes: transient evoked (TEOAEs), DPOAEs, and stimulus frequency (SFOAEs). TEOAEs may be elicited by transient click or toneburst stimuli. DPOAEs are elicited by introducing two pure tones into the ear canal. The distortion product most often examined is $2f_1 - f_2$, which will only be present when the OHCs in the corresponding frequency ranges are of sufficient integrity. SFOAEs are elicited by a pure tone and elicit a response from the cochlea at the stimulus frequency. All of the above types of OAEs are more robust for women than men, and more robust in right ears than in left ears (for a comprehensive review of OAEs see Hall, 2000; Robinette and Glattke, 2002).

Acoustic stimulation, whether contralateral, ipsilateral, or binaural, during OAE recording has the effect of reducing the OAE amplitude by activating the MOCB. This suppressive effect is small, typically 1 – 4dB. Binaural suppression of TEOAEs has shown a greater degree of suppression than ipsilateral and contralateral suppression. Ipsilateral suppression of OAEs yields more suppression than a contralateral method (Thornton, 1994; Tavartkiladze, Frolenkov, Kruglov, and Artamasov, 1994). These

results suggest that contralateral suppression of OAEs may not reveal the full extent of the suppressive effect (Berlin, Hood, Hurley, Wen, and Kemp, 1995). The majority of OAE suppression research has investigated the effects of contralateral acoustic stimulation. Binaural and ipsilateral suppression studies require the use of a custom-made probe. The cost and rarity of this type of probe prohibits widespread research using this method. Equipment used for TEOAEs and contralateral suppression is widely used in clinical practice, and additional instrumentation is generally not required. Suppression of DPOAEs has not been researched to the extent of TEOAEs, in part, due to the small decreases in the level of distortion products (Moulin, Collet, and Duclaux, 1993; Williams and Brown, 1995).

Giraud, Collet, Chéry-Croze, Magnan, and Chays (1995) found that patients who had undergone unilateral vestibular neurotomy (which severed the OCB) showed a significant decrease in contralateral TEOAE suppression at the neurotomized side. The same study found that patients with Bell's palsy and paralyzed middle ear muscles had symmetric, unaffected OAE suppression, indicating that the stapedial reflex has a minimal role in OAE suppression.

Harkrider et al. (2001) examined the effects of transdermal nicotine administration on the number and power of SOAEs and magnitude of CEOAEs of non-smokers. Although the results were not statistically significant, they found that nicotine administration had the effect of increasing the CEOAE level in left ears while decreasing CEOAE level in right ears. The authors suggested that this finding may be due to a differential effect of nicotine on the efferent, MOCB pathways in these subjects.

However, MOCB activity was not directly measured. In the published literature, there are no reports of the effect of smoking on OAEs or OAE suppression. As discussed previously, nicotine is an acetylcholinomimetic drug that could possibly have an effect on OAEs by acting on the nAChRs in the MOCB efferent auditory system. The current study compared suppression of CEOAEs in smokers versus non-smokers.

Corticotectal Pathways

Efferent pathways also arise from primary and non-primary areas of each auditory cortex and indirectly influence the SOC and OCB via synapses in the inferior colliculus. These descending tracts are arranged tonotopically, just as the ascending tracts. Neural feedback loops are present between each level of the CANS (for a complete review see Sahley, Nodar, and Musiek, 1997; Spangler and Warr, 1991).

Measurement of Corticotectal Pathways - P50

In normal listeners, the electrophysiological response to the second of a tone- or click-pair delivered closely together will be reduced. This wave component occurs at about 50ms. Intrastimulus delay is typically 500ms. This reduction in neural response to the second signal of the pair is representative of the brain's selective filtering ability. This measure also corresponds to the ability to attend to relevant stimuli. Generators for wave P50 include the temporal lobe (Weate, Moore, and Drake Jr, 1995). Deficiencies in auditory sensory gating are shown by the wave P50 remaining at the same amplitude or by a non-significant decrease in response amplitude to the second click.

Sensory gating, as measured by the P50 response, is diminished in schizophrenic patients. Adler et al. (1993) measured the P50 in schizophrenic patents before and after smoking. They found that smoking significantly lowered the P50 ratio, indicating an increase in sensory gating. This effect was non-significant in non-schizophrenic smokers. Crawford et al. (2002) found significantly greater sensory gating in heavy tobacco smokers when compared to never-smokers. Normalization of sensory gating by nicotine has also been observed in cocaine addicts (Adler et al, 2001). Hetrick et al. (1996) found that women had higher P50 ratios than men, suggesting less sensory gating in females.

Late Latency Response

The auditory LLR consists of four waves in the latency range of 5-350 ms. This potential is mesogenous, in that is affected by stimulus parameters and subject factors, such as arousal and attention (for review see Stapells, 2002). Neural generators for P1 are believed to be the pathways traveling from the inferior colliculus to the medial geniculate body of the thalamus to the auditory cortex (Teas and Kiang, 1964; Woods, Clayworth, Knight, Simpson, and Naeser, 1987). Generators for N1, P2, and N2 are believed to include bilateral auditory cortices and non-specific midline structures (Woods et al, 1987). In addition to arousal, N1, P2, and N2 are also affected by attention (for review see McPherson, 1996). Their amplitude is higher when attended to, as opposed to ignored. Prior to P1, auditory evoked potentials are generally not affected by state of arousal, in which the reticular activating system plays a large role. The effects of

smoking and transdermal nicotine on the LLR reflect both excitatory and inhibitory processes (discussed previously), and responses from non-smokers and smokers were compared in this study. The effects of smoking on auditory inhibition are summarized in Table 1.

Behavioral Measures

Word Recognition in Noise

Speech perception testing is typically performed in quiet during clinical evaluations. However, speech performance testing in noise is a more realistic measure. Wide inter-subject variability in word recognition scores has been seen in listeners with normal hearing, particularly as the SNR decreases (Cooper and Cutts, 1971; Wilson and Strouse, 2002; Beattie, 1989). This variability suggests that, in addition to pure tone thresholds, other factors and/or processes play an integral role in speech perception. Previous studies examining speech-in-noise have presented stimuli monaurally (Cooper and Cutts, 1971; Wilson and Strouse, 2002; Beattie, 1989; Studebaker, 1994) or binaurally (Snell, Mapes, Hickman, and Frisina, 2002) with either multi-talker babble (Cooper and Cutts 1971; Beattie, 1989; Snell et al, 2002; Wilson and Strouse, 2002) or noise of various spectra as a masker (Studebaker, 1994). Studebaker (1994) found that intensity function of listeners with normal hearing; a masker with a frequency spectrum the spectrum of the masker had substantial effects on the slope of the performance-similar to speech would yield the sharpest performance-intensity curve. In contrast, a high-pass masker, which did not resemble the speech spectrum, yielded the flattest

Table 1. Previously reported excitatory and inhibitory (*) effects of smoking/nicotine.

	Response	Latency	Amplitude
Knott (1987)	ABR	No effect	Increased wave V
Kumar and Tandon (1996)	ABR	Waves I and III delayed *	No effect
Harkrider, et al. (2001)	ABR	Wave I delayed *	Wave I reduced *
Harkrider and Champlin (2001a)	MLR/ 40Hz	Wave Nb delayed */ Inter-peak latencies reduced *	Na-Pa increased
Harkrider and Champlin (2001b)	LLR	N2 latency reduced	P1 –N1 increased
Friedman et al. (1974)	LLR	No effect	N1-P2 reduced *
Knott (1985)	LLR	No effect	P1-N1 increase P2-N2 decrease *
Crawford et al. (2002)	P50	No effect	Increased sensory gating *
Adler et al. (1993)	P50	No effect	Increased sensory gating *
Duncan et al. (2001)	Auditory Startle Response	No effect	Reduced pre-pulse inhibition *

performance-intensity function. Some investigators have held the intensity of the word lists steady and varied the intensity of the masker (Cooper and Cutts, 1971; Beattie, 1989; Snell et al, 2002), others have varied the level of the word lists and held the masker intensity steady (Wilson and Strouse, 2002; Studebaker and Taylor, 1994).

Wilson and Strouse (2002) sought to design a clinically applicable word recognition task for hearing-impaired populations. In this study they included a group of normal hearing listeners. The task consisted of seventy monosyllabic words from lists 3 and 4 of the N.U.6 presented in competition with multi-talker babble. Ten words were presented at seven signal-to-babble ratios, ranging by 5dB increments from –10 to +20dB. In the babble condition there was less variability for both the normal and hearing-impaired groups, when compared to the quiet condition. Speech discrimination in noise likely reflects inhibitory processes within the CANS, such as auditory filtering. In this study, it was hypothesized that smokers would perform better than controls on word recognition in noise tasks due to increased auditory inhibition from nicotine. There are no published studies examining the effect of smoking/nicotine on word recognition in noise performance.

Rationale

The purpose of this study was to compare the responses of normal-hearing, female smokers and non-smokers on physiological and behavioral tests that measure auditory inhibition. It was hypothesized that responses from smokers would reflect

stronger inhibitory activity than those from non-smokers. This hypothesis was based on the evidence that nicotine enhances auditory inhibitory processes in various populations.

Objectives include:

I. To determine if the smoking status of the listener causes differences in the amount of efferent, suppressive feedback, as measured by contralateral OAE suppression and acoustic reflexes.

II. To examine the effect of smoking status on auditory inhibition as measured by the auditory late latency response.

III. To determine if the smoking status of the listener has an effect on auditory gating tasks such as word recognition in competition with noise.

IV. To determine if the chronic effects of smoking, if any, on behavioral and physiological responses will correlate.

CHAPTER III

Method of Procedure

Participants

Participants consisted of two groups of females: smokers and non-smokers. Thirteen non-smokers (age 21 - 38) and ten smokers (19 - 37) participated. All participants had pure tone thresholds at or less than 15dB HL at 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000Hz. Smokers were defined as females who smoked ≥ 5 cigarettes per day for at least 1 year. Non-smokers were females who had not smoked more than the occasional cigarette and had not smoked for three years. All participants had healthy appearing outer ears, as examined by otoscopy, and normal acoustic immitance measures, as recorded by tympanometry. Each participant completed consent and case history forms prior to testing. The case history inquired about current prescription medications, otologic pathologies, noise exposure, head trauma, and smoking history. Subject characteristics for smokers and non-smokers can be seen in Tables 2 and 3, respectively. Participants taking central-acting medications at the time of testing were excluded from this study. Smokers continued to smoke ad-hoc prior to testing in order for results to represent their everyday performance. Total test time was approximately 1.5 hours.

Table 2: Smoker demographic and cigarette (cig) smoking information.

Name	Age	Smoking Years	Cigs/day (average)	Cigs at day of test	Time interval between last cig and test session
CR	20	1.5	5	1	30 minutes
EM	19	7	6	1	4 hours
SL	30	9	6	1	15 minutes
RB	24	6	5-8	1	2 hours
LS	19	2	10	3	30 minutes
SM	22	5	10	6	2.5 hours
EM2	37	20	10-15	1	40 minutes
MS	19	3	10-15	2	30 minutes
LF	20	5	10-20	5	30 minutes
CH	25	7	20	5	5 minutes

Table 3: Non-smoker demographic information and smoking history.

Name	Age	Smoking History
SG	32	N/A
AA	23	N/A
RS2	24	N/A
KL	25	N/A
JD	21	N/A
RS	25	N/A
LR	22	N/A
JK	29	N/A
JR	22	N/A
HB	24	N/A
KK	38	Occasional social smoker 17 years ago
KK2	24	Occasional social smoker 4 years ago
AH	32	Social smoker for 7 years, has not smoked in 5 years

Physiologic Measures

Acoustic Reflex

Acoustic reflex thresholds (ARTs) to broadband noise (BBN) were recorded through ipsilateral and contralateral stimulation of each ear. A Grason-Stadler GSI 33 Middle Ear Analyzer was used for these measurements. Tympanometric tracings were obtained prior to acoustic reflex thresholds, using a starting pressure of +200 daPa with a probe tone of 226 Hz. Presentation levels ranged from 50-110 dB HL for ARTs to BBN. A proper fitting Grason Associates, Inc. Single Use Eartip presented stimuli to the ear. Size and insertion depth of the ear-tips were selected for each participant based on anatomical landmarks.

CEOAEs

CEOAEs were recorded using an Otodynamics Ltd. ILO88/92 Otoacoustic Emission System. Click stimuli with duration of 80 μs were delivered to the right and left ears via the standard system probe containing a receiver and microphone. An Otodynamics Ltd soft foam tip was placed on the end of the probe and inserted into the ear of the participant. Stimuli were presented linearly at a rate of 50/s. This linear mode presents each group of four clicks in the same phase to maximize responses at low presentation levels. Three trials of 260 sets of responses were summed and each response was stored alternately in one of two buffers, totaling 1040 responses per trial. Each CEOAE waveform consisted of 512 data points in a 20-ms post-stimulus time window.

The recorded frequency range of the CEOAEs was approximately 0-5000 Hz. If the noise level in the external auditory canal exceeded the rejection level during recording, then recording was paused until the noise level dropped below the rejection level. Each participant was seated in a comfortable chair in a sound-treated booth that conformed to acceptable ambient noise levels (ANSI, 1996).

Contralateral Suppression of CEOAEs

Three trials of CEOAEs were recorded without a BBN contralateral suppressor (as described above) and three CEOAE trials were recorded with a BBN contralateral suppressor. These two conditions were alternately recorded. A 65 dB SPL BBN contralateral suppressor was generated by a Grason-Stadler, Inc. audiometer (GSI 61) and presented to the left ear of the participant via an EAR Tone ER-3A insert earphone.

Late Latency Response

The late latency response (LLR) was recorded from each participant using BioSig software and Tucker-Davis Technologies hardware. Gold-plated electrodes were placed on the scalp or face and held in place by conductive paste and medical tape after scrubbing the area with a mild facial scrub. A vertical two-channel electrode array was used to record the LLR with right ear stimulation. Inverting electrodes were placed at the ipsilateral and contralateral earlobes (A2 and A1, respectively) and a non-inverting electrode was placed at the vertex of the head (Cz). A ground electrode was placed on the low-forehead (Fpz). Prior to recording, each participant was asked to blink naturally

several times. The smallest deflection caused by the eye-blinks was recorded and the artifact-reject set to match it. An online artifact rejection algorithm was applied to the averaging waveform. Electrode impedances were measured at 30 Hz and kept below 5 kΩ and within 1 kΩ of each other. Responses were differentially amplified (gain: 1 x 10^4) and band-pass filtered from 1-30 Hz. The rejection rate for these filters was 6dB/octave. The LLR was converted from an analog to a digital signal at a sampling rate of 10 kHz. The time window was 750 ms, allowing for a pre-stimulus baseline of 350 ms. Click stimuli (100μs) were delivered to the right ear by an electrically shielded Etymotic ER-3A insert earphone at a rate of 1.8/sec and intensity of 70 dBnHL. Each LLR recording consisted of 130 sweeps. Two runs were collected per subject. In the event that a recording has poor morphology, another recording was obtained. Each participant was in a magnetically shielded, sound-treated booth during recording. They were reclined in a comfortable chair; their head and neck were well supported.

Behavioral Measures

Word Recognition in Noise

Participants were instructed to verbally repeat their perception of each word they heard to their best ability, even if they were not sure of the correctness of their response. BBN and four groups of 25 monosyllabic words from lists 1A and 2A of the N.U. 6 word recognition list and were presented to the right ear by an Etymotic insert earphone. The word lists and BBN were pre-recorded onto a compact disc. To assess word recognition

performance at different signal-to-noise ratios (SNRs), the level of the multi-talker babble was fixed and the level of the word lists was changed. The SNRs were –5 and 0 dB.

Response Analysis

Acoustic Reflex

Ipsilateral and contralateral acoustic reflex thresholds were obtained to BBN using a bracketing method. The acoustic reflex threshold was recorded as the level at which a repeatable .02mmho acoustic reflex was elicited.

CEOAEs

The CEOAE amplitudes were analyzed using the same ILO-88 software that was used for CEOAE recording. A total of six CEOAE recordings were obtained, three from each ear. The average CEOAE amplitude from each ear was derived from the three CEOAE recordings obtained from that ear.

Contralateral Suppression of CEOAEs

CEOAE suppression was analyzed using Kresge EchoMaster software. The CEOAE recording without noise and the CEOAE recording with noise that were most similar with regard to stimulus stability, stimulus level, noise rejection, etc. were compared for each subject. As recommended by Hood, Berlin, Goforth-Barter, Bordelon, and Wen (1999), the time window of 8-18 ms was analyzed for CEOAE suppressive

effects. The greatest effects of contralateral suppression are seen in this 8-18ms window (for review see Hood et al., 1999). More refined suppression analysis was examined in 2 ms blocks from 8 – 18 ms. Analysis of the 2 ms windows allowed for examination of frequency specific effects that may exist.

Late Latency Response

The analyzed response from each participant was an average of two ipsilateral waveforms. Averaged waveforms were analyzed using Tucker-Davis Technologies BioSig software. Wave component peaks were selected based on time windows from normative data collected in the laboratory. Absolute latencies of P1, N1, P2, and N2, as well as peak-to-peak amplitudes of P1-N1, N1-P2, and P2-N2 were measured. If a waveform component was absent, the peak-to-peak amplitude was recorded as 0 nV and its absence was noted. The insert earphone tubes introduced a 0.9 ms stimulus delay and the amplifier introduced a 2.0 ms delay. Thus, for reporting purposes these latency differences were added to the observed latency of LLR components. Likewise, the 350 ms pre-stimulus baseline was subtracted from the observed latency.

Word Recognition in Noise

Participants were instructed to repeat the words they believed they heard, even if they were not confident in their response. Their verbal responses were scored by number of phonemes correct and words correct. A percentage of correct phonemes was derived

at each SNR by dividing the total number of phonemes in the group of words by the total number of phonemes correctly repeated for that group of words. The percentage of words correct was calculated by dividing the total number of words in each list by the number of words correct.

Statistical Analysis

Four analyses of variance (ANOVAs) and one multivariate ANOVA (MANOVA) were performed. A three-factor ANOVA was conducted on acoustic reflex threshold. Factors were smoking status (2 levels, smoker, never smoker), stimulus ear (repeated measures on 2 levels, ipsilateral, contralateral), and probe side (repeated measures on 2 levels, right, left). A two-factor ANOVA was conducted on CEOAE amplitude. Factors were smoking status and stimulus ear (repeated measures on 2 levels, right, left). A two-factor ANOVA was conducted on amount of CEOAE suppression. Factors were smoking status and time window (repeated measures on 6 levels, 8 – 18 ms, 8 – 10 ms, 10 – 12 ms, 12 – 14 ms, 14 - 16 ms, 16 – 18 ms). A one-factor MANOVA was conducted on absolute latencies of P1, N1, P2, and N2, as well as peak-to-peak amplitudes of P1-N1, N1-P2, and P2-N2. The factor was smoking status. Two two-factor ANOVAs were conducted, one on percent correct phoneme recognition and one on percent correct word recognition. Factors were smoking status and SNR (repeated measures on 2 levels, -5, 0dB SNR).

A Pearson-product moment correlation analysis between percent correct phoneme identification and the physiologic measures will yield an intercorrelation matrix for each

of the two groups (female non-smokers, female smokers). Due to the large number of correlations, a Bonferonni correction will be applied for tests of significance.

CHAPTER IV

Results

General Statistical Approach

The purpose of this study was to compare the responses of normal hearing female smokers and non-smokers on physiological and behavioral tests that measure auditory inhibition. It was hypothesized that responses from smokers would reflect stronger inhibitory activity than those from non-smokers. This hypothesis was based on the evidence that nicotine enhances auditory inhibitory processes in various populations.

Analysis of variance statistics were run with the between-subject factor as smoking status (2 levels, smokers, non-smokers). Additional statistics were run after breaking subjects into subgroups by never-smokers versus non-smoker versus light smoker (< 10 cigarettes per day) versus heavy smoker (≥ 10 cigarettes per day). However, none of these subdivisions changed statistical findings. Thus, statistics are reported with the two main divisions (non-smoker vs. smoker).

Within-subject factors varied dependent on the measure being tested. All statistics were first conducted as repeated measures univariate or multivariate analysis. With some measures, within-subject factors were significant as expected by previous reports (for example: probe side for acoustic reflex). These findings were not pertinent to our study and so are not discussed in any detail, but do indicate current data are consistent with past findings. Post-hoc statistics were run on individual dependent variables that indicated a trend with smoking status as dictated by multivariate analysis

($p < 0.1$) or with single factors due to a pattern observed in the means. On some measures, patterns in the data were sought by dividing smoking subjects by number of cigarettes smoked on the day of testing, prior to the testing session. Lastly, correlations were run between physiologic tests and behavioral tests for each group, smokers and non-smokers.

Physiologic Measures

Acoustic Reflex

A three-factor ANOVA was conducted on acoustic reflex threshold. Factors were probe side (repeated measures on 2 levels, ipsilateral, contralateral), stimulus ear (repeated measures on 2 levels, right, left), and smoking status. The main effect for probe side was significant, $F(1, 20) = 10.63, p = .004$. The main effects for stimulus ear, $F(1, 20) = 0.72, p = .79$, and smoking status, $F(1, 20) = .001, p = .98$, were not significant, nor were any interactions. Data from one non-smoking participant were not included in the analysis of acoustic reflexes, due to an absent crossed acoustic reflex. ART means and standard deviations are listed in Table 4.

CEOAEs

A two-factor ANOVA conducted on CEOAE amplitude was conducted. Factors were stimulus ear (repeated measures on 2 levels) and smoking status (2 levels). The main effect of ear was not significant, $F(1, 21) = 2.138, p = .159$. The main effect of

Table 4: Mean acoustic reflex thresholds (dB SPL) and standard (Std.) deviations measured from non-smokers and smokers divided by stimulus (stim) ear and probe side.

Stimulus and Probe side	Mean	Std. Deviation	*N*
Stim right, probe right			
Non-smokers	74.5	11.6	12
Smokers	75.5	11.9	10
Stim left, probe right			
Non-smokers	69.5	8.1	12
Smokers	71.5	9.1	10
Stim left, probe left			
Non-smokers	70.4	7.8	12
Smokers	69.5	7.6	10
Stim right, probe left			
Non-smokers	77.1	8.1	12
Smokers	75.5	11.6	10

smoking status was not significant, $F(1, 21) = .006$, $p = .938$, nor was the interaction between smoking status and stimulus ear. Mean CEOAE values are listed in Table 5.

Contralateral Suppression of CEOAEs

A two-factor ANOVA conducted on the amount of contralateral CEOAE suppression was tested. The factors were analysis time window (repeated measures on 6 levels, suppression between 8 – 18 ms, 8 – 10 ms, 10 – 12 ms, 12 - 14 ms, 14 – 16 ms, and 16 – 18 ms) and smoking status (2 levels). A significant main effect for analysis time window, $F(5, 17) = 8.067$, $p = .005$, was found. A marginally significant difference was revealed for smoking status, $F(1, 21) = 3.685$, $p = .069$, with non-smokers having greater contralateral suppression of CEOAEs than smokers. Subsequent ANOVAs revealed marginally significant differences between groups at the following time windows: 8-18ms, $F(1, 21) = 3.60$, $p = .069$, 8-10ms, $F(1, 21) = 3.736$, $p = .067$, and 12-14ms, $F(1, 21) = 4.162$, $p = .054$. In all analysis time windows, non-smokers had greater contralateral CEOAE suppression than smokers. See Table 6 for mean values of contralateral OAE suppression in smokers and non-smokers.

Late Latency Response

A one-factor MANOVA was conducted on the LLR. Dependent variables were P1 latency, P1-N1 amplitude, N1 latency, N1-P2 amplitude, P2 latency, P2-N2 amplitude, and N2 latency. The factor was smoking status (2 levels). The main effect of

Table 5: Mean CEOAE amplitude (dB SPL) and standard (Std.) deviations measured in right and left ears of non-smokers and smokers.

Ear	Mean	Std. Deviation	*N*
Right			
Non-smokers	9.1	4.8	13
Smokers	9.8	5.8	10
Left			
Non-smokers	8.8	4.4	13
Smokers	8.5	6.1	10

Table 6: Mean contralateral CEOAE suppression (dB SPL) and standard deviations in smokers and non-smokers for each of 6 analysis time windows (ms).

Time Window	Mean	Standard Deviation	*N*
8 – 18			
Non-smokers	2.6	1.2	13
Smokers	1.7	1.0	10
8 – 10			
Non-smokers	1.9	1.0	13
Smokers	1.2	.6	10
10 – 12			
Non-smokers	2.6	1.4	13
Smokers	1.3	2.4	10
12 – 14			
Non-smoker	3.3	1.5	13
Smoker	2.1	1.3	10
14 – 16			
Non-smoker	2.4	1.4	13
Smoker	2.2	2.0	10
16 – 18			
Non-smoker	3.3	1.8	13
Smoker	2.2	1.5	10

smoking status was not significant, F (7, 15) = .522, p = .805. However, a trend in the means compelled post-hoc ANOVAs for two of the dependent variables (P2 latency and N2 latency). For the ANOVAs, the main effect of smoking status was not significant for P2 latency, F (1, 21) = 1.988, p = 1.73, or N2 latency, F (1, 21) = 1.277, p = .271. However, P2 and N2 latencies were consistently later in non-smokers versus smokers. Thus, an additional one-factor ANOVA was conducted on the P2 and N2 latency data from smokers only. The factor was number of cigarettes smoked prior to the test session. A significant main effect of number of cigarettes was found for P2 latency, F (4, 5) = 13.696, p = .007, but not N2 latency, F (4, 5) = .525, p = .724. Generally, P2 latency measured from smokers increased with the number of cigarettes smoked. See Table 7 and A-10 for mean values of all LLR components.

Behavioral Measures

Word Recognition in Noise

A two-factor ANOVA was conducted on percent word correct. The factors were SNR (repeated measures on 2 levels, 0 dB, -5 dB) and smoking status. The main effect for SNR was significant, F (1, 21) = 42.891, p < .001. The main effect for smoking status was not significant, F (1, 21) = 2.039, p = .168, nor was the interaction.

A two-factor ANOVA was conducted on percent phoneme correct. The factors were SNR (repeated measures on 2 levels) and smoking status. The main effect for SNR was significant, F 1,21 = 31.484, p < .001. The main effect for smoking status was not significant, F (1,21) = 1.196, p = .287, nor was the interaction. However, smokers were

Table 7: Mean LLR wave component absolute latencies (ms) and peak-to-peak amplitudes (μV).

LLR Component	Mean	Standard Deviation	*N*
P1 latency [a]			
Non-smokers	51.9	15.3	13
Smokers	49.1	15.8	10
P1N1 [b]			
Non-smokers	1.8	0.8	13
Smokers	1.6	0.7	10
N1 [a]			
Non-smokers	80.9	17.1	13
Smokers	83.6	21.1	10
N1P2 [b]			
Non-smokers	3.4	1.2	13
Smokers	3.2	1.5	10
P2 [a]			
Non-smokers	138.8	10.1	13
Smokers	132.6	10.8	10
P2N2 [b]			
Non-smokers	4.3	1.7	13
Smokers	4.0	1.7	10
N2 [a]			
Non-smokers	228.2	21.6	13
Smokers	219.6	11.9	10

a = absolute latency measured in milliseconds (ms)
b = peak-to-peak amplitude measured in microvolts (μV)

consistently poorer than non-smokers, especially at the 0 dB SNR. This pattern in the means compelled subsequent analysis on the data from smokers only. A one-factor ANOVA was conducted. The factor was number of cigarettes smoked on day of test. A significant main effect was found, $F(4,5) = 8.494$, $p = .019$, indicating correct phoneme identification improved with number of cigarettes smoked. Mean data for phoneme recognition in noise at each SNR are located in Table 8.

Correlations between Physiologic and Behavioral Measures

Pearson product-moment correlations were performed between percent correct phoneme identification at 0 dB SNR and percent correct word identification at 0 dB SNR for non-smokers and smokers. As expected for non-smokers, the correlation was high ($r = .923, p < .001$). Unexpectedly, for smokers, the correlation was low ($r = .259$, $p = .471$). Scatterplot analysis revealed an outlier within the smoking subjects at the 0 dB SNR (Figure 1). Excluding this subject from the analysis improved the correlation ($r = .931, p < .001$). For this reason, this subject was excluded from correlations reported below. Because correlations between percent correct phoneme identification at 0 dB SNR and percent correct word identification at 0 dB SNR for non-smokers and smokers were high, subsequent correlations were run between percent correct phoneme identification and physiologic measures.

Pearson product-moment correlations were performed between percent correct phoneme identification at 0 dB SNR and physiological responses measured from non-smokers and from smokers. No significant correlations were found between percent

Table 8: Mean data for phoneme recognition at each signal-to-noise ratio (SNR) for each group.

SNR	Mean Percent Correct	Standard Deviation	*N*
-5 dB			
Non-Smokers	59	13	13
Smokers	57	11	10
0 dB			
Non-Smokers	76	10	13
Smokers	69	10	10

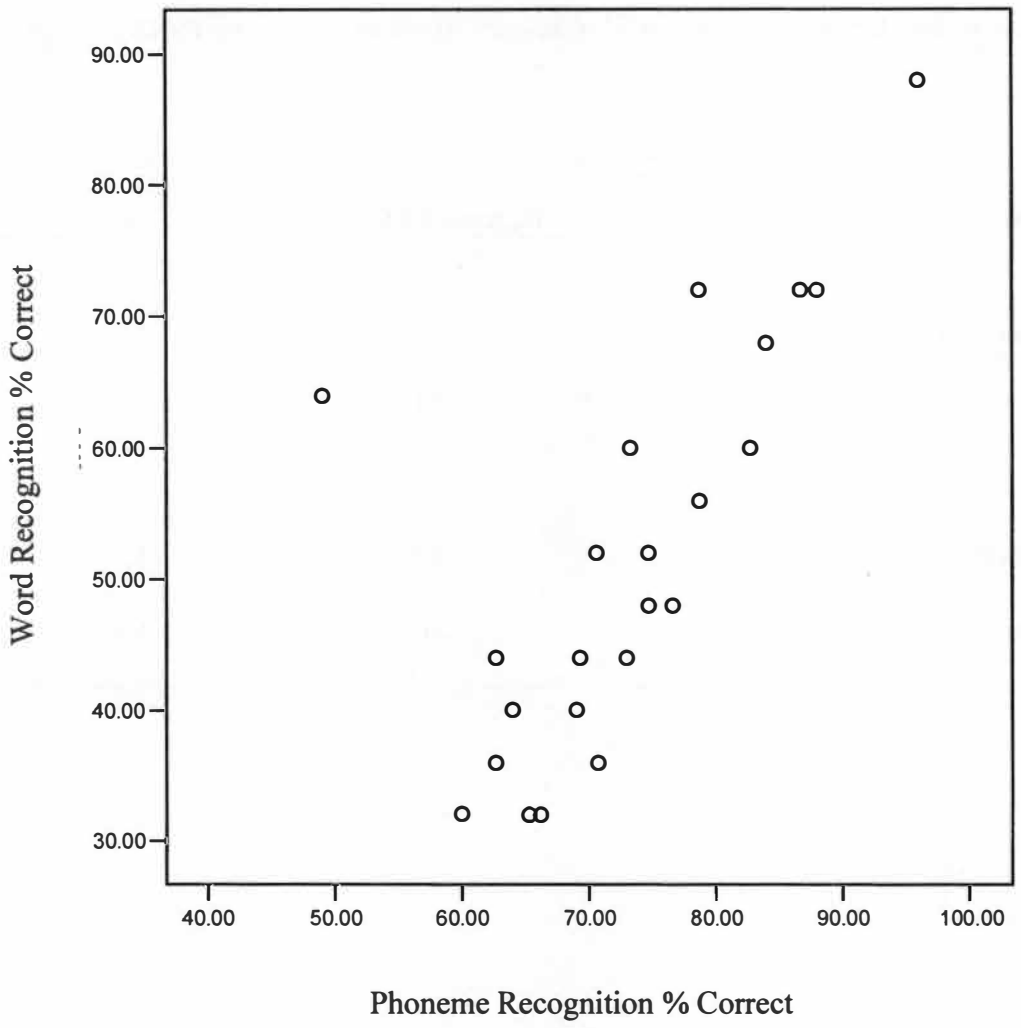

Figure 1: Correlation ($r = .923, p < .001$) between word recognition and phoneme recognition percent (%) correct at the 0 dB SNR for all participants.

correct phoneme identification at 0 dB SNR and any of the physiological measures in data from nonsmokers or smokers (Table 9).

Table 9: Correlations of physiologic variables with phoneme recognition at the 0 dB SNR.

Smoking Status	OAE Suppression (8 – 18ms)	Acoustic Reflex (Probe right, stim left)	LLR Component	
			P2	N2
Non-Smokers	r = -.015	r = -.172	r = -.310	r = .003
	p = .960	p = .573	p = .303	p = .992
Smokers	r = .057	r = .296	r = .371	r = .310
	p = .876	p = .841	p = .291	p = .383

CHAPTER V

Discussion

The purpose of this study was to compare certain physiological and behavioral measures of auditory inhibition in young, normal-hearing non-smokers and smokers to determine if there is a chronic effect of nicotine/smoking on these responses. It was hypothesized that these responses would indicate stronger inhibition in smokers, due to long-lasting effects on nAChRs by chronic levels of nicotine in the CANS of these individuals. Previous studies have documented *acute* effects of nicotine/smoking on similar inhibitory responses (Adler et al., 1993; Bhargava, 1978; Harkrider et al., 2001; Harkrider and Champlin, 2001a, 2001b; Knott, 1985, 1986; Knott and Venables, 1978; Wesnes and Warburton, 1983). Generally, smoking status did not appear to significantly influence auditory inhibition as reflected by acoustic reflex thresholds, OAE suppression, components of the LLR, or word recognition in noise. When a difference was reported, the means indicated weaker inhibition in the smokers versus the non-smokers. It is possible that smokers have weaker than normal inhibitory systems as reflected by the responses obtained in this study, although these findings are in contrast to the acute effects of nicotine/smoking reported on the same or other inhibitory responses measured from smokers. It is also possible that the findings from this study are in conflict with previous reports due to methodological differences. For example, many of the previous studies reported the acute effects of nicotine/smoking while the present study measured chronic effects. Further, in the current study, amount of cigarettes smoked prior to the

experimental sessions was not controlled. Interestingly, in some cases the number of cigarettes smoked prior to the experimental session had a significant effect on a measure such that it reflected an increase in auditory inhibition in the direction of the nonsmokers. These and other explanations will be discussed below.

Physiologic Measures

The first research question was to determine if the smoking status of the listener causes differences in the amount of efferent, suppressive feedback, as measured by contralateral OAE suppression and acoustic reflexes. Generally, there were no differences on these measures between smokers and non-smokers.

ARTs were not significantly different between ears or groups. These results are consistent with previous reports of ART ear differences being minimal, typically less than 15dB in normal-hearing listeners (for review see Gelfand, 2002). There was no correlation between the right crossed ART (probe right, stimulus left) and OAE suppression (Table 6), indicating that little to none of the OAE suppression could be accounted for by the acoustic reflex. Smith (2003) found significant interactions between BBN ART and OAE suppression, suggesting that the acoustic reflex may have contributed to the amount of CEOAE suppression that was measured.

Despite a lack of correlation, a contribution of the acoustic reflex to CEOAE suppression cannot be entirely ruled out for all participants. Three of the twenty-three participants had uncrossed right ear BBN ARTs (probe right/stimulus right) at the level of the CEOAE click stimulus (60 dB SPL), and seven of the twenty-three participants had

crossed BBN ARTs (probe right/stimulus left) at or below the level of the contralateral CEOAE suppressor (65dB SPL). It is possible that the acoustic reflex may have contributed to CEOAE suppression in these individuals. However, the methodology of this study used a relatively low click stimulus level and low noise level in order to minimize the effect of acoustic reflex contribution. Most published studies measuring contralateral CEOAE suppression have not reported BBN ARTs, making it difficult to compare this aspect of the current study to previous reports.

Consistent with results from the current study, previous studies have shown OAE amplitudes to be larger for right ears than left ears (for a comprehensive review of OAEs see Hall, 2000; Robinette and Glattke, 2002). Additionally, OAE amplitude data from the current study are in accord with previous data suggesting the lack of an effect of smoking or nicotine on outer hair cell function (Harkrider et al., 2001; Fuchs and Murrow, 1992).

The amount of contralateral CEOAE suppression reported in this study is comparable to that from other studies of young normal-hearing subjects (Hood et al., 1996; De Ceulaer, G, 2001; Giraud, A, 1995; Velenovsky and Glattke, 2002; Smith , 2003). As expected, the amount of suppression varied depending on the analysis time window, indicating a frequency-dependent effect. As shown in Table 6, the greatest amount of suppression (3.3dB) was seen at the 12-14 ms window in non-smokers. This 12-14 ms time window was the same window that had a marginally significant difference between groups, $F(1, 21) = 4.162, p = .054$.

To date, there are no previous reports of the effects of smoking/nicotine on CEOAE suppression. In this current study, marginally significant effects for smoking status were seen at the 8 – 18, 8 – 10, and 12 – 14 ms time windows. Larger group differences in CEOAE suppression may not have been seen in this study due to the lack of an effect of smoking on this physiologic function, or the smokers' continuation of everyday smoking patterns may not have provided adequate stimulation to the appropriate parts of the CANS. Additionally, binaural CEOAE suppression is of a greater magnitude than contra- or ipsilateral suppression and may be a more sensitive measure of the effects of smoking on this process.

The differences that were seen at the 8 – 18, 8 – 10, and 12 – 14 ms time windows indicated greater suppression in nonsmokers versus smokers. This finding was contradictory to the hypothesis that smokers would exhibit greater OAE suppression than non-smokers. Inhibitory effects of nicotine discussed in the review of literature are largely central in nature. While CEOAE suppression has a central mechanism, the MOCB, it is the most peripheral of these central mechanisms that was examined in this study. The peripheral location of the MOCB compared to the cortical and subcortical generators involved with the LLR and speech recognition in noise, may be responsible for the relative lack of differences between groups seen in this study. Nicotine may act differently on these separate levels of the brain. It may also be the case that only high doses of nicotine not present in this group of smokers acts on these more peripheral pathways.

The second research question was to examine the effect of smoking status on auditory inhibition as measured by the auditory late latency response. Generally, there were no differences between smokers and non-smokers on the earlier components of the LLR. However, there were some interesting patterns in the means. Examining the mean data indicated that, although not statistically significant, P2 (p = .173) and N2 (p = .271) latencies were consistently longer in non-smokers versus smokers. These findings are not consistent with previous reports on the acute effects of nicotine/smoking (Freidman et al., 1974; Knott, 1985a, 1985b, 1986; Harkrider and Champlin, 2001b).

Freidman, Goldberg, Horvath, and Meares (1974) found that the N1-P2 peak-to-peak amplitude of the late latency response (LLR) was significantly greater in male smokers after twelve hours of abstaining from tobacco when compared to amplitudes obtained when the smokers had followed their normal smoking patterns; no significant latency effects were seen. Knott (1985a, 1985b, 1986) examined the effects of smoking in groups of female smokers and found significantly larger P2-N2 amplitudes in non-smoking sessions.

Harkrider and Champlin (2001b) examined the LLR and transdermal nicotine in non-smokers. The amplitude of P1 – N1 increased in the right hemisphere and the latency of N2 decreased, suggesting nicotine increased the excitability of the primary auditory pathways responsible for the LLR. N1-P2 and P2-N2 amplitudes were reduced with nicotine, suggesting simultaneous enhanced and inhibitory activity.

In the current study, although not statistically significant, smoking status consistently appeared to affect P2 and N2 latency. Because of this, smokers were divided

into subgroups by number of cigarettes smoked on day of testing, and a significant relationship was found with P2 latency. Both of these later components tended to increase in latency with the number of cigarettes smoked (Figures 2 and 3). Previous studies (Duncan et al., 2001; Rasmussen et al., 1997; Crawford et al., 2002) have suggested that smoking serves to normalize reduced or impaired stimulus gating (discussed below).

Behavioral Measures

The third research question was to determine if the smoking status of the listener has an effect on auditory gating tasks such as word recognition in competition with noise. Although a significant difference between groups was not observed, smokers consistently performed worse than non-smokers on phoneme recognition in noise. When the smokers were divided by number of cigarettes smoked on day of testing, interesting patterns emerged. A significant correlation between number of cigarettes smoked and percent phoneme recognition in noise ($p = .019$) was found, such that phoneme recognition became more accurate with number of cigarettes smoked. In other words, responses from smokers became more like those from non-smokers the more cigarettes they had smoked prior to the test session. This is consistent with the P2 and N2 latency data from this study and with previous research that suggests smoking serves to improve, or restore deficits in, auditory gating (Duncan et al., 2001; Rasmussen et al., 1997; Crawford et al., 2002).

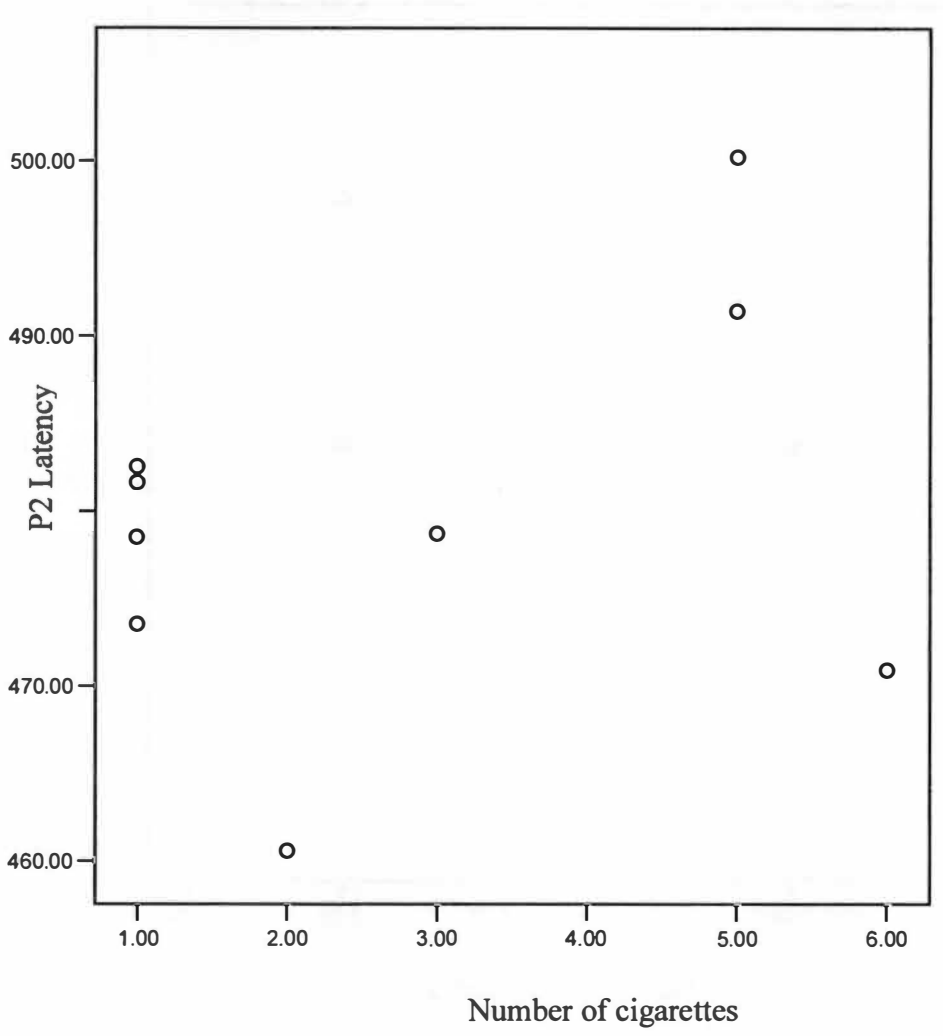

Figure 2: P2 latency (ms) as a function of number of cigarettes smoked on day of testing.

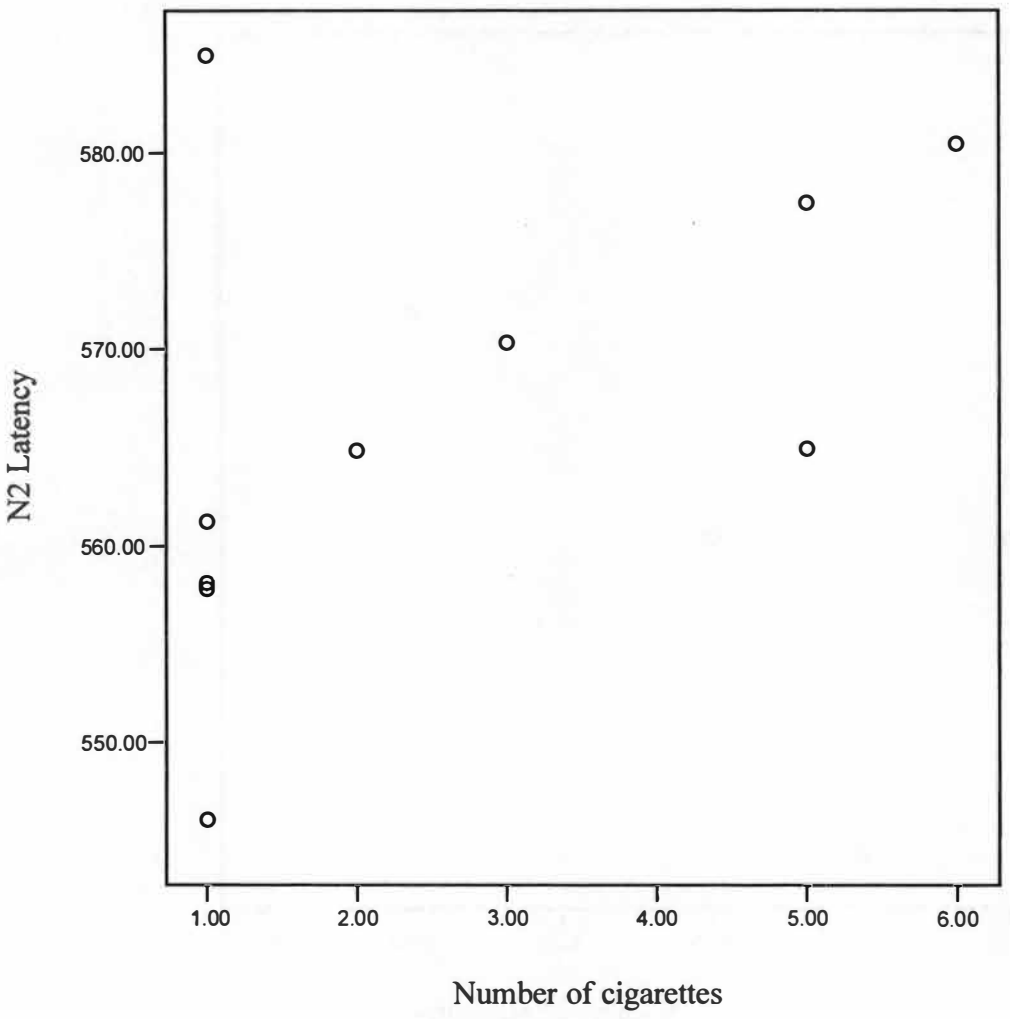

Figure 3: N2 latency (ms) as a function of number of cigarettes smoked on day of testing.

Wesnes and Warburton (1983) found that smoking improved information processing accuracy among smokers. They also reviewed previous reports of smokers who experienced improvement in information processing accuracy as a function of the nicotine content of the cigarettes smoked. Smoking cigarettes with nicotine content below and comparable to their regular brand resulted in increasing amounts of improvement, but improvement was not as great after smoking cigarettes whose nicotine content exceeded their normal dose. This may indicate the existence of an optimal level of nicotine. If there is such an optimal level, it may be different for every smoker. Tong et al. (1980) also found that smoking has the effect of strengthening auditory information processing. Unfortunately, these studies did not contain non-smoking control groups so it is difficult to know if the performance of smokers overall was worse than that of nonsmokers as reported in the current study.

If smoking is affecting the smoker's phoneme recognition, it seems likely that an improvement in auditory gating plays a role. Recent studies (Harkrider et al., 2001; Harkrider and Champlin, 2001a, b) indicate that transdermal delivery of nicotine to non-smoking subjects enhances responses associated with arousal (e.g., 40-Hz response; Na, Pa of the MLR; P1 of the LLR; high-frequency bands of EEG), primary auditory pathway transmission (Na, Pa of the MLR; P1 of the LLR) and cortical excitation (EEG), and suppresses responses associated with efferent activity from the cortex to the midbrain (P2, N2 of the LLR) and to the 8th nerve (wave I of the ABR). Similar findings have been reported for acute cigarette smoking (Friedman et al., 1974; Friedman and Meares, 1980; Knott, 1985a, 1985b, 1986). It has been hypothesized that this paradoxical action

of nicotine in the CNS may result in an initial enhanced focused attention to a stimulus with a subsequent improved stimulus filtering (Knott, 1985). Typically, stimulus filtering is defined as the ability to screen out task-irrelevant stimuli while at the same time focusing on relevant stimuli. It is an informational processing task that has been documented in all sensory modalities using both behavioral and physiological measures and, in part, may be due to central cholinergic receptors. Models of this hypothesis incorporate modulation of arousal and enhanced focused attention (Friedman et al., 1974). The hypothesis that nicotine normalizes stimulus filtering has been investigated in schizophrenic smokers (e.g., Adler et al., 1993), as well as persons with Alzheimer's (Newhouse et al., 1987; Sahakian and Jones, 1991) and Parkinson's (Fagerstrom, Pomerleau, Giordani, and Stelson, 1994). In these populations, histological studies have indicated marked degeneration of cholinergic receptors in CNS pathways (Adler et al., 1982). One common symptom to all of these diseases is the inability to filter irrelevant stimuli and appropriately respond to relevant stimuli. Interestingly, when nicotine is administered to these patients, this symptom is transiently relieved (e.g., Adler et al., 1993).

Relationship Among Physiological and Behavioral Measures

The fourth research question was to determine if the effects of smoking, if any, on behavioral and physiological responses would correlate. Consistent with previous reports (e.g., Smith, 2003), physiological and behavioral measures were not well correlated and smoking status had no effect on these correlations. However, an interesting trend

developed involving P2 latency and phoneme recognition at the 0 dB SNR such that, generally, the smokers who had smoked a greater number of cigarettes prior to the experimental session had better phoneme recognition at the 0 dB SNR and longer P2 latencies than those smokers who had smoked fewer cigarettes that day ($p = .007$). Thus, the general tendency was for P2 latency to increase with number of cigarettes smoked (Figure 2). This relationship, although not significant, was observed between phoneme recognition and N2 latency as well (Figure 3). The trend for P2 and N2 latencies to increase with number of cigarettes smoked, brings them closer to the latencies of non-smokers. This is consistent with the effect of number of cigarettes smoked on phoneme recognition at 0 dB SNR and provides further support for the idea that smoking may act to normalize some weaker aspects of cortical auditory processing in smokers.

Methodological Issues

This study has differed from most other studies examining AERs in smokers in that this study did not control for smoking. Nearly all published reports of smoking and AERs control for this factor, usually by smoking immediately before data collection and including a session where smokers abstain from tobacco. The chronic, rather than acute, effects of smoking on the auditory system were examined in this study. Additionally, withdrawal effects were minimized by not requiring subjects to abstain from cigarette use prior to the experimental session. Subjects were instructed to smoke as usual on the day of testing. The advantage to this method was that any measured effects of nicotine on the individual's responses were likely to be typical. The disadvantage was that the effects

varied greatly from individual to individual, perhaps minimizing a chance at finding group differences. However, individual variability is one of the most consistent findings reported in the literature and trying to collapse the data may result in a finding of no significant difference while examination of subgroups or individual subject data often will provide a more complete picture of the effect of the drug (Levin, 2002; Perkins, 1999). In that same regard, controlling for the method or amount of nicotine administered may obscure individual differences in the effects and vulnerability of nicotine.

As discussed in the review of the literature, there are various methods of nicotine administration. The nicotine patch is the only current method of delivery that steadily administers a dose of nicotine. The ad-hoc smoking procedure used in this study was chosen to reflect the everyday, real-life performance of smokers' auditory systems. A methodology other than ad-hoc smoking may have revealed different results in some or all measures. Most other studies have used a methodology that involves smoking immediately before data collection and so, examine the acute effects of smoking. In this study, subjects were instructed to smoke as usual on the day of testing and to take breaks during testing as needed to continue on their regular smoking pattern. None of the 10 smokers opted to smoke during the test session and the last time a cigarette was smoked prior to the test session varied (Table 2). Testing sessions typically lasted 1.5 hours. If a participant smoked immediately prior to the session, nicotine levels would have dropped during the test session. It is unknown what effect varying stages of nicotine withdrawal has on the auditory system. The delay between last cigarette smoked and the time of

response measurements may be partly responsible for the small group differences between smokers and nonsmokers because any effects of nicotine measured would be considered chronic, not acute. It should be noted, however, that the time since last cigarette smoked was not found to be significantly related to these responses. On the other hand, the number of cigarettes smoked the day of testing was significantly related to some of the measures.

Relatively small differences on the measures between the smokers and nonsmokers may be due to the fact that half of the smokers in this study were light smokers (average of 5 cigarettes/day) and half were heavy smokers (10-15/day), although no obvious patterns in the data were observed for these subgroups. It is possible that the chronic effects of nicotine in the light smokers are not substantial enough to produce significant differences between smokers and nonsmokers. Additionally, all of the subjects in this study were female. Sex differences in the effects of nicotine and smoking on various responses are inconsistently reported. However, the majority of studies measuring the effects of smoking on performance have used male subjects (Tong, Leigh, Campbell, and Smith, 1977; Tong et al., 1980; Wesnes & Warburton, 1978). No justification for using primarily male subjects could be found. However, pharmacologically, it has been shown that male rats that receive chronic doses of nicotine have higher nAChR densities than male controls. In contrast, female rats chronically exposed to nicotine did not differ from female controls (Koylu et al, 1997). Sex differences in the pharmacological action of nicotine in the CNS gives rise to the possibility that nicotine may affect males and females differently. Sex differences have

been reported in overall tobacco use and pain inhibition (Jamner, Girdle, Shapiro, and Jarvik, 1998).

Future Research

Data from this study suggest that the inhibitory system in smokers is less active than that of nonsmokers. This weaker inhibition in smokers appears to be strengthened (or normalized) with the administration of nicotine through tobacco use. The effects of number of cigarettes smoked per day on auditory measures should be more closely examined, and compared to responses from nonsmokers, to determine if smoking is "normalizing" the inhibitory auditory systems of smokers. Similar data should be measured in male smokers and non-smokers to reveal any sex differences in the effects of nicotine/smoking on these measures. To document acute effects of nicotine/smoking on these measures, the length of time between last cigarette smoked and the tests should be controlled. Nicotine delivered by a patch would provide the most steady, constant form of nicotine administration and maximize the likelihood of seeing acute effects.

It would be interesting to examine how changes in this length of time might alter the effects of nicotine on behavioral and physiological responses. Smokers involved in the current study typically smoked fewer cigarettes than smokers in previous studies, and may not reflect performance for heavier smokers. Similar data should be measured in heavy smokers.

Conclusions

(1) Generally, smoking status did not appear to significantly influence auditory inhibition as reflected by acoustic reflex thresholds, OAE suppression, components of the LLR, or word recognition in noise.

(2) When a difference was reported, the means indicated less inhibition in the smokers versus the non-smokers.

(3) The number of cigarettes smoked prior to the experimental session had a significant effect on P2 latency and phoneme recognition at the 0 dB SNR, demonstrating an increase in auditory inhibition in the direction of the nonsmokers.

(4) The chronic effects of smoking/nicotine on the auditory responses measured in this study are different than previously reported acute effects of smoking/nicotine, suggesting that cigarette smoking produces effects on these measures that do not persist.

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APPENDICES

APPENDIX A

Laboratory Data

Table A-1: Participant Audiometric Data.

Thresholds (dB HL)																	
		Right Ear (kHz)								Left Ear (kHz)							
ID	Subject	.25	.5	1	2	3	4	6	8	.25	.5	1	2	3	4	6	8
1	JR	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2	HB	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3	JK	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4	LR	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
5	RS	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
6	JD	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
7	KL	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
8	RS2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
9	AA	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
10	SG	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
11	KK	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
12	AWH	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
13	KK2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
14	EM	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
15	SL	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
16	RB	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
17	CR	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
18	CH	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
19	EM2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
20	LS	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
21	SM	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
22	MS	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
23	LF	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

Note: P = behavioral threshold $\leq$ 15 dB HL

Table A-2: Participant Right Ear Immittance Data.

Right Ear Immittance Measures				
ID	Name	Ear Canal Volume (cc)	Static Compliance (mmho)	Equivalent Air Pressure (daPa)
1	JR	1.5	0.6	5
2	HB	1.5	1.1	25
3	JK	1.4	1.2	5
4	LR	1.6	0.6	5
5	RS	1.1	0.5	5
6	JD	1	0.5	-45
7	KL	1.4	0.5	5
8	RS2	1.1	0.4	-5
9	AA	1.3	0.5	-35
10	SG	1.5	0.8	5
11	KK	1.3	0.6	20
12	AWH	1.1	0.9	10
13	KK2	0.8	0.4	5
14	EM	1.2	1	5
15	SL	1.3	0.3	5
16	RB	1.3	1	15
17	CR	1.1	0.4	5
18	CH	1.7	1.1	5
19	EM2	1.5	0.5	0
20	LS	1.9	2.1	-15
21	SM	1.9	5	0.7
22	MS	0.9	0.6	5
23	LF	1	0.3	15

Table A-3: Participant Left Ear Immittance Data.

Left Ear Immittance Measures				
ID	Name	Ear Canal Volume (cc)	Static Compliance (mmho)	Equivalent Air Pressure (daPa)
1	JR	1.4	0.8	5
2	HB	1.2	1.2	25
3	JK	1.5	1.4	5
4	LR	1.4	0.9	5
5	RS	0.9	0.6	5
6	JD	1.1	0.4	-60
7	KL	1.1	0.4	5
8	RS2	1.2	-10	0.5
9	AA	1.1	0.7	-10
10	SG	1.4	0.9	10
11	KK	1.3	0.6	10
12	AWH	1.2	0.7	10
13	KK2	0.6	0.2	10
14	EM	1.1	0.9	5
15	SL	1.4	0.4	10
16	RB	1.6	2.4	10
17	CR	1.1	0.6	5
18	CH	2.3	1.5	5
19	EM2	1.4	0.4	-5
20	LS	1.8	1.4	15
21	SM	1.9	0.7	5
22	MS	1.1	0.8	10
23	LF	1.1	0.4	15

Table A-4: Participant Acoustic Reflex Thresholds.

Acoustic Reflex Thresholds (dB SPL)					
ID	Name	Stimulus Right/ Probe Right	Stimulus Left/ Probe Right	Stimulus Left/ Probe Left	Stimulus Right/ Probe Left
1	JR	75	80	75	80
2	HB	75	85	90	*
3	JK	75	80	75	80
4	LR	70	95	75	90
5	RS	85	90	80	90
6	JD	60	60	60	65
7	KL	70	60	70	75
8	RS2	60	85	55	80
9	AA	70	70	70	65
10	SG	80	70	75	75
11	KK	65	65	65	75
12	AWH	60	65	65	70
13	KK2	65	75	80	80
14	EM	65	75	65	75
15	SL	85	80	80	90
16	RB	80	90	80	90
17	CR	60	60	65	60
18	CH	65	70	60	65
19	EM2	80	80	65	70
20	LS	70	80	80	85
21	SM	60	65	65	60
22	MS	70	60	70	75
23	LF	80	95	65	85

* No acoustic reflex was present in this condition

Table A-5: Participant Right Ear CEOAE Amplitude.

Right Ear CEOAE Amplitude (dB SPL)					
ID	Name	Run 1	Run 2	Run 3	Mean
1	JR	6.4	6.5	6.6	6.5
2	HB	9.5	11.6	11.8	10.97
3	JK	7.2	5.7	7.9	6.93
4	LR	7.1	6.9	6.7	6.90
5	RS	2.9	3.3	3.4	3.20
6	JD	4.3	4.8	4.7	4.60
7	KL	17.6	19.4	18.4	18.47
8	RS2	14.8	16.1	15.9	15.60
9	AA	9.3	9.6	9.3	9.40
10	SG	7	7.6	9.7	8.10
11	KK	4.2	3.8	3.6	3.87
12	AWH	14.7	15.5	15.8	15.33
13	KK2	8.5	8.7	9.6	8.93
14	EM	5.6	5.2	7.1	5.97
15	SL	10.2	9.7	10.7	10.20
16	RB	7.6	8.5	9.3	8.47
17	CR	23	21.8	22.5	22.43
18	CH	5.1	5.6	5.6	5.43
19	EM2	5.1	5.4	5.5	5.33
20	LS	6.6	7.8	7.9	7.43
21	SM	14.3	18.5	18.9	17.23
22	MS	4.6	5.6	5.2	5.13
23	LF	10.5	10.9	10.9	10.77

Table A-6: Participant Right Ear CEOAE Amplitude with Contralateral Suppressor.

Right Ear CEOAE Amplitude with Contralateral Suppressor (dB SPL)					
ID	Name	Run 1	Run 2	Run 3	Mean
1	JR	4.5	5.6	5.4	5.17
2	HB	10.3	10.9	11	10.73
3	JK	3.4	3.6	4.8	3.93
4	LR	5.2	5.5	5.5	5.40
5	RS	1.3	1.8	2.3	1.80
6	JD	2.4	2.3	2.6	2.43
7	KL	17.6	18	18.3	17.97
8	RS2	14.4	15.2	15.2	14.93
9	AA	6.6	6.5	6.5	6.53
10	SG	5.6	6.5	7.8	6.63
11	KK	2.1	2	2.3	2.13
12	AWH	13.1	13.7	14.1	13.63
13	KK2	7.5	8.1	8.6	8.07
14	EM	3.6	2.8	5.1	3.83
15	SL	8.2	8.8	9.5	8.83
16	RB	7.3	7.4	7.6	7.43
17	CR	21	20	20.4	20.47
18	CH	3.6	4.2	4.5	4.10
19	EM2	4.8	4.5	5.2	4.83
20	LS	6.7	7.6	3.2	5.83
21	SM	15.5	16.3	16.3	16.03
22	MS	3.4	3.8	4.4	3.87
23	LF	9.2	9.3	9.3	9.27

Table A-7: Participant Left Ear CEOAE Amplitude.

Left Ear CEOAE Amplitude (dB SPL)					
ID	Name	Run 1	Run 2	Run 3	Mean
1	JR	5.5	5.2	5.6	5.43
2	HB	7.4	6.9	7.2	7.17
3	JK	7.9	8.2	8.4	8.17
4	LR	5.3	5.4	5.4	5.37
5	RS	2.1	2.6	2.6	2.43
6	JD	2.7	2.9	2.4	2.67
7	KL	18.3	18.5	18.6	18.47
8	RS2	10.4	11.3	11.5	11.07
9	AA	8.1	8.8	9	8.63
10	SG	11.5	11.1	11.2	11.27
11	KK	10	10.3	10.4	10.23
12	AWH	12.2	12.6	12.6	12.47
13	KK2	11.5	11.5	11.6	11.53
14	EM	3.5	3.2	3.2	3.30
15	SL	6.9	6.3	6.9	6.70
16	RB	5.2	5.2	5.4	5.27
17	CR	18.2	18.7	19	18.63
18	CH	2.5	2.8	2.6	2.63
19	EM2	6.8	6.6	6.3	6.57
20	LS	5.5	5.1	5.3	5.30
21	SM	18.9	19.4	19.4	19.23
22	MS	4.6	5.1	4.9	4.87
23	LF	12	12.3	12.3	12.20

Table A-8: Participant CEOAE Suppression at Each Time Window.

Amount of Contralateral CEOAE Suppression by Time Window (ms)							
ID	Name	8 – 18	8 – 10	10 – 12	12 – 14	14 – 16	16 -18
1	JR	2.485	0.59	3.507	1.996	5.214	3.283
2	HB	0.936	0.955	0.991	1.808	0.973	3
3	JK	3.569	2.718	4.053	4.849	3.071	3.464
4	LR	2.905	2.155	3.067	3.149	2.895	4.097
5	RS	3.328	2.44	3.686	4.404	3.045	3.977
6	JD	2.28	2.545	0.674	3.44	0.263	2.788
7	KL	1.053	0.743	1.201	1.143	-0.296	2.627
8	RS2	1.251	0.598	1.035	1.044	1.424	2.354
9	AA	4.748	3.015	4.493	5.753	3.039	6.702
10	SG	3.679	2.672	4.477	3.811	2.995	4.478
11	KK	2.478	3.489	1.989	3.698	2.779	-1.202
12	AWH	3.184	2.484	3.048	4.9	3.016	4.597
13	KK2	1.395	0.756	1.278	2.481	2.627	2.217
14	EM	2.546	1.041	4.048	4.229	3.895	0.92
15	SL	1.31	0.813	-0.024	1.527	1.321	1.832
16	RB	2.191	1.896	1.158	3.024	2.354	2.316
17	CR	2.199	1.472	2.509	2.346	3.243	3.595
18	CH	-0.509	0.693	-1.777	-0.38	-0.486	0.227
19	EM2	1.913	0.402	3.024	0.954	5.221	0.812
20	LS	1.147	2.016	-3.326	2.006	-0.901	2.903
21	SM	2.205	1.436	2.276	1.998	3.034	3.171
22	MS	1.204	0.682	2.525	1.518	0.815	0.778
23	LF	2.723	1.796	2.893	3.312	3.406	5.019

Table A-9: Participant LLR Absolute Latency and Peak-to-Peak Amplitude Data.

LLR Absolute Latencies (ms) and Peak-to-Peak Amplitudes (μV)								
ID	Name	P1	P1-N1	N1	N1-P2	P2	P2-N2	N2
1	JR	43.25	0.36	60.45	2.92	140.06	4.43	228.28
2	HB	61.75	1.26	83.46	2.84	120.66	3.81	206.87
3	JK	37.65	1.26	54.55	3.78	141.07	6.23	252.18
4	LR	50.85	1.63	72.86	4.65	151.27	6.76	235.68
5	RS	79.66	1.96	102.86	3.37	133.56	4.18	204.67
6	JD	70.86	2.51	107.36	2.322	138.16	1.79	203.57
7	KL	42.95	1.55	67.26	3.29	146.07	3.8	251.38
8	RS2	42.55	0.61	65.96	1.68	125.36	2.3	224.78
9	AA	41.55	2.3	74.16	3.35	136.66	5.42	218.58
10	SG	41.25	2.31	79.66	5.97	143.67	6.05	216.88
11	KK	78.46	1.54	101.66	1.547	155.27	1.56	204.17
12	AWH	39.05	2.89	85.26	3.68	127.16	4.87	254.08
13	KK2	44.45	3.2	96.36	4.56	145.17	4.64	264.98
14	EM	43.65	0.97	108.56	1.6	135.46	2.61	214.17
15	SL	44.05	0.89	71.86	2.1	126.46	2	237.88
16	RB	51.85	0.82	98.96	2.57	131.46	3.97	210.77
17	CR	41.25	1.52	59.15	3.64	131.46	4.76	198.97
18	CH	39.85	1.24	71.46	3.67	144.37	6.02	230.38
19	EM2	39.25	1.77	99.66	3.59	134.56	3.95	211.07
20	LS	83.26	2.11	103.86	1.517	131.66	2.54	223.28
21	SM	38.45	2.17	55.35	6.16	123.86	6.44	233.38
22	MS	37.25	2.92	63.25	4.82	113.46	5.88	217.78
23	LF	72.16	1.85	103.66	2	153.17	1.96	217.88

Table A-10: Participant Word Recognition and Phoneme Recognition Scores.

Word and Phoneme Percent Correct					
		-5 dB SNR		0 dB SNR	
ID	Name	Word	Phoneme	Word	Phoneme
1	JR	68	88	88	96
2	HB	36	72	65	79
3	JK	16	52	44	75
4	LR	28	60	58	73
5	RS	32	44	63	69
6	JD	20	72	55	87
7	KL	24	60	55	83
8	RS2	16	36	47	71
9	AA	28	56	53	79
10	SG	16	40	45	64
11	KK	40	44	77	63
12	AWH	36	68	65	84
13	KK2	36	32	56	60
14	EM	12	48	45	75
15	SL	28	36	57	63
16	RB	44	32	69	66
17	CR	16	32	44	65
18	CH	16	48	56	77
19	EM2	36	52	69	71
20	LS	40	44	68	73
21	SM	32	72	64	88
22	MS	12	64	43	49
23	LF	20	40	52	69

APPENDIX B

Subject Consent Form

Subject Consent Form

"Smoking and Sex Differences in Measures of Auditory Inhibition"

You are being asked to participate in a study examining the effects of smoking on the inhibition of the auditory system. The purpose of this study is to investigate the role that smoking has on the inhibitory pathways in the central auditory nervous system. If you are a never-smoker, you may be one of 20 subjects chosen to participate in this study. If you are a smoker, you may be one of 20 subjects chosen to participate in this study. To participate in this study you need to consent to have a hearing evaluation and otoacoustic emission screening. This evaluation will include a brief case history, a hearing screening, tests of middle ear function, and tests of eardrum and ear canal health. **If you do not pass all parts of the evaluation, you will be excluded from further participation.**

If you have none of the exclusionary criteria and agree to participate in the study, I will administer several tests of auditory function. These procedures are all slightly modified versions of tests that are commonly performed in standard audiological evaluations. The following steps are involved in these noninvasive procedures:

Case History – answer questions about or related to your hearing and smoking history.

Hearing Screening – respond to weak tones presented at various tone frequencies to each ear via insert earphones

Immitance Screening – Your ear canals will be examined with a light to make sure they are free from obstruction. A soft plastic earplug will be placed at the entrance to your ear canal. You will hear a moderately loud tone. You will also feel the pressure in your ear canal increase and decrease slightly, and you may experience a brief, mild sensation of aural fullness, but should not feel pain or discomfort.

Acoustic Reflexes – The same soft plastic earplug will be inserted at the entrance to your ear canal. You will feel a slight increase in air pressure as described above. You will hear a moderately loud tone. A different noise, lasting about one second, will be presented, and the reflexive response from the muscles in the middle ear will be indirectly measured. This procedure will be repeated until the lowest level that causes the middle-ear reflex to contract is determined. The signals are loud enough to elicit an acoustic reflex, but are not at the level and duration that pose a danger to hearing. You may feel slight aural fullness and startle from the stimuli, but this procedure should not cause pain or discomfort.

Evoked Otoacoustic Emissions – A different soft rubber plug will be paced in your ear canal. Sounds will be presented via small speakers and will be recorded via a sensitive microphone that is contained in the earplug. These measurements will be made both in the presence and absence of a moderate-level noise presented to your opposite ear. This noise will be presented through an insert earphone that will be placed in your ear canal.

Word Recognition – A list of 80-recorded words will be presented to your right ear through an insert earphone at a comfortable level. At the same time, you will hear a static-like noise in the same ear. The words will be presented at four different loudness levels, with each level getting softer. You will be asked to say each word as you hear it. Your responses will be audio-recorded to ensure accurate interpretation and analysis.

Late Latency Response and P50 Response – Several electrodes will be placed on your scalp, earlobe, and forehead. These areas will be cleaned with a mild facial scrub and the electrodes will be held in place with a small amount of paste and medical tape. An insert earphone will deliver sounds at a moderately loud level to your right ear. The electrodes will indirectly record electrical activity from your brain. You will be asked to relax and focus on a point on the wall.

For all measurements, you will be asked to sit in a chair in a sound treated room. You will be given time to rest, if needed. Completion of all tests will take approximately 1-1.5 hours. None of the sounds you will hear pose any risk of damaging your hearing. There are no known psychological, social, legal, or physiological risks or side effects associated with participation in this study. Although it is not expected,

you should inform the investigator immediately if you experience discomfort of any kind during the experiment. The investigator will discuss the results of the tests with you. If you wish, a copy of these results can be given to you.

Benefits of the study include a free hearing screening, and a free examination of the health of the outer and middle ear. The scientific and clinical communities will benefit from greater understanding of the physiologic mechanisms affected by smoking.

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission. Any publication resulting from this study will identify you only in accordance with a code. All information (consent form, history report, data sheets) will be kept in a locked filing cabinet on the UT campus for three years and then destroyed.

If you have any questions, please ask me now. I will be happy to answer any questions that you may have in the future. My number and email is listed at the bottom of this form.

You will receive a copy of this form to keep.

You are making a decision whether or not to participate. Your decision whether or not to participate will not affect your future relations with the Department of Audiology and Speech Pathology or The University of Tennessee. Your signature indicates that you have read the information provided above, understand the possible risks, discomforts, and benefits of this study, and have decided to participate. You may withdraw at any time after signing this form, without penalty, should you choose to discontinue participation in this study.

Under federal privacy regulations, you have the right to determine who has access to your personal health information (called "protected health information" or PHI). PHI collected in this study may include information regarding health history, hearing tests, smoking status, as well as basic demographic information. By signing this consent form, you are authorizing the research team at the University of Tennessee to have access to your PHI collected in this study. The Institutional Review Board (IRB) at the University of Tennessee may review your PHI as part of its responsibility to protect the rights and welfare of research subjects. Your PHI will not be used or disclosed to any other person or entity, except as required by law, or for authorized oversight of this research study by other regulatory agencies, or for other research for which the use and disclosure of your PHI has been approved by the IRB. Your PHI will be used only for the research purposes described in this consent form. Your PHI will be used indefinitely.

You may cancel this authorization in writing at any time by contacting the principal investigator listed on the first page of the consent form. If you cancel the authorization, continued use of your PHI is permitted if it was obtained before the cancellation and its use is necessary in completing the research. However, PHI collected after your cancellation may not be used in the study. If you refuse to provide this authorization, you will not be able to participate in the research study. If you cancel the authorization, then you will be withdrawn from the study. Finally, the federal regulations allow you to obtain access to your PHI collected or used in this study.

Signature of Participant Date

Investigator's Assurance:

The individuals whose names appear below are responsible for carrying out this research program. They assure that you are informed of any changes in the procedures or risks and benefits if any should occur during or after the course of this study. They assure that all information remains confidential.

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Christopher Gray Clinard was born in Cape Girardeau, Missouri on May 23, 1977. He was raised in East Prairie, Missouri and graduated from East Prairie High School in May 1995. He received the degree of Bachelor of Business Administration in Music Business in 1999 from Belmont University in Nashville, Tennessee. Chris attended the University of Tennessee at Knoxville from 2001 to 2004 and received a Master of Arts in Audiology in May 2004. He is currently pursuing his Ph.D. in Speech and Hearing Science at the University of Tennessee at Knoxville.