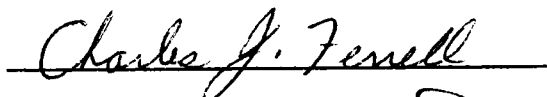
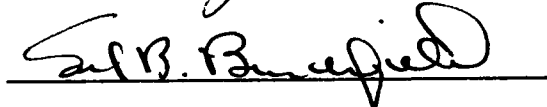


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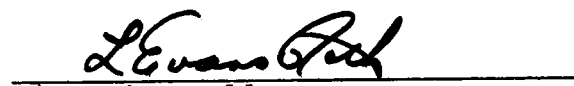
I am submitting herewith a thesis written by Brian Grove King entitled "Effects of Aspirin and Caffeine on the Acoustic Reflex Threshold in Chinchilla." I recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Arts, with a major in Audiology.


David M. Lipscomb
Major Professor

We have read this thesis and
recommend its acceptance:

Accepted for the Council:


Vice Chancellor
Graduate Studies and Research

EFFECTS OF ASPIRIN AND CAFFEINE ON THE
ACOUSTIC REFLEX THRESHOLD IN
CHINCHILLA

A Thesis
Presented for the
Master of Arts
Degree
The University of Tennessee, Knoxville

Brian Grove King
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DEDICATION

This thesis is dedicated to the author's family; his father Hueston, his mother Wilma, and his sister Melinda, for without whose love, confidence, and faith in the author, this thesis would never have been undertaken.

B.G.K.

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B.G.K.

ABSTRACT

The purpose of the study was to determine the effects, if any, of aspirin and caffeine, individually and in combination on the acoustic reflex threshold in chinchilla. Animals were selected from the available herd of The University of Tennessee Noise Research Laboratory, and randomly allocated into the following groups; aspirin recipients (ten animals); caffeine recipients (ten animals); aspirin/caffeine recipients (ten animals); and control (five animals).

The primary means of data assembly was through audiological assessment of stapedial reflex thresholds by impedance audiometry. A stimulation tube was acoustically coupled to an American Electromedics impedance bridge to provide contralateral ear acoustic stimulation. Reflex thresholds were measured from the probe ear through readings of external ear canal air pressure change on the impedance bridge compliance change meter. Acoustic reflex thresholds were measured both prior to, and following administration of each experimental substance.

A paired-sample t-test for related measures was used to evaluate the data. Primary findings included significant differences between pretreatment and posttreatment thresholds for 1000 Hz and 4000 Hz in the aspirin/caffeine combination

group at the left ear. Significant differences were also found at 1000 Hz in the control group at the right ear.

Impedance audiometry has been shown to be affected by certain substances which depress the acoustic reflex threshold. Aspirin and caffeine, substances commonly ingested in moderate amounts, have been shown to affect the hearing sensitivity threshold, however, have not been thoroughly investigated with regard to acoustic reflex threshold change. Findings of the study showed isolated significant differences. Reliability of the results was questioned because of the ipsilateral group and frequency differences, and the control group differences at the right ear.

Further investigation was recommended in which hearing sensitivity threshold shift, as a result of substance administration, could be determined, and correlative studies performed with related acoustic reflex threshold shift data. Once in possession of more reliable data, researchers could further investigate effects of substance ingestion on the acoustic reflex threshold.

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CHAPTER I

INTRODUCTION

The purpose of this study was to determine any effects of aspirin and caffeine, alone and in combination, on the acoustic reflex threshold using pure tone and white noise stimulation.

The experimental questions under study were:

1. Does aspirin elevate or decrease the level of elicitation of the acoustic reflex threshold in chinchilla?
2. Does caffeine elevate or decrease the level of elicitation of the acoustic reflex threshold in chinchilla?
3. Do aspirin and caffeine in combination elevate or decrease the level of elicitation of the acoustic reflex threshold in chinchilla?

Importance of the Study

In the routine audiometric evaluations of pure tone hearing sensitivity and speech acuity, the accuracy of data gathered is largely dependant upon the voluntary responses of subjects. Occasionally, a reliable response cannot be obtained due to several factors such as physical or mental limitations, immaturity, or an unwillingness to respond appropriately on the part of the subject. In these instances, a hearing test such as the acoustic stapedial reflex

threshold can give insight into the estimate of true hearing sensitivity. Impedance audiometry, utilizing the acoustic reflex threshold, is a relatively recent development in the field of audiology. Jerger (1974) indicated that various physiologic functions such as yawning, swallowing, and vocalizing could cause contraction of the stapedius muscle which might be misinterpreted as a reflex to sound stimulation during testing. Other researchers have indicated that certain drugs such as pentobarbital sodium (Borg and Moeller, 1967), secobarbital sodium (Borg and Moeller, 1967), secobarbital (Robinette, et al., 1974), and toxic agents such as ethylalcohol (Borg and Moeller, 1967) may have the effect of depressing the stapedial reflex magnitude, resulting in elevated acoustic reflex thresholds when measured by impedance audiometry. The use of these more potent drugs would likely be known to the audiologist. However, common substances which are generally ingested in moderate to extreme amounts, such as aspirin, aspirin substitutes, caffeine, nicotine, saccharin, and vitamins have not been satisfactorily investigated with respect to their potential influence on the acoustic reflex threshold. The present study concentrated on the possible effects of aspirin and caffeine.

Human acoustic reflex threshold to pure tone stimulation occurs at sensation levels of about 70 to 95dB (Chiveralls

and FitzSimons, 1973). If aspirin is shown to have a depressive effect on the acoustic reflex threshold, it could have implications on the diagnostic significance of impedance audiometry. While the specific locus of aspirin effects regarding hearing loss is not known, it is possible that the addition of sodium salicylate to the blood serving the inner ear is a factor. Bernstein and Weiss (1967) suggested a possible relationship between the degree of hearing loss and the level of plasma salicylate in the blood. This excess sodium salicylate level could be transmitted to the stria vascularis and on into the scala media fluid as well as to other areas of the inner ear through the various circulatory routes. In doing so, the delicate balance of sodium and potassium could be affected, rendering a pseudo-sensori neural hearing loss, which in fact might not be as significant as it appears. If such an alteration results in a depressive effect on the acoustic reflex threshold, it could have implications regarding the diagnostic significance of impedance audiometry. This information is particularly important when testing patients who can only be evaluated with impedance audiometry, since diagnostic inferences are often made regarding hearing sensitivity as relates to dynamic range.

The majority of patients seen in the audiologic clinic setting are probably not influenced by aspirin alone.

Caffeine is commonly used as a catalyst in aspirin products. It also occurs naturally in coffee, cola products, and other foods. Caffeine acts as a stimulant to the central nervous system and may effect the elicitation level of the acoustic reflex threshold (Merck Index, 1978).

The specific effects of caffeine on the threshold of hearing sensitivity have not been reported. However, related studies show caffeine to influence hearing detection. Wojnaroska (1966) noted that a 375 mg dose of caffeine had the effect of reducing or alleviating auditory fatigue to an irritating tone. Certain auditory tests such as the Supra-Threshold Adaptation Test (STAT) involve relatively long periods of high intensity sound exposure. If the auditory system fatigues, and the acoustic reflex testing is attempted shortly thereafter, the effect could possibly be depressive, and the reflex thresholds would be seen at sensation levels different from those which would otherwise be found. However, the converse is also possible, as in patients experiencing a recruiting phenomenon resulting in reflexes elicited at normal sensation levels. The effect of caffeine in reducing or alleviating this fatigue could be significant in the elicitation of the acoustic reflex. Threshold could be found at levels not influenced by the amount of previous sound exposure.

Null Hypotheses

For statistical analysis purposes, it was hypothesized that:

1. Aspirin does not elevate nor decrease the level of elicitation of the acoustic reflex threshold in chinchilla.
2. Caffeine does not elevate nor decrease the level of elicitation of the acoustic reflex threshold in chinchilla.
3. Aspirin and caffeine in combination do not elevate nor decrease the level of elicitation of the acoustic reflex threshold in chinchilla.

Definition of Terms

The following terms were defined to clarify their usage in the present study:

Dynamic Range. The dynamic range is the difference in intensity level necessary to find the hearing sensitivity threshold and the intensity level necessary to elicit the acoustic reflex threshold.

Impedance Audiometry. Impedance audiometry is a clinical audiological test which includes at least three separate types of measurement: tympanometry, absolute or static compliance, and acoustic (stapedius) reflex thresholds.

Stapedial (Acoustic) Reflex. The stapedial reflex is the reflex response of the stapedius muscle to an intense

sound stimulus. The action of the stapedius muscle, through its attachment to the neck of the stapes, is to pivot the footplate of the stapes ventrolaterally from the oval window. This increases tension within the middle ear mechanism. The reflex occurs bilaterally upon stimulation of either ear by an intense sound.

Stapedial (Acoustic) Reflex Threshold. The stapedial reflex threshold is defined as the intensity (in dB above the threshold of hearing in the stimulated ear) which is just capable of inducing a reflex contraction of the stapedius muscle, as evidenced by a change in the impedance of the tympanic membrane (Jepsen, 1963).

CHAPTER II

REVIEW OF THE LITERATURE

Through a MEDLAR (interlibrary computer) search, several articles were located which pertained to this study. However, these were either related primarily to aspirin effects or caffeine effects upon hearing. No article related to studies on both substances simultaneously. Also, all articles regarding aspirin and caffeine related their effects on hearing sensitivity threshold changes or hearing detection changes and not to their effects on the acoustic reflex threshold, per se.

The Effects of Aspirin

Bernstein and Weiss (1967) studied the effects of high dosages of aspirin on the threshold of human hearing sensitivity. All twelve subjects were patients with rheumatoid arthritis already receiving aspirin compounds. Any salicylate substance was removed from consumption prior to admission to the study so that plasma salicylate levels at the start of the study were zero. Results indicated that high intake of aspirin for as few as three days could elevate the hearing sensitivity threshold to pure tone stimulation from 25 to 45 dB. It was suggested that this elevation was possibly in relation to the plasma

salicylate level in the blood. Plasma salicylate levels ranged from 22.5 mg per 100 ml in patients with 25 dB threshold shifts through 47.5 per 100 ml in patients with 45 dB threshold shifts. Plasma salicylate levels appeared to correspond well with the degree of hearing loss. It was also noted that the threshold shift was entirely reversible with 24 to 48 hours after salicylates had been withdrawn. Whether the decrease in hearing sensitivity was associated with depression of the acoustic reflex threshold was not reported. If, however, the decrease in hearing sensitivity threshold is indeed related to a change in acoustic reflex thresholds, this could provide further diagnostic information to the clinical audiologist. Possibly remediation efforts would be resolved by the removal of salicylates instead of other means such as amplification.

Warren and Rhem (1975) studied the effects of salicylates on nineteen female subjects' temporary threshold shift (TTS) following high intensity noise exposure. All subjects were exposed to 110 dB of white noise to the left ear for fifteen minutes and following two minutes of rest, completed automatic audiometer threshold tracings. Subjects were then placed on a 48-hour schedule of salicylate ingestion and the procedure was repeated. Results indicated that the amount of TTS was greater in those patients following salicylate ingestion than from noise exposure alone. This TTS difference between shift due to noise alone and shift

due to noise and salicylate was equivalent to the hearing threshold shift as a result of salicylate toxicity. Warren and Rhem suggested that the part of the TTS due to salicylate toxicity would recover completely, and that the only TTS which could ultimately result in hair cell damage would be that from the noise. This further evidences the effect of salicylate, a primary ingredient in aspirin, on the hearing mechanism. This additive effect of salicylate and noise could influence the findings of reflex threshold testing. A depression of the acoustic reflex threshold along with the depression of the hearing sensitivity threshold as a result of the noise and salicylate would indicate more of a hearing loss to be present than would normally be true. Also, this impairment would return to preexposure thresholds following removal of the noise and the salicylates.

The Effects of Caffeine

Murphy and Venables (1971) studied the effects of caffeine citrate on human hearing in the detection of two clicks in the presence and absence of white noise. Thirty-six subjects were used; eighteen male and eighteen female. All subjects were right-handed. Click stimuli were approximately 90 dB intensity (no dB reference given). Interclick intervals were selected individually per subject at the level each made 30% errors. Fifteen subjects received an

interclick interval at 1.0 msec; fifteen at 1.5 msec; and six at 2.0, 2.5, or 3.0 msec. The task was to identify whether a single click was presented or whether two clicks, with the subject's interclick interval, were presented. The conditions were: detection in quiet; detection with white noise to the contralateral ear; detection in quiet under caffeine citrate influence; and detection with white noise to the contralateral ear under caffeine citrate influence. Results indicated that a 375 mg dose of caffeine citrate allowed the detection of two clicks with a significantly greater number of correct responses, with and without contralateral white noise. The improved detection of the two clicks could also appear as improved detection of pure tone stimuli in conventional clinical audiometric testing. In this instance, patients being evaluated shortly after consumption of heavy dosages of caffeine could present an audiogram illustrating better hearing than would be shown without the caffeine intake. This could be important in the rehabilitation of borderline cases which might benefit from amplification.

Clicks in this study were presented to the patients through earphones at 90 dB. This level should be sufficient to elicit the acoustic reflex in most normal-hearing patients. Many patients have acoustic reflex thresholds at or just greater than 120 dB. This is the intensity

limit for most impedance bridges. An increased detection ability in this instance, could serve to elicit the stapedial reflex at slightly lesser intensity levels. Another possibility is that the acoustic reflex would occur with greater stapedial contraction, allowing it to be seen more easily on the impedance bridge compliance change meter.

In patients evaluated only through impedance audiometry measures, the presence or absence of the acoustic reflex may influence the further recommendations of the audiologist. An absence of acoustic reflexes does not necessarily indicate normal hearing or a loss of hearing. However, stapedial reflexes present at any intensity level indicate hearing at some measureable point. Further testing to locate this point can then be attempted.

Wojnaroska (1966) examined the effects of several calmatives and stimulants on human auditory fatigue as it relates to temporary threshold shift (TTS) after the presentation of an irritating tone. Twenty subjects ranging in age from 18 to 60 years were administered the calmatives and stimulants; three of each type. The results pertaining to the stimulant caffeine will be examined here.

A base test with no drug was administered first to define a baseline of fatigue to an irritating tone. The baseline was found at 25 dB/12 minutes.

Tests on caffeine were performed fifteen minutes after an oral administration of a dose of 200 mg of the caffeine. Subjects were required to abstain from drinking coffee on the day of the test. An analysis of her results indicated that a dose of 200 mg of caffeine had the effect of decreasing auditory fatigue. This effect was much more manifest in young adults, however, it was also noticeable in older adults. The diminished effect in older adults was possibly related to their having habituated to the stimulant, and to general reduction of reactivity to certain calmatives and stimulants with the progress of age.

Many times extensive auditory testing may last several hours, often with acoustic reflex testing being administered near the end of the testing period. Such supplementary tests as the SupraThreshold Adaptation Test (STAT) as described by Jerger (1974) may require relatively long periods of high intensity pure tone exposure. It is possible that this amount of high intensity sound exposure could fatigue the auditory system in patients without recent caffeine intake so as to make the acoustic reflex more difficult to elicit at lower sound intensity levels. In patients with recent caffeine intake, especially younger patients, this fatigue factor could be ruled out as a cause of depressed hearing sensitivity and/or acoustic reflex thresholds.

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Summary

Aspirin has been indicated to cause a predictable sensori-neural hearing impairment. This impairment may elevate hearing thresholds from 25 to 45 dB in patients taking heavy daily doses, such as arthritics. If this depression in threshold occurs for the acoustic reflex threshold also, the reflex might be altered enough so that it would not be seen at the limits of the test equipment. With this information missing, the audiologist could encounter difficulties in patient care. Removing aspirin for a few days could allow hearing sensitivity and acoustic reflex thresholds to return to nonsalicylate influenced levels, and thereby give the audiologist more accurate information.

Caffeine has been shown to provide better detection of two click stimuli and to reduce auditory fatigue. This effect was found at hearing sensitivity suprathreshold levels. It is at these levels that acoustic reflex testing is performed. Through this increased detection ability, the lack of fatigue, or a combination of factors, the acoustic reflex threshold might be enhanced sufficiently to be elicited at lower stimulus intensity levels. This could prove beneficial in patients with acoustic reflex thresholds just beyond the upper stimulus intensity levels of the test equipment.

Many brand-name aspirin products contain caffeine, acting as a catalyst in the dispersion of the aspirin into the blood stream. Caffeine is also an ingredient in coffee, cola products, and some chocolate products. Therefore, it is highly probable that aspirin and caffeine would be present in combination in many patients with high aspirin consumption. The effects of each separate substance on the hearing mechanism, the acoustic reflex in particular, could possibly cancel when occurring in combination. It is also possible that the effects could be synergistic. That is, one substance would show an even greater effect when combined with the other substance than when individually introduced. These possible effects were investigated in this study.

CHAPTER III

METHODS AND PROCEDURES

Subjects

Thirty-five chinchilla between the ages of six months and two years inclusive were randomly selected from the herd of experimental animals of the University of Tennessee Noise Research Laboratory. Animals maintained in the herd had no apparent disease processes and no history of prior experimental treatments. Prior to acceptance to the study, subjects were tested by impedance audiometry at each ear for acoustic reflex thresholds for 500, 1000, 2000, and 4000 Hz and broad band noise. Animals were disqualified and replaced if their acoustic reflex thresholds were not obtained within the limits of the equipment (120 dB maximum intensity output) for at least three of the frequencies tested at each ear. Reflexes could not be elicited at any frequency bilaterally for one animal, and were present at only one frequency bilaterally for two animals. These three subjects were replaced by three animals meeting test criteria.

Dosage

Ten animals received the average arthritic dosage of aspirin as indicated by the Merck Index (1978), 12.9 mg/kg

body weight four times per day (total daily dosage of 50.8 mg/kg body weight) for three days. Ten animals received 5.1 mg/kg body weight caffeine, equivalent to the 375 mg dose to humans of the Murphy and Venables (1971) study, in a single dosage. Caffeine dosages were administered at the same time the other experimental groups received the final aspirin dosage. Ten animals received a combination of aspirin and caffeine dosages (12.9 mg/kg body weight aspirin four times per day for three days, and 5.1 mg/kg body weight caffeine administered with the final aspirin dosage). Five animals receiving neither aspirin nor caffeine served as a control group.

Experimental Substance Administration

Each substance dosage was dissolved in 1 cc distilled water. A gastric tube was inserted down the animal's throat and into the stomach. Adequate insertion was completed when the tube met with slight resistance to further insertion. The substance mixture was administered to the animal through the tube using a hypodermic syringe. The tube was then removed. Control group animals received distilled water in the same manner.

All animals' acoustic reflexes were tested for elicitation one hour following final substance dosage administration. This period of time was considered sufficient

for dispersion of the substance throughout their circulatory system. However, it was not considered sufficient time for the substance to be metabolized from the system.

Acoustic Reflex Measures

Chinchilla were prepared for acoustic reflex testing by placing them inside a cloth sleeve with their heads exposed to the neck. A surgical hemostat was clipped to the sleeve beside the animal's neck at a point which provided an adequately tight collar. This prevented the animal from slipping its head back into the sleeve, however, was not so restricting so as to prevent respiration. A second hemostat was clipped to the sleeve wrapped tightly around the region of the base of the tail. This procedure sufficiently restricted movement by the animal so that sedating drugs would not be necessary.

The chinchilla test ear was sealed using an 8 mm diameter, 9 mm long flanged impedance probe insert. An adequate seal was determined by adjusting the equivalent-to-water air pressure meter until 200 mm of positive air pressure could be contained in the ear canal without leakage. The compliance change meter was adjusted to the zero dial reading. The pressure was then removed from the ear canal by adjusting the air pressure meter with the test ear remaining sealed. The compliance change meter was observed

as the air pressure was varied until the largest relative number was found.

Stimuli were presented to the contralateral ear through a stimulation tube inserted into the ear canal. The stimulation tube was held in place by securing the pinna around the tube with masking tape. An American Electromedics impedance bridge (model 83) was used to provide pure tone and broad band noise stimuli. The stimulation tube was acoustically coupled to the TDH 39 earphone for presentation of the stimuli to the test ear through the stimulation tube. Calibration information is provided in the appendix.

The major criterion for an acceptable acoustic reflex threshold included movement of the compliance change meter needle from an arbitrary point of rest to a point at least one compliance change unit different than that of the point of rest. Additional criteria for this movement included needle movement concurrent with the presentation of the stimuli, and returning to the point of rest immediately after cessation of the stimulus presentation.

Acoustic reflex stimuli were presented at 500, 1000, 2000, and 4000 Hz and broad band noise. The intensity level necessary to elicit a response for each stimulus was recorded prior to experimental substance administration, and again following the final experimental substance dosage.

Pretreatment reflex thresholds at each stimulus condition were averaged for each experimental group and compared with the averaged scores for the corresponding stimulus condition and group.

A paired sample t-test was applied to the acoustic reflex threshold measures for the following groups at each ear:

pretreatment aspirin vs. posttreatment aspirin

pretreatment caffeine vs. posttreatment caffeine

pretreatment combination vs. posttreatment combination

pretreatment control vs. posttreatment control

A t-value was computed for each group for each of the stimulus conditions; 500, 1000, 2000, and 4000 Hz and broad band noise. The resultant t-values were tabled for each ear for comparison purposes (Table 1).

Table 1. T-Test Values Obtained from Pairing the Pre- vs. Posttreatment Acoustic Reflex Thresholds for the Three Experimental and the One Control Groups for the Test Frequencies 500, 1000, 2000, and 4000 Hz and Broad Band Noise

	T-Scored Group	Frequency			
		500 Hz	1000 Hz	2000 Hz	4000 Hz BBN
Right Ear	Control	3.270	7.333*	4.543*	3.162
	Aspirin	0.155	0.000	-0.206	0.000
	ASA/Caf	0.132	-1.274	-1.000	-1.271
	Caffeine	-0.228	-0.634	-0.158	0.067
Left Ear	Control	0.886	0.388	1.534	1.725
	Aspirin	-2.085	-2.506	-2.449	-2.871
	ASA/Caf	-0.843	-3.911*	-2.335	-3.023*
	Caffeine	0.190	0.331	-0.859	0.352

* = significant difference given t-value with $P < 0.01$

α 0.01 = 3.747 for control group

α 0.01 = 2.821 for ASA/caffeine; caffeine

α 0.01 = 2.896 for ASA

CHAPTER IV

RESULTS AND DISCUSSION

Results

Data analysis was utilized to answer the following questions:

1. Does aspirin elevate or decrease the level of elicitation of the acoustic reflex threshold in chinchilla?
2. Does caffeine elevate or decrease the level of elicitation of the acoustic reflex threshold in chinchilla?
3. Do aspirin and caffeine in combination elevate or decrease the level of elicitation of the acoustic reflex threshold in chinchilla?

A paired sample t-test was used to compute differences between pretreatment and posttreatment acoustic reflex threshold levels for the thirty-five adult chinchilla. It was hypothesized that there would be no significant differences between the pretreatment and posttreatment acoustic reflex threshold levels with or without substance dosages. An alpha level of .01 was selected for rejection or nonrejection of the questions being tested.

Data for the pretreatment vs. posttreatment differences were obtained through observation of the movement of the American Electromedics impedance bridge compliance change

meter needle. The lowest stimulus intensity level (in dB) for each condition, 500, 1000, 2000, and 4000 Hz and broad band noise at which the compliance change meter needle moved a minimum of one compliance change unit, was recorded for each group prior to experimental treatments (pretreatment). The same procedure was performed on each group for each condition after final substance dosage administration (posttreatment).

The posttreatment reflex intensity level was subtracted from the pretreatment acoustic reflex intensity level in the paired sample t-test computation of the t-values. Negative t-values (Table 1) indicated that the acoustic reflex threshold was elicited at a greater intensity level for the posttreatment elicitation than for the pretreatment elicitation.

Table 1 contains the computed t-values. Murphy and Venables (1971) indicated that increased ability in the detection of two clicks after administration of caffeine citrate may be related to differential arousal of the cerebral hemispheres, so the right ear t-values in the table for each frequency condition were tabled separately from the left ear t-values. If there were differences between pretreatment and posttreatment acoustic reflex threshold levels in the caffeine groups of this study, it might have been possible that an "ear difference" could have been statistically compared.

Results for the right ear for each experimental group at each test condition are as follows:

Statistical differences were found for the control group at the test conditions 1000 and 2000 Hz. No other group for any of the experimental conditions showed any statistical differences. This probably indicates the extent of test-retest reliability. Significant differences occurred only for the control group. The absence of significant differences for all other test conditions indicates that aspirin and caffeine had no effect on the chinchilla acoustic reflex threshold elicitation levels.

Results for the left ear for each experimental group at each test condition are as follows:

Statistical differences were found only for the combination group at the test conditions 1000 and 4000 Hz. No other group for any of the experimental conditions showed any statistical significant differences.

The only significant differences for any experimental group appeared at 1000 Hz and 4000 Hz for the left ear. Significant differences also appeared at 1000 Hz and 2000 Hz at the right ear for the control group. This control group difference suggests that artifact is present in the experiment or the measurement procedures and, therefore, places doubt as to the true significance behind the left ear statistical differences. In addition, the unilateral effects also indicate an artifactual influence.

Discussion

Bernstein and Weiss (1967) found a predictable sensori-neural type hearing loss associated with aspirin ingestion. The present study attempted to find whether there was a related change in the acoustic reflex threshold. The only significant differences found in animals receiving aspirin were at 1000 Hz and at 4000 Hz for the aspirin-caffeine combination group, for the left ear only. Bernstein and Weiss' study indicated that the hearing sensitivity threshold shift was for more than these two frequencies. In addition, the aspirin induced loss occurred bilaterally, while the effects in the present study were unilateral. Also, no significant differences were found for those animals receiving aspirin alone. Therefore, the differences noted for the aspirin caffeine combination group could, at most, be partly attributed to the effects of the aspirin.

Wojnaroska (1966) found that caffeine aids in reducing auditory fatigue. This effect is probably a central effect, not directly related to the hearing mechanism per se. However, the association with auditory function would indicate that it is in some way affecting auditory areas of the brain. In another study related to caffeine effects on hearing, Murphy and Venables (1971) found that detection of two sequential clicks could be improved through moderate

caffeine dosage ingestion. It was postulated that this effect could be due to differential arousal of the brain hemispheres by the stimulant. An effect of this type could possibly partially explain the ear difference related to the aspirin-caffeine combination group in the present study.

Both the Wojnaroska study and the Berstein and Weiss study were performed at suprathreshold levels. The stimuli were presented at intensity levels high enough to elicit the acoustic reflex, which may have been a factor in the results of the studies. The central auditory areas may be affected to some degree by caffeine ingestion as far as heightened arousal to the listening task. The present study did not show any significant differences for the caffeine-alone group. The caffeine related significant differences were found at 1000 Hz and 4000 Hz for the aspirin-caffeine combination group, only at the left ear. This supports the Murphy and Venables theory that caffeine provides differential hemispheric arousal of the brain. However, caffeine is not indicated to affect the acoustic reflex threshold sufficiently when in isolation to produce noticeable effects.

The combination of aspirin and caffeine was indicated to elevate the acoustic reflex threshold at 1000 Hz and 4000 Hz in the left ear only. Artifact of measurement or an unproven test-retest reliability could be influencing

the data, resulting in these significant differences. When compared to the control group, at which significant differences were also indicated, artifact is the most probable influencing factor.

Sites of action of aspirin and caffeine could also be factors in the two-frequency significant differences. Caffeine has its main effect at the level of the central nervous system in a stimulating mode. No studies could be found relating the effects of caffeine on the inner ear anatomy. While aspirin also has its main effect at the level of the central nervous system, studies (Warren and Rhem, 1975) have shown it to have an evidently protective function at the cochlear hair cells. By depressing hearing sensitivity thresholds, aspirin aids in protecting the ear from otherwise potentially damaging high intensity sound by providing a buffer zone. The addition of caffeine may accentuate this type of effect for the acoustic reflex threshold, however, in a differential manner for particular frequencies. The amount of caffeine in the circulatory system necessary to react with aspirin, and elevate the stapedial reflex threshold for 1000 Hz and 4000 Hz may not be sufficient to elevate 500 Hz and 2000 Hz reflex thresholds.

The null hypotheses were not rejected at the $\alpha = .01$ rejection level. For the statistical analysis of the results of this experiment:

1. Aspirin did not significantly change the level of elicitation of the acoustic reflex threshold in chinchilla.

2. Caffeine did not significantly change the level of elicitation of the acoustic reflex threshold in chinchilla.

3. A combination of aspirin and caffeine did not significantly change the level of elicitation of the acoustic reflex threshold in chinchilla.

In summary, these results appear to indicate that aspirin and caffeine, individually and in combination, have no measurably significant effect on the level of elicitation of the acoustic reflex threshold in chinchilla. Data were tabled comparing the ranges of the acoustic reflex threshold scores and pretreatment/posttreatment differences (Tables 2 and 3). There was no indication that the ranges of the statistically different groups were any greater or less than the nonsignificant difference groups.

Standard deviations of the acoustic reflex threshold scores and differences were also tabled (Tables 4 and 5). There was no indication that the standard deviations for the statistically different groups were any greater or less than the nonsignificant difference groups.

The range of differences and the standard deviation of scores for the experimental groups in each condition are shown in Tables 2 and 3. There is essentially no difference in range or standard deviation between the

Table 2. Range of Acoustic Reflex Thresholds for the Pretreatment and Posttreatment Conditions

		Frequency				White Noise
		500	1000	2000	4000	
Right Ear	Control	95-125	90-125	95-125	95-125	90-125
	Aspirin	85-105	75-105	85-105	85-115	70-105
	Asp/Caf	85-115	85-120	85-125	85-125	80-120
	Caffeine	85-125	75-125	80-125	80-125	75-125
Left Ear	Control	90-125	90-125	90-125	95-125	85-125
	Aspirin	85-120	85-120	85-110	85-120	85-100
	Asp/Caf	85-125	85-125	85-125	90-125	85-125
	Caffeine	90-115	80-125	85-115	80-125	75-125

Table 3. Range of Differences for Acoustic Reflex Thresholds for the Pretreatment and Posttreatment Conditions

		Frequency				White Noise
		500	1000	2000	4000	
Right Ear	Control	+5--+30	+15--+30	+10--+30	+5--+30	+5--+30
	Aspirin	-20--+	-15--+10	-15--+5	-20--+20	-20--+15
	Asp/Caf	-20--+20	-25--+10	-25--+10	-30--+20	-15--+10
	Caffeine	-30--+35	-35--+25	-30--+30	-35--+25	-35--+25
Left Ear	Control	-15--+30	-25--+25	-5--+30	-5--+20	+5--+30
	Aspirin	-25--+10	-30--+10	-15--+5	-15--+5	-5--+10
	Asp/Caf	-25--+20	-35--+10	-35--+10	-35--+5	-30--+5
	Caffeine	-15--+10	-15--+30	-15--+15	-35--+20	-25--+30

Table 4. Standard Deviation of Pretreatment vs. Posttreatment Acoustic Reflex Thresholds

		Frequency					White Noise
		500	1000	2000	4000		
		Pre-Post	Pre-Post	Pre-Post	Pre-Post	Pre-Post	Pre-Post
Right Ear	Control	8.3-10	10-3.5	10.2-4.5	12.4-6.5	11.4-8.2	
	Aspirin	8.3-8.9	7.7-8.4	5.0-6.9	7.4-9.6	8.8-11.2	
	Asp/Caf	7.4-8.3	5.9-11.0	5.9-13.0	6.9-11.8	8.2-11.5	
	Caffeine	8.8-14.2	11.1-15.2	7.5-15.5	10.8-16.0	11.8-16.5	
Left Ear	Control	11.4-15.5	11.5-17.5	12.4-17.5	6.1-13.0	11.5-15.5	
	Aspirin	7.5-9.8	5.1-8.9	3.6-5.6	6.8-9.5	4.3-5.5	
	Asp/Caf	8.1-11.8	4.8-14.2	6.1-13.3	5.4-13.7	4.9-16.8	
	Caffeine	8.2-6.8	11.2-7.2	8.7-5.9	12.7-11.2	15.1-7.1	

Table 5. Standard Deviation of Differences in Pretreatment vs. Posttreatment Acoustic Reflex Thresholds

		Frequency				White Noise Pre/Post
		500 Pre/Post	1000 Pre/Post	2000 Pre/Post	4000 Pre/Post	
Right Ear	Control	9.6	6.7	8.4	10.6	9.7
	Aspirin	10.7	8.3	7.9	11.6	11.7
	Asp/Caf	11.8	12.4	0.0	12.8	7.8
	Caffeine	20.8	22.2	19.9	23.6	22.7
Left Ear	Control	20.2	23.0	14.5	10.3	9.6
	Aspirin	11.9	11.3	8.8	8.6	6.1
	Asp/Caf	13.1	14.6	17.2	12.0	16.6
	Caffeine	8.2	14.3	9.2	17.9	17.9

significantly different (by t-test) group conditions and the nonsignificantly different group conditions. Significant differences were noted for the control group. These occurred at 1000 Hz and 2000 Hz at the right ear only. Significant differences for the control group essentially define the limits of tolerance for test-retest reliability. This shows that significant differences at the right ear might be the result of unreliable test results. However, since no other group at any other condition for the right ear showed a statistical significance, the limits of tolerance were not violated. Control group results for the left ear fell within normal limits. Therefore, results for both ears were expected to be valid for all conditions.

In clinical audiometry, these results are not diagnostically significant. A two frequency difference in acoustic reflex threshold for the left ear does not provide enough audiometric information to invalidate clinical impedance audiometry testing. Aspirin and caffeine, in separate dosages, did not affect the acoustic reflex threshold. The combination of aspirin and caffeine was found to provide an effect for one ear at two frequencies. Therefore, in clinical impedance audiometry, the effects of the two substances are not sufficient to affect audiometric test results or diagnostic interpretations.

CHAPTER V

SUMMARY AND CONCLUSIONS

Summary

It was the purpose of this study to investigate the possible alteration of the intensity level necessary for the elicitation of the acoustic reflex threshold with the administration of aspirin and caffeine, both individually and in combination.

Thirty-five adult chinchilla, ranging in age from six months to two years inclusive, were randomly selected as subjects from the herd maintained at The University of Tennessee Noise Research Laboratory. The criteria for selection were that the animals had no apparent disease processes and had no previous history of experimental participation. Further criteria for acceptance in the study was that the acoustic reflex thresholds had to be elicited for at least three of the desired frequency conditions at each ear within the limits of the equipment specified.

Each subject was administered acoustic reflex threshold testing both prior to experimental procedures, and following the complete administration of the study parameters. Ten animals were placed into each of the following groups:

aspirin-only, caffeine-only, and aspirin/caffeine combination. Five animals served as a control group. Measurements of the acoustic reflex threshold were taken the morning of the initial substance dosage to obtain the pretreatment acoustic reflex threshold levels. Posttreatment acoustic reflex threshold measurements were taken one hour following the administration of the final substance dosage.

The data obtained from these measures were compared statistically using the paired sample t-test. Statistical differences were noted for the right ear control group at 1000 and 2000 Hz. Statistical differences were noted for the left ear aspirin/caffeine combination group at the conditions 1000 and 4000 Hz.

Conclusions

The results of this study indicate that the usefulness of the acoustic reflex threshold as part of the impedance test battery is apparently influenced to a very limited degree, if at all, by the presence of aspirin or an aspirin/caffeine combination in the system of the subject. This observed influence, limited to the left ear at two specific frequencies, is probably not significant when comparing dynamic ranges between hearing sensitivity thresholds and acoustic reflex thresholds.

Moderate dosages of aspirin have been shown to elevate the hearing sensitivity threshold when administered over a period of three days of systematic sequential dosages (Bernstein and Weiss, 1967). Aspirin alone was not shown to cause a statistically significant difference between the pretreatment and the posttreatment acoustic reflex threshold levels. Caffeine alone also does not appear to alter the intensity level necessary for the elicitation of the acoustic reflex. Aspirin and caffeine in combination were shown to elevate the acoustic reflex threshold in the left ears of subjects at 1000 and 4000 Hz test conditions. However, this effect is probably a result of artifact of measurement, or a result of limited test-retest reliability.

Therefore, the bilateral aspirin-induced hearing loss found by Bernstein and Weiss (1967) is apparently not directly related to an influence of aspirin on the acoustic reflex threshold. Instead, aspirin may have its effect on the acoustic reflex threshold elicitation at some level of the brain-stem or brain which may interfere with the reflex arc of the stapedius muscle at intensity levels which, prior to aspirin ingestion, would have adequately produced the reflex. It is also possible that aspirin acts in a catalytic manner or in an excitatory function when occurring in combination with caffeine. However, it must be noted that

since this effect was seen at one ear only, it is possibly an artifactual effect.

Limitations of the Study

Prior to experimental procedures, hearing sensitivity thresholds were not determined. It was not determined whether any of the substance dosages resulted in a change in hearing sensitivity thresholds. If this procedure had been accomplished, more accurate conclusions could have been drawn regarding the possible alterations of the acoustic reflex threshold levels by aspirin and caffeine.

Animals were administered substance dosages via a gastric tube to approximate human intake of the substances as closely as possible, however, this procedure seemed to agitate the animals. Occasionally, an animal would collapse shortly following substance administration. However, most recovered fully within 30 minutes of the collapse. One animal died shortly after the final aspirin dosage for its group. Therefore, the aspirin-only group was reduced to nine subjects, with ten subjects remaining in the caffeine-only group and combination group, and five subjects remaining in the control group.

Tone decay measurements were attempted, however, the animals would not tolerate prolonged stimulation and struggled against the impedance probe and stimulation tube. This

resulted in unreliable tone decay responses due to excessive needle movement of the compliance change meter needle.

Implications for Further Study

1. The study could be replicated using human subjects (e.g. arthritic patients medically prescribed daily aspirin dosage), to examine the effects in humans and to predetermine hearing threshold shift prior to acoustic reflex threshold testing.

2. The study could be replicated with animals conditioned to respond to hearing sensitivity threshold stimuli. This would enable the experimenter to assure a hearing threshold shift to relate to the acoustic reflex threshold results.

3. The study could be replicated using other substances commonly ingested in moderate to extreme amounts. These substances could include nicotine, saccharin, salts (sodium), or vitamins known to be stored by the body.

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APPENDIX

CALIBRATION AND SPECIFICATIONS OF AMERICAN ELECTROMEDICS
IMPEDANCE BRIDGE MODEL 83¹

CALIBRATION: The instrument is calibrated acoustically by means of a cavity with rigid walls at any barometric pressure. Calibration of this unit is performed at the regional facility in Atlanta, Georgia once per annum. Periodic calibration checks are performed at the University of Tennessee Hearing and Speech Center Electronics Laboratory.

SPECIFICATIONS:

Power Supply: 110-220 volts 50-60 Hz

Power Consumption: 25 Watts

Test Frequency: 220 Hz Accuracy $\pm 1\%$

Distortion: Less than 1%

Compliance Range: 0.2 to 5 cc with accuracy better than 10%

Acoustic Impedance Range: 10000 to 200 acoustic Ohms

Accuracy: Better than 5%

¹Impedance Audiometers By American Electromedics (pamphlet) American Electromedics Corporation 145 Palisade Street Dobbs Ferry, New York, 10522.

Compliance Change Meter: Range sensitivity.

Sensitivity for full deflection: 0.0; A_D :

± 2 cc; T $\pm .7$ cc; R: ± 0.125 cc; SR: $\pm$

0.05 cc

Sound Pressure: 55 dB above threshold (85 dB SPL)

Pure Tone Frequencies: 250, 500, 1000, 2000, 4000

Hz $\pm 3\%$, HTL ISO output 40-125 dB HTL,

250 Hz 40-110 dB HTL

Broad-Band Noise Output: 40-125 dB SPL

Low Pass Noise: 40-125 dB SPL

High Pass Noise: 40-125 dB SPL

Attenuation Range: 40-125 dB HTL (pure tone), 40-125

dB SPL (broad-band noise and low and high pass

filtered noise).

VITA

Brian Grove King was born April 21, 1954 in New York, New York. He graduated from Miami Palmetto Senior High School in Miami, Florida in 1972. He attended Florida State University where he became a member of Phi Sigma of Phi Gamma Delta fraternity, and was recognized as a campus leader through election to membership in such academic honor societies as Garnet Key (Vice-President), Gold Key, and Who's Who in American Colleges and Universities. Brian received a B.A. in Audiology and Speech Pathology from Florida State University in March 1976.

He attended Baylor Medical School in Houston, Texas from 1976 through 1977 studying medical aspects of audiology. In 1977 he entered the Master of Arts program in Audiology and Speech Pathology at The University of Tennessee, Knoxville, completing the program in December 1979.

Brian is currently pursuing a doctorate in Hearing and Speech Science at The University of Tennessee, Knoxville. He is also completing his Clinical Fellowship Year at The University of Tennessee Memorial Research Center and Hospital and at The University of Tennessee Hearing and Speech Center.