THE EFFECTS OF SITUATIONAL CUES ON THE CHANGE OF NICOTINE TOLERANCE

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1989

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Submitted to the Faculty of the
Graduate College of the
Oklahoma State University
in partial fulfillment of
the requirements for
the Degree of
DOCTOR OF PHILOSOPHY
July, 1994

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CUES ON THE CHANGE OF
NICOTINE TOLERANCE

Thesis Approved:

Thesis Adviser

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ACKNOWLEDGMENTS

I wish to extend my deepest gratitude to my dissertation chair, Dr. Frank Collins, for his guidance and patience during my pursuit of this degree. His mentorship has been invaluable in helping me to attain my goals. I would like to express my thanks to my committee members, Dr. David Thomas, Dr. Maureen Sullivan, and Dr. Donald Boswell, for their contributions of time, comments, and recommendations that helped to make this a stronger study. To Dr. Dan McNeil, I I extend my appreciation for his early mentorship and continuous support. My thanks also to Dr. Steve Miller who donated the toothbrushes for this study.

To my family (Jeanne Kirk, DaMaris Corzatt, Stacy and Peter, Mildred Laible, Bill, and all others), I wish to express my most heartfelt thanks for their unceasing love and support during what has seemed to be the never-ending quest for my Ph.D. My thanks to Dr. Henry Croes, whose support and teaching have contributed to the personal strength that has helped me to achieve my goals. I extend my gratitude to my wonderfully supportive friends: Jennifer B., Jennifer F., Carolyn and Rick, Margarita, Lisa, Mary, Greg, and Chuck, without whom I would not have been as sane during this endeavor. Their presence has helped me to maintain perspective in my life and to cope with the sacrifice that has been associated with achieving this goal.

I extend my loving appreciation to my late father, Wayne Corzatt, who instilled in me not only his faith but also his belief in life's constant quest for knowledge. I also extend my appreciation to my late stepfather, Frank Kirk, who made my early education possible and who was always supportive of my goals.

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Abstract

Research has indicated that some situations are "high risk" for cigarette smoking, while other situations appear more neutral and do not result in increased smoking. For example, smoking is more likely following a meal, but is not typically associated with events such as tooth brushing. Previous studies suggest that eating may result in a reduction of smoking tolerance. Most theories of tolerance emphasize the importance of situational cues in the development (and reduction) of tolerance, thus it is hypothesized that "high risk" situations which result in increased smoking may reduce tolerance more than "low risk" situations not typically associated with smoking.

In Study 1, each of 18 subjects participated in three conditions: High Risk Change (Eating), Low Risk Change (Tooth Brushing), and No Change (Resting). Tolerance was measured during each puff of a Pre-Condition cigarette (Pre-Cigarette) and a Post-Condition cigarette (Post-Cigarette) by (a) self-report (i.e., hedonic ratings of smoking satisfaction, enjoyment, and taste) and (b) physiological (i.e., heart rate) measures. Results indicated that mean hedonic ratings for the Post-Cigarette differed significantly across conditions. Eating exhibited the greatest increase in hedonic ratings; whereas, Resting exhibited a slight decrease and Brushing a moderate decrease in hedonic ratings.

A second study (Study 2) was conducted to determine the extent to which the findings of Study 1 were the result of the possible interactive effects of eating and nicotine. Each of 20 subjects participated in the Eating condition (two groups of 10 smokers each, based on subjects' reporting that they frequently or rarely smoke following eating). Results indicated an increase in hedonic ratings of the Post-Cigarette only for the group that reported frequently smoking following eating.

In Study 1, hedonic ratings for the three conditions at the Post-Cigarette were not consistent with ratings that would be expected if tolerance reduction had occurred (i.e., both risk conditions resulting in increases). Overall, the findings of both studies were consistent with subjects' self-report of their frequency of smoking following eating and tooth brushing events. Results suggest that a person's smoking history provides a better predictor of "high risk" smoking situations and smoking pleasure than the reduction of tolerance.

The Effects of Situational Cues on the Change of Nicotine Tolerance

Approximately 32.7 percent of men and 28.3 percent of women in the United States are regular cigarette smokers (United States Department of Health and Human Services [USDHHS], 1988). The National Status Report to Congress (1986) reported that 16 states had restrictions on smoking in restaurants and 17 states had restrictions on smoking in the workplace. Only nine states did not have some type of restriction on smoking in public places. Thus, cigarette smoking in certain environments is becoming increasingly restrictive.

Public information about the hazards of smoking has steadily increased since the 1960s (USDHHS, 1988). Smoking is known to be causally related to deaths from cardiovascular disease, cancer, and chronic obstructive lung disease (Klesges, 1989). Despite these statistics, however, many individuals continue to smoke. Research suggests that nicotine, the addictive drug found in cigarettes, serves as a powerful reinforcer (USDHHS, 1988) and may account for the difficulty smokers have in quitting smoking, despite the decreasing number of smoking environments and an increasing awareness of the associated health risks.

Drug effects are modified through the process of tolerance. Tolerance is typically defined as a decrease in drug effects following repeated administration (Baker & Tiffany, 1985; Cagiulla et al., 1991; Poulos & Cappell, 1991). For example, when people smoke, inhaling an initial puff increases heart rate and blood pressure (Frankenhaeuser, Myrsten, Post, & Johansson, 1971). Following a second puff, there is less of an increase. As tolerance develops, an increase in the amount of the drug used is necessary to achieve the initial drug effect (F. L. Collins, Epstein, & Caggiula, 1993).

The duration of tolerance is characterized as either acute or chronic. Acute tolerance develops within one or two doses of a drug, is relatively short-lived, and may be lost and regained during short periods of abstinence from the drug (Russell, Jarvis, Jones, & Feyerabend, 1990; USDHHS, 1988). Acute tolerance may also be conceptualized as occurring when the effect of identical drug dose administrations is less following the second administration of the drug than following the first administration of the drug (Fischman, Schuster, Javaid, Hatano, & Davis, 1985; Poulos & Cappell, 1991). Contrastingly, chronic tolerance is acquired after more prolonged use of a drug and is longer lasting (USDHHS, 1988).

There is an enormous literature on drug tolerance. The present review will focus on animal research for morphine (Siegel, 1975, 1976, 1978a, 1978b; Siegel, Hinson, & Krank, 1978, 1981), cocaine (Fischman et al., 1985; Smith, 1990), and nicotine (Caggiula, Epstein, & Stiller, 1989; Morgan & Ellison, 1987; Porchet, Benowitz, & Sheiner, 1988). Environmental factors have been found to contribute to the development and disruption of both acute and chronic drug tolerance. Although environmental factors and their association with tolerance have experienced extensive investigation, research has not examined the extent to which certain environmental situations reduce nicotine tolerance, and thus, directly contribute to the maintenance of smoking.

In order to better understand the factors contributing to nicotine tolerance and the role of tolerance in the maintenance of smoking, several areas will be addressed. First, models used to explain the development of tolerance will be presented in order to provide a more detailed understanding of the paradigms that have been proposed for tolerance. Second, tolerance to drug effects, as measured by heart rate, blood pressure, body weight, and hedonic ratings, will be reviewed. Third, the contribution of environmental cues in the development

of tolerance to drug effects will be discussed. Fourth, the role of certain situational cues to smoking, such as stress and eating, will be examined. Fifth, a proposed association between situational cues and nicotine tolerance reduction will be presented as the focus of a first study (Study 1). Finally, a second study (Study 2), will be proposed to address a potential confound regarding possible interactive effects between a particular situational cue and nicotine.

Models of Tolerance Development

Pavlovian Conditioning Model

Pavlovian principles of conditioning have been used extensively in the explanation of learned phenomena. Siegel (1975) proposed a model of tolerance based on these principles of conditioning. According to the Pavlovian conditioning model of tolerance, emphasis is placed on the association between cues preceding drug administration and the systemic effects of the drug.

According to Siegel's (1977) initial model of tolerance development, drug administration under specific cues results in an anticipatory compensation in addition to the usual drug effect. When drug delivery (unconditioned stimulus) is repeatedly paired with these environmental cues (conditioned stimulus), an anticipatory compensation (conditioned response) opposite to the drug effect (unconditioned response) develops.

However, the development of a CR in opposition to the UCR is a violation of Pavlovian principles; thus, Siegel has proposed a revision in his initial model. According to the revised Pavlovian conditioning model, there is not an anticipatory compensation, but rather a conditioned drug effect. For example, the disturbance created by morphine (UCS) elicits the adaptive response of hyperalgesia (UCR). This hyperalgesia may be repeatedly paired with environmental stimuli (CS), resulting in a conditioned response which is similar to the unconditioned hyperalgesic response, but is lesser in strength. This

diminished response to a drug following repeated administrations is tolerance (Siegel, 1988; Siegel, Krank, & Hinson, 1987).

Opponent-Process Model

The opponent-process model of tolerance also utilizes the Pavlovian principles found in Siegel's (1975) model; however, different terminology is used. Ternes (1977) suggests that tolerance occurs as a result of the development of physiological processes that counteract disruptions in homeostasis. The introduction of the drug into the organism initiates an a-process, or drug effect. In order to counteract the a-process, the organism produces an opponent process, or b-process, which acts to return the body to homeostasis.

Furthermore, in order to determine the affective or hedonic state of the organism, the mathematical absolute value of the a-process minus the b-process is obtained (Solomon, 1980). If the a-process is greater than the b-process, the organism is said to be in State A. However, if the b-process is greater than the a-process, the organism is said to be in State B. Assuming that State A is the state desired by the organism, efforts will be made to alleviate State B through the use of more frequent drug administrations. However, with repeated presentations of the drug, the b-process takes longer to decay and becomes stronger in its ability to maintain homeostasis, whereas, the a-process weakens. As a result, an increasing quantity of the drug is needed to produce the initial effect, or State A. The strengthening of the b-processes results in a decreased drug effect and is considered to be tolerance (Solomon & Corbit, 1973; Solomon, 1980).

Solomon and Corbit (1973) contend that previously neutral environmental events (CS) may be paired with drug administration (UCS), resulting in the elicitation of either the State A or State B (CRs), depending on when the pairing

occurs. For example, in the use of opiates, conditioned stimuli which are paired with the A State, such as a drug syringe, a needle prick, or familiar surroundings should be able to function to activate the A state and oppose the B state. Contrastingly, if a conditioned stimulus which is associated with the lack of the drug, such as lack of money or confinement, is paired with the peak of the B state, the most intense craving state, then it is possible that the conditioned B state will exacerbate an already existing unconditioned B state. As a result of this conditioning phenomenon, the frequency of drug administration should increase.

Habituation Model

Baker and Tiffany (1985) propose a model of tolerance which states that tolerance development is similar to the behavioral characteristics of habituation. The distinction between habituation and tolerance is minimal in that habituation is also a process of decreased responding following repeated administrations (MacKintosh, 1987). Tolerance, as it relates to habituation, has been described as a decreased effectiveness in eliciting a response to a drug which develops when knowledge about the context of drug delivery and the environment matches information in short-term memory (STM) concerning prior drug doses (Siegel, 1977).

The habituation model (Baker & Tiffany, 1985) is different from the Pavlovian and Opponent-Process models in that it suggests that the mechanisms for tolerance are more cognitively linked. Baker and Tiffany (1985) make extensive use of concepts proposed by Wagner's (1979) theory of habituation. For example, if an event or stimulus is unexpected, then it is not considered to be primed in STM and processing of the stimulus will be activated. The extent to which the stimulus is processed depends on the magnitude of the unconditioned responding to the stimulus. If, however, the stimulus is primed in

STM, a process is also initiated, but it is a diminished response. Therefore, habituation is evident when the stimulus is primed in STM prior to its presentation.

Moreover, two types of priming may occur. Self-generated priming refers to a stimulus primed in memory due to a prior, recent exposure to the stimulus (Baker & Tiffany, 1985). With regard to drug administration, if traces of the drug stimulus properties remain in memory, then less processing is needed and the response to the stimulus is decreased, resulting in nonassociative tolerance. In associative priming, when two stimuli have previously been paired, one stimulus is able to evoke the priming of the second stimulus in STM. For example, if drug administration is consistently paired with particular environmental cues, then reexposure to the cues would elicit the priming of drug properties in STM. As a result, the presentation of the drug would be expected, and a diminished, or habituated, response would occur. This response as it relates to drug administration is considered to be associative tolerance (Baker & Tiffany, 1985).

Tolerance development also varies as a function of the pharmacological variables of drug dose and interdose interval (IDI; Baker & Tiffany, 1985). If reliable drug cues for administrations are not present, then the development of nonassociative tolerance will vary directly with dose and inversely with IDI. For example, if dose is high and IDI is short, then nonassociative tolerance will be exhibited more readily due to the priming of drug properties remaining in STM; whereas, if drug dose is low and IDI is long, then little nonassociative tolerance will develop due to the decreased likelihood that drug properties from a previous stimulus remain in STM. Associative tolerance, however, is not dependent on the presence of a drug's stimulus properties in STM; therefore, it will develop more readily at lower drug doses and longer IDIs. Associative

tolerance is also more likely to be acquired rapidly when drug administration is paired with salient environmental cues (Baker & Tiffany, 1985).

Homeostatic Model

Poulos and Cappell (1991) provide an alternate view of tolerance which they call a homeostatic process. This model attempts to provide an explanation for tolerance which the other models do not. This model states that "functional disturbances are necessary to drive the processes of physiological adaptations that serve to restore homeostasis" (Poulos & Cappell, 1991, p. 391). In order for a functional disturbance, or a behavioral demand, of a drug effect to be detected, an organism must interact with relevant features of the environment and the systemic presence of the drug. There are two forms of systemic tolerance: Associative and nonassociative.

The homeostatic model differs from the habituation model in its utilization of the terms associative tolerance and nonassociative tolerance. Whereas the habituation model uses these terms as they refer to priming in STM (Baker & Tiffany, 1985), the homeostatic model uses them to refer to the role environment plays in the development of tolerance (Poulos & Cappell, 1991).

According to Poulos and Cappell (1991), associative tolerance incorporates Pavlovian conditioning in its explanation. Associative tolerance occurs when the unconditioned homeostatic response to a drug administration becomes paired with predictive cues. In order for associative tolerance to be extinguished, an opposite counteradaptation must occur. In addition, the organism must interact with relevant features of the environment. Nonassociative tolerance involves a functional drug disturbance which is not tied to specific cues. The loss of nonassociative tolerance also requires a counteradaptation.

Each of these models is compatible with the others. Environment is consistently utilized as a factor affecting tolerance development, whether it be

through conditioning processes or priming in memory. Each model suggests that when environmental cues associated with drug administration are changed, tolerance is reduced.

Drug Effects and Tolerance

The assessment of drug tolerance has been conducted using both physiological and self-report measures of drug effects. According to the Surgeon General's Report (USDHHS, 1988) some of the most commonly used physiological measures of tolerance have been heart rate, drug administration, analgesia, EEG activity, and performance of a behavioral task. Other physiological measures of tolerance have included skin temperature (Pomerleau, Fertig, & Shanahan, 1983) and body weight (Morgan & Ellison, 1987). Self-report measures of tolerance have included hedonic ratings (F. L. Collins et al., 1991). Studies of drug effects have focused on a variety of drugs including morphine, cocaine, and nicotine.

Physiological Measures

Cardiovascular Measures. Heart rate is an important measure in the study of drug tolerance. Changes in heart rate following cocaine administrations have been found to decrease with repeated administrations (Fischman et al., 1985). This acute tolerance to the heart rate effect of cocaine disappeared within a 24 hour period.

Acute tolerance to nicotine has also been studied by measuring heart rate. West and Russell (1988) found that a decrease in the degree of heart rate boost indicated that acute tolerance had developed to nicotine; however, this tolerance disappeared after 24 hours of abstinence from smoking. The cigarette smoked following the abstinence period raised the heart rate by approximately 14 beats per minute to the pre-abstinence levels. Given that a decrease in heart rate

boost is indicative of tolerance, this increase in heart rate following the abstinence period is indicative of tolerance reduction.

Furthermore, in a study by Pomerleau et al. (1983), acute tolerance was produced through cigarette smoking in the laboratory. Heart rate boost following smoking was found to be greater in subjects who were less dependent on nicotine than those who were more dependent on nicotine. In the same study, measurement of skin temperature indicated greater tolerance to nicotine in heavy rate smokers than in light rate smokers. These findings provide empirical support for the widely held belief that subjects who are more dependent on nicotine experience a greater degree of tolerance to nicotine.

The development of tolerance as assessed by increases in blood pressure and heart rate following repeated administration of nicotine was observed by Benowitz, Jacob, Jones, and Rosenberg (1982). Following the infusion of nicotine, blood pressure and heart rate increased rapidly, reaching a peak within 5 to 10 min after drug administration. In subsequent administrations, blood pressure and heart rate did not increase as substantially as during the initial drug infusion, indicating tolerance had occurred.

Rapid tolerance to the blood pressure and heart rate changes resulting from intravenous nicotine has also been documented (Rosenberg, Benowitz, Jacob, & Wilson, 1980). Subjects were presented with six series of nicotine injections, 30 min apart. Each series contained 10 injections spaced 1 min apart. Although blood pressure and heart rate values remained above baseline, suggesting that complete tolerance had not developed, there was little increment with repeated injections. This minimal increment in heart rate and blood pressure occurred despite nicotine blood level increases which were comparable to those initially observed after the first series of injections.

Body Temperature. Although not as commonly researched, A. C. Collins, Burch, de Fiebre, and Marks (1988) and A. C. Collins and Marks (1991) investigated body temperature and nicotine tolerance in mice and found that with repeated infusions of nicotine, animals developed tolerance to the effect of nicotine on body temperature.

Body Weight. The effect of nicotine tolerance on the body weight of rats was measured in a study by Morgan and Ellison (1987). Tolerance was found to develop to the weight reducing (anorectic) effects of nicotine, contributing to an increase in body weight in response to nicotine administration. Tolerance, however, was found to occur only in rats continuously infused with the drug.

Similarly, with repeated injections of nicotine paired with cues signaling drug administration, milk intake in rats increased suggesting tolerance to the anorectic effects of nicotine. When these cues were changed, milk intake decreased, indicating tolerance reduction (Caggiula et al., 1989).

Self-Report Measures

Tolerance to the affective responses of smoking has been reported. F. L. Collins et al. (1992) found that ratings of positive aspects of smoking, such as the satisfaction, enjoyment, and taste of the cigarette reduced significantly across time. Subjective reports indicate that a cigarette following a meal is always the most enjoyable, and enjoyment tends to decrease across cigarettes when not eating.

Tolerance has been found to develop to the negative subjective effects of nicotine (Russell et al., 1990), such as light-headedness and dizziness, and the positive subjective effects of nicotine (Rosenberg et al., 1980), such as pleasure. Rosenberg et al. (1980) found that following an initial injection of nicotine, subjects reported a pleasant sensation. This response was not observed beyond the first series of injections.

Tolerance and the Environment

The investigation of the relationship between tolerance and the environment is an important component in the study of drug tolerance. Siegel (1984) used heroin to investigate the contribution of environment to the Pavlovian conditioning model of tolerance development. According to Siegel, as the frequency of drug administration increases, an association is made between the drug effects and the environmental cues. The effects of anticipating drug administration contribute to tolerance and lessen the drug effects. However, when the drug is presented in a novel environment, tolerance is reduced due to the environment not having any previously established association to the drug. Therefore, the drug effect is not anticipated and drug-compensatory responses are not activated. The resulting effects are a reduction of tolerance, an increase in the drug effect, and in some instances, heroin overdose.

Tolerance to the drug effects of nicotine is also influenced by environmental stimuli. The research in the area of nicotine tolerance and environment yields results consistent with those found in the investigation of other drugs. Epstein et al. (1989) induced tolerance to nicotine in rats in a laboratory setting. Rats were provided drug administrations within the same environmental context. Tolerance developed through the repeated pairing of nicotine with the distinct environmental and procedural cues. Changes in these situational cues were found to reduce tolerance. The resurgence of the initial drug response suggests that mechanisms responsible for tolerance are conditioned to the cues present in the environment which are associated with drug administration.

Studies of opiate use have investigated the role of environment in the development and maintenance of tolerance. Baker and Tiffany (1985) reported that morphine tolerance was reduced when the drug was presented in an environment other than the one typically associated with drug administration.

Smith (1990) studied the situational specificity of tolerance in using cocaine. Rats were found to develop tolerance only "for responding in the presence of environmental stimuli that were coincident with pharmacologic effects of the drug" (p. 476). Findings indicated that drug effects in one environment were not generalizable to other environments. Smith (1991) found similar results in an animal study of the situational specificity of tolerance to the effects of morphine.

Studies have also indicated that tolerance development is affected by the timing of cues signaling drug administration. When these cues are changed, tolerance is reduced, and the effect of the drug increases (Caggiula et al., 1989; Caggiula et al., 1991).

Situational Cues and Smoking

As indicated by Epstein et al. (1989) and Caggiula et al. (1991), a significant area of investigation related to smoking behavior is that of the influence of situational cues on smoking. Studies have shown that certain situations, or events, such as stress and eating, may affect a person's urges to smoke and contribute to the frequency with which a person smokes (Pomerleau & Pomerleau, 1987). Variations in smoking behavior have been found to be a result of the function of situational factors in the natural environment (Hatsukami, Morgan, Pickens, & Champagne, 1990). In addition, smokers have been found to smoke more in certain situations, suggesting that some situations are more associated with smoking than others (Epstein & Collins, 1977).

Smoking in conjunction with a stressor may result in smoking functioning as a cue for that stressor (Perkins, Epstein, & Jennings, 1991). The temporal contiguity of smoking and a stressor contributes to the development of an association between the two. If a smoking cue which predictably precedes a repeated stressor is removed, the responses to the stressor may be affected.

Many authors have found smokers to smoke more following eating. Jarvik, Saniga, Herskovic, Weiner, and Oisboid (1989) reported that subjects preferred the cigarette after a meal more so than a cigarette following no meal. F. L. Collins et al. (1991) found that subjects' hedonic ratings before and after smoking cigarettes indicated increased positive sensations from the cigarette (i.e., more satisfaction, more enjoyment, and more taste) and an increased craving to smoke following a meal, suggesting that tolerance had previously developed and was then reduced following a meal.

Similar conclusions were found by Hasenfratz, Pfiffner, Pellaud, and Battig (1989). Craving to smoke, smoking enjoyment, and subjective tobacco taste all increased with smoking after eating. It was suggested that a meal might intensify the effects of smoking. One possible explanation for this intensification was that a transient reduction of nicotine tolerance occurred, possibly as the result of metabolic effects.

Another study investigated the extent to which smoking a cigarette following a meal was influenced by the acceleration of metabolism of nicotine (Lee, Jacob, Jarvik, & Benowitz, 1989). Results demonstrated variable decreases in nicotine blood concentrations during a 45-min period following a meal, with the decrease being minimal for some subjects. It was suggested that this small decrease was due to the long half-life of nicotine (2 hr). The investigators concluded that it was "unlikely that, for most people, a small, gradual decline in nicotine levels could explain why a cigarette is smoked following a meal" (p. 624).

Models of Tolerance as Related to Situational Cues

Each of the four models previously discussed, the Pavlovian, opponent-process, habituation, and homeostatic models, contributes an increased understanding to the role of situational cues and their association with the

development and reduction of tolerance to drug effects. The Pavlovian model suggests that if smoking is paired consistently with a particular situational cue, such as eating, across multiple administrations, a drug effect similar to the original effect but lesser in strength would be expected. As a result, it would be expected that the drug effect (e.g., as measured by hedonic ratings) following eating would be at consistently lower levels. This model, however, does not explain how hedonic ratings for satisfaction, enjoyment, and taste have exhibited a notable increase with a cigarette immediately following eating. Therefore, this model is not appropriate to explain the role of situational cues in the reduction of nicotine tolerance following eating.

The habituation model states that if a situational cue were to be repeatedly paired with a drug presentation, the connection of the drug and cue would result in associative tolerance, with the situational cue predicting the drug effect. As a result, the presentation of the drug would be expected, and a diminished response would occur. This tolerance is different from nonassociative tolerance, where situational cues are not present; there is an initial drug effect followed by a diminution in responding due to priming in short-term memory.

Based on the habituation model, eating, an event which is typically associated with smoking, would elicit the priming of drug properties in STM. As a result of its ability to predict the presentation of the drug, eating would result in a diminished drug effect across time (e.g., a decrease in hedonic ratings), or associative tolerance. An event such as tooth brushing which is a situational cue not typically associated with smoking would result in an increase in drug effect following the drug administration. Across repeated administrations, however, this response would become lesser in strength due to traces of the drug stimulus properties remaining in memory, or nonassociative tolerance. A control condition in which no situational cue is present would be

expected to result in a continuation of previously developed tolerance from an initial cigarette. The habituation model provides an explanation for tolerance development; however, this model would predict that hedonic ratings would not increase following eating due to the presence of associative tolerance. Therefore, habituation does not account for studies which have shown increased hedonic ratings after a meal.

The homeostatic model would predict that with associative tolerance, a decrease in the drug effect of a cigarette would be the result of repeated pairing of the drug effect with the predictive cues associated with a particular event, such as eating. Eating immediately prior to smoking a cigarette, however, might serve to initially disrupt previously developed tolerance (from a previous cigarette), thus, resulting in increased hedonic ratings followed by a decrease in hedonic ratings. This disruption would be expected due to the predictive cues of eating and their association with smoking. Nonassociative tolerance is defined as tolerance development to the drug effect of a cigarette when it is not tied to specific situational cues. Tooth brushing would be considered an activity which has not been repeatedly paired with the drug effects of smoking. An increase in hedonic ratings as the result of eating or tooth brushing would suggest that both situations serve to reduce tolerance, with one situation typically associated with smoking (eating) and one situation not typically associated with smoking (tooth brushing). A control condition would be expected to exhibit a continuation of tolerance development from a previous cigarette. This model does not account for the extent to which situations may differentially reduce tolerance and does not provide a framework for investigating different situational cues.

The final model, the opponent-process model, best fits with the preliminary research that has shown smoking a cigarette following an eating condition (a

situation typically associated with smoking) to result in an increase in hedonic ratings. This model states that tolerance develops to repeated administrations of the drug thus accounting for tolerance which develops to an initial cigarette (i.e., a pre-experimental cigarette) as measured by a decrease in hedonic ratings and a decrease in heart rate boost. If eating is repeatedly paired with smoking, the opponent-process model would predict that there would be a lesser drug effect given that the b-process had strengthened and the a-process had weakened (i.e., tolerance had developed). As a result, an increased amount of the drug would be needed to achieve the a-process. A smoker would then use more of the drug to achieve the desired A-state, which would result in an increase in hedonic ratings for a second cigarette (i.e., a post-experimental cigarette). The compensatory nature of this drug use would indicate that an initially large increase in hedonic ratings would occur. The opposing b-process elicited by the onset of State A would then be expected to cause a decrease in hedonic ratings across puffs.

Tooth brushing is a situation not typically associated with smoking, and is therefore a novel stimulus. Smoking a cigarette immediately following a tooth brushing condition would be expected to promote an a-process. Although an increase in hedonic ratings would be expected, the elicitation of the a-process would be of lesser intensity than the elicitation of the a-process exhibited following the eating condition, given that tooth brushing condition would lack the compensatory quality of smoking like that associated with the eating condition. With a rest (control) condition, it would be expected that the tolerance exhibited as measured by the hedonic ratings of an initial cigarette would continue to show a decrease, with any increase in hedonic ratings for a second cigarette attributed to the time between the first and second cigarettes.

The opponent-process model offers a theoretical foundation for the effects of eating and tooth brushing conditions on tolerance. However, it is also important to interface this model with the literature regarding environmental cues. Both eating and tooth brushing are activities that occur in the mouth, which serves as an "environment" that may be changed. The types of foods that may be eaten vary greatly. Therefore, each food presentation serves as a novel disruptor of this environment, resulting in a reduction of tolerance (i.e., an increase in hedonic ratings). Tooth brushing tends to be less novel of an event (i.e., the same toothpaste is used in each presentation). As a result, tooth brushing might cause some disruption in the environment by virtue of its presentation (i.e., a slight increase in hedonic ratings); however, the disruption would not be as great as that found with eating.

It is important that each of the four models used to explain tolerance be taken into account with the research findings concerning the role of situational cues in the development and reduction of tolerance and how hedonic ratings of a cigarette have been shown to be consistent, and at times contradictory, to what would be predicted by the models of tolerance. This study will serve to clarify the role of tolerance in a paradigm investigating hedonic ratings and their potential ability to be representative of tolerance to the drug effects of smoking.

Goals of Study 1 and Study 2

Given that situational cues such as eating and stress have been found to influence smoking behavior and that nicotine tolerance has been found to develop to the drug effects of smoking, one possible explanation for the maintenance of smoking behavior is that situational cues associated with increased smoking reduce nicotine tolerance. For example, many smokers report that they enjoy smoking a cigarette following a meal. Increased urges to smoke and increased pleasure following a meal may indicate tolerance

reduction. This reduction may be explained by the presentation of food as a new situation or event. F. L. Collins et al. (1992) found that when subjects did not eat in the laboratory for 5 hr, hedonic ratings showed tolerance. Following a meal, however, hedonic ratings increased, indicating a reduction in tolerance.

Preliminary Research

Increased smoking following a meal may be related to the reduction of nicotine tolerance (Hasenfratz et al., 1989). Preliminary research supports this position. Hedonic ratings of the satisfaction, enjoyment, and taste of a cigarette were obtained from a pilot subject following each puff of two cigarettes; one cigarette before eating a small snack, and the second following the snack. The second cigarette was smoked following a 5 min period during which time the subject ate a muffin. A muffin was selected as opposed to a meal due to its ease of use in the lab and for its ability to represent a situational cue for smoking. Hedonic ratings during the initial puffs of the post-eating cigarette were noticeably higher compared to the pre-eating cigarette, suggesting tolerance reduction.

With the opponent-process model providing a conceptual framework for tolerance, the goal of Study 1 was to determine the extent to which situational cues, or events, highly associated with smoking (i.e., eating) and less associated with smoking (i.e., tooth brushing) differentially affect the reduction of nicotine tolerance. Studying the development and reduction of nicotine tolerance is important in order to determine those events which make smoking either more or less reinforcing following the event, and therefore, contribute to the maintenance of smoking behavior.

Study 2 was designed to determine the extent to which the findings were the result of eating or the result of the possible interactive effects of eating and nicotine. Eating a snack is a different event from tooth brushing in that it

produces basal metabolic changes which may interact with smoking, thus, providing a methodological confound. As stated previously, Lee et al. (1989) found that nicotine levels decreased gradually due to a 2-hr half-life. As a result, it was unlikely that this slow metabolism of nicotine could account for increased smoking immediately following eating or for a reduction of tolerance. However, in order to be able to more accurately interpret the findings of Study 1, a second study was developed.

In Study 2, a High Risk Change eating group (High Risk Eating group; i.e., smokers who reported frequently smoking following eating) was compared with a Low Risk Change eating group (Low Risk Eating group; i.e., smokers who reported rarely smoking following eating). The intent of this design was to determine if self-report of smoking frequency or metabolism associated with eating was the primary factor in the findings.

Statement of Hypotheses

All subjects were observed in three conditions: High Risk Change (i.e., a condition typically associated with cigarette smoking), Low Risk Change (i.e., a condition not typically associated with cigarette smoking), and No Change. It was hypothesized that more tolerance would be observed in the condition involving no change in environment as opposed to the conditions involving change in the environment. This finding would provide support for the opponent-process model which would predict that no change in environment would result in a continuation of tolerance development and that changes in environment would cause a reduction in tolerance. In addition, it was expected that more tolerance would be observed in the Low Risk Change condition as opposed to the High Risk Change condition. This finding would suggest that the opponent-process model accurately predicted that a Low Risk Change

condition would elicit less reduction of tolerance than a High Risk Change condition.

It was hypothesized in Study 2 that differences would be found between the High Risk Eating and the Low Risk Eating groups on tolerance measures. This finding would suggest that the differences were attributable to the frequency that eating was reported to elicit smoking, and not due to metabolic factors associated with eating.

Study 1

Method

Subjects

Nineteen subjects were recruited from Oklahoma State University (OSU) Introductory Psychology classes, OSU employee workplaces, and from the surrounding community. Recruitment was conducted through the use of class screenings and the posting of fliers advertising the study. Based on information obtained through the smoking questionnaire presented to Psychology 1113 classes and from responses to fliers, subjects were contacted by telephone for participation in the study.

Prior to participation in the three conditions, subjects were interviewed to obtain a smoking history and to verify the frequency with which they smoked immediately following a snack and immediately following brushing their teeth. In addition, each subject had to meet the following inclusion criteria: (a) 18 years of age or older, (b) history of smoking for at least 1 year, and (c) smoke more than 15 cigarettes per day. Subjects were given the option of receiving either four extra credit points towards a Psychology 1113 grade or $12 as compensation for participation in the study.

The final subject pool consisted of 18 subjects, 5 males and 13 females. A nineteenth subject was recruited for participation in the study to replace a

subject who had repeated the tooth brushing condition due to a computer malfunction. Counterbalancing of the condition orders was conducted. Given that there were three conditions, six orders were used. Subjects were randomly assigned to these orders with three subjects in each order. In addition, the same female experimenter was used to run all subjects through all three conditions. No additional experimenters were used.

The mean age of the 18 participants was 26.94 years (SD = 11.14). Subjects smoked an average of 25.0 cigarettes per day (SD = 7.67) with a mean length of time smoked of 7.69 years (SD = 8.92). The mean alveolar carbon monoxide (COa) rating for the interview session was 19.0 ppm (parts per million; SD = 9.91).

Alveolar carbon monoxide (COa) is an indirect measure of smoking history. As a general rule, COa levels < 10 parts per million (ppm) typically indicate a condition of total abstinence, whereas, smoking COa levels are typically $\geq$ 10 ppm. Frederiksen and Martin (1979) found abstinence COa levels ranging between 5 and 11 ppm, whereas, COa levels for smokers continuing to smoke ranged between 36 and 80 ppm. For purposes of this study, smokers with COa levels < 10 ppm at the interview session were excluded from participation with two exceptions. One subject reported fasting at the time of the interview and thus had smoked less. This subject obtained a COa of 8 ppm during the interview; however, during Session 1, the subject's initial COa was 19 ppm. A second subject was sick during the interview and obtained a COa of 9 ppm; however, the subject's initial COa measure during Session 1 was 11 ppm. A second criterion for COa measures stated that if a subject received a COa rating of < 5 ppm on any of the three experimental days, he or she would not participate on that day.

Event Selection

A smoking survey was presented to a Psychology 1113 class. Smokers were asked to rate the frequency with which they smoked immediately following nine events, such as eating a snack, reading, and studying. A 5-point Likert scale was used with ratings of never (1), seldom (2), sometimes (3), frequently (4), and always (5). In the initial screening, smoking immediately following eating a snack was typically either a 4 or a 5 rating. A separate inquiry of smokers suggested that smoking following tooth brushing would typically result in either a 1, 2, or 3 rating.

Subject selection included an assessment of ratings for eating a snack and for tooth brushing events. Smokers who rated a 4 or 5 on eating a snack, and who rated a 1, 2, or 3 on tooth brushing, with an increment greater than one rating (e.g., 2-4, 3-5), and who met the previously stated inclusion criteria, were eligible for the study.

Measures

Alveolar Carbon Monoxide (COa). Alveolar carbon monoxide (COa) measures were taken to exclude nonsmokers from the study and to determine COa boost following cigarette smoking. Samples of each subject's breath were obtained using a Vitalograph BreathCOa monitor (Model 29.700). Each subject was asked to inhale and hold the air in his or her lungs for 20 s, then to exhale the air into the sterile mouthpiece of the COa monitor. Time of inhaling and exhaling during COa measures was regulated using a stopwatch. A digital value of COa comprised each measure.

Hedonic ratings. Hedonic ratings for satisfaction, enjoyment, and taste of each cigarette puff were taken. Each subject smoked eight, paced cigarette puffs and made hedonic ratings following each puff using an IBM Personal System/2 (Model 70 386) computer program. Each subject made hedonic

ratings using a 9-point Likert scale initially developed by Jarvik et al. (1989; see Appendix for complete scale).

Heart Rate. Heart rate was taken using a J & J Photoplethysmograph (PPG) Module (Model P-401). The PPG provides an estimate of average heart rate by measuring small variations in blood volume by using an infrared emitter and detector in the sensor. The magnitude of the variations indicates relative blood flow immediately below the sensor. The time interval from the peak of one pulse waveform to the peak of the next was converted to a voltage representing 0 to 200 beats per minute. The heart rate signal was a new value after each pulse. The averaging required was done with a J & J Enterprises (1988) software package.

The sensor was placed against the pad of a proximal digit of a finger on the nondominant hand of each subject. The emitter and detector were placed squarely in the center of the pad. The Velcro cuff was then tightened to hold it in place without causing throbbing in the finger. Subjects were instructed to keep the hand motionless in order to obtain accurate signals from the sensor.

General Procedure

All subjects participated in a 30 min initial interview session and then three, 1 hr experimental sessions on three separate days, one experimental condition per day. During the initial interview, each subject was asked questions regarding his or her smoking habits and the frequency with which he or she smoked immediately following eating a snack and tooth brushing. In addition, for each subject, his or her preference for brand of cigarettes, brand of toothpaste, and muffin flavor was obtained. These items were then purchased for the experimental conditions for each subject based on the preferences reported. Each subject received an explanation of all aspects of the study and was asked to sign an informed consent which stated his or her rights as a human

participant. A breath sample was obtained to establish a smoking COa level to verify that the subject was a smoker and to use for later comparisons. Finally, each subject was instructed to abstain from smoking for 1 hr prior to coming to the lab for the first experimental session. Assessment of compliance was based on verbal report by the subject at the time of the session.

All subjects participated in each of the three conditions: High Risk Change, Low Risk Change, and No Change. Subjects were selected based on their reporting that they frequently or always smoked immediately after eating a snack, suggesting that for them this event was associated with increased smoking. Due to this event's ability to influence increased smoking, it was considered to be a High Risk Change in environment. Subjects were also selected based on their reporting that they never, seldom, or sometimes smoked immediately following tooth brushing, suggesting that for them this event was not typically associated with smoking and would not be likely to elicit smoking. Thus, tooth brushing was considered a Low Risk Change in environment. For the High Risk Change condition, subjects were asked to eat a muffin during a 5 min period. In the Low Risk Change condition, subjects were asked to brush their teeth during a 5 min period. In the No Change condition, subjects rested for 5 min.

The time of day for the three sessions was held constant as determined by the first time the subject came into the lab. For example, if the subject were scheduled for 10:00 a.m. for the first session, then he or she was scheduled for 10:00 a.m. for the remaining two sessions. In addition, the scheduled interval between any two sessions was no less than one day (e.g., Monday-Wednesday) and no more than four days (e.g., Wednesday-Monday).

Given that each subject received all three conditions, the effects of the session number (i.e., whether the session was 1, 2, or 3) on the findings were a

concern. As a result, each subject was assigned to one of six counterbalanced condition orders (e.g., Eating-Brushing-Resting, Brushing-Resting-Eating) as a method of ensuring that any differences noted were not due to the order in which the conditions were presented.

At the lab, each subject was instructed to sit in a large chair in a soundproof room. The PPG Module was connected to a proximal digit of a finger of the nondominant hand, and each subject was asked to keep the attached hand as motionless as possible during the experiment. The computer monitor and keyboard for paced smoking and hedonic ratings were placed on a table to the right of each subject. A subject whose right hand was connected to the PPG module was asked to reach gently across to his or her right and make the hedonic ratings with his or her left hand. Each subject was asked to rest for 10 min prior to the smoking of the Pre-Experimental Cigarette (Pre-Cigarette).

A pre-smoking COa measure (pre-COa) was taken prior to smoking the Pre-Cigarette. Each subject smoked eight puffs of the cigarette and made hedonic ratings for each puff using his or her dominant hand. The computer program for paced smoking and hedonic ratings consisted of timed instructions presented to each subject on the computer monitor. Each subject was instructed to light the cigarette without inhaling. After 10 s, the program prompted each subject for 4 s with "Ready" on the monitor, at which time the subject was instructed to bring the cigarette to his or her lips. The monitor then cleared and was followed by the instruction to "Inhale" (display time = 4 s) and then to "Exhale" (display time = 4 s). The computer monitor then displayed a screen with three, 9-point Likert scales, one for each of the three hedonic ratings. A rating of 0 represented the least pleasure and 9 represented the most pleasure on the hedonic scales. Each subject pressed the number corresponding to the degree to which the puff was satisfying, was enjoyable, or tasted good. The program

provided an opportunity to verify the ratings made and to change the ratings if necessary. Each subject had 30 s to make the three hedonic ratings for one puff. During each 30 s interval, heart rate was also measured. Following the last hedonic rating for a puff and the completion of the 30 s interval, instructions for beginning the next puff appeared on the computer monitor. If a subject completed the hedonic ratings in less than 30 s, the computer provided the message to wait for the next puff. The program continued until eight puff and rating trials were completed. Following the hedonic ratings for the eighth puff, the instruction to extinguish the cigarette and to sit quietly until the experimenter provided additional instructions was displayed for 5 s on the computer monitor. A post-smoking COa measure (post-COa) was taken for the Pre-Cigarette. Each subject was then requested to rest quietly for 25 min. During the 25 min period, subjects were able to read magazines. Following the 25 min rest period, each subject was asked to either eat a muffin, brush his or her teeth, or continue resting for 5 min, depending on which of the three conditions he or she was assigned to for that session.

Eating Condition -- High Risk Change. During the 5 min presentation of the manipulation for the eating condition, each subject was asked to eat a muffin. Otis Spunkmeyer muffins (blueberry, apple-cinnamon, banana-nut, or almond poppy seed) were used. Each subject selected his or her preference regarding muffin flavor. The muffin was cut into fourths and each subject was instructed to eat at least one-quarter of the muffin. A glass of water was also provided with the muffin. If the subject finished eating before the end of 5 min, he or she was asked to rest for the remainder of the period.

Tooth Brushing Condition -- Low Risk Change. During the initial interview session, each subject was asked what brand of toothpaste he or she typically used. This brand was purchased by the experimenter for use by the subject for

the tooth brushing condition. During the 5 min presentation of the experimental manipulation for tooth brushing, a small, 1-qt, white bowl, a sterile toothbrush, the subject's brand of toothpaste, a cup of water, and a paper towel were used. To ensure subject comfort regarding sterility during the condition, the package containing the new toothbrush was opened in front of the subject. A half-inch of toothpaste was placed on the toothbrush, the toothbrush wetted, and then handed to the subject. The subject was instructed to brush his or her teeth for 2 min. The experimenter left the room and began timing 2 min. At the end of this time, the experimenter reentered the room and assisted the subject with rinsing his or her teeth. The subject was provided with the 1-qt bowl for expectorating the toothpaste. A glass of water was provided for rinsing his or her teeth. The subject was asked to rest for the remainder of the 5 min period.

Resting Condition -- No Change. Each subject was instructed to continue the 25 min resting period for an additional 5 min.

Immediately following the 5 min presentation of the experimental manipulation, a pre-COa measure for the Post-Experimental Cigarette (Post-Cigarette) was obtained. Each subject then smoked eight puffs of the cigarette and made hedonic ratings. A post-COa for the Post-Cigarette was taken, thus completing the experimental session. At the end of the third experimental session, each subject was given the remainder of the pack of cigarettes and given either 4 points of extra credit towards his or her Introductory Psychology grade or paid $12 as compensation for his or her participation.

Data Analyses

The five dependent measures used in the current study were heart rate, puff satisfaction, puff enjoyment, puff taste, and alveolar carbon monoxide (COa). Heart rate was measured for each of the eight puffs of each cigarette by calculating a mean for the average interbeat intervals for the 30 s period

following each puff. For analyses purposes, heart rate data were filtered by excluding any value greater than one standard deviation above the mean and any value less than one standard deviation below the mean for any 30 s period. Heart rate data were filtered as a means of eliminating extraneous values due to movement artifact. A new mean for each puff was then calculated based on the remaining values. All analyses of heart rate used these filtered data. The mean for the eight puffs served as the dependent variable. Measures of puff satisfaction, enjoyment, and taste were taken following each puff. A single score was computed for each cigarette representing the mean of the eight puffs.

Analyses for Alveolar Carbon Monoxide (COa). Alveolar carbon monoxide (COa) is an indirect estimate of nicotine dose. Given that the way in which individuals smoke (i.e., depth of inhaling, frequency of cigarettes) may influence the amount of nicotine received from a puff, COa boost was analyzed to determine if subjects obtained the same dose of nicotine for each cigarette. This measure was also used to determine the extent to which compensatory smoking was a factor in the reduction of tolerance, thus contributing to a greater drug effect.

Carbon monoxide boost was calculated for each cigarette (post-cigarette COa minus pre-cigarette COa) to determine the extent to which nicotine dose may have been a factor in the Session Data results. These data were analyzed using an Session (3) X Cigarette (2) repeated measures univariate analysis of variance (ANOVA).

As with the data analyses for session, COa boost was calculated for each cigarette (post-cigarette COa minus pre-cigarette COa) to determine the extent to which nicotine dose may have been a factor in the Condition Data results. Data were analyzed using a Condition (3) X Cigarette (2) repeated measures univariate analysis of variance (ANOVA).

Analyses Comparing Session 1, Session 2, and Session 3. Data were analyzed without regard to condition to determine possible differences related to session number (1, 2, or 3). The hedonic ratings were subjected to a Session (3) X Cigarette (2) repeated measures multivariate analysis of variance (MANOVA). If significant, this analysis was followed by a Session X Cigarette ANOVA for each dependent variable. Due to computer memory constraints and in order to more accurately interpret the MANOVA findings, heart rate data were analyzed separately from hedonic ratings using a Session X Cigarette ANOVA. Significant interactions were further analyzed using T-tests for Pre- and Post- Cigarettes.

Analyses Comparing Eating, Tooth Brushing, and Resting Conditions. Data were analyzed without regard to the order in which the conditions were presented. To test the hypotheses that more tolerance would be observed in the condition involving no change in environment as opposed to the conditions involving change in the environment and that more tolerance would be observed in the Low Risk Change condition as opposed to the High Risk Change condition, the hedonic ratings were subjected to a Condition (3) X Cigarette (2) repeated measures multivariate analysis of variance (MANOVA). If significant, this analysis was followed by a Condition X Cigarette ANOVA for each dependent variable. Heart rate data were analyzed separately from hedonic ratings using a Condition X Cigarette ANOVA. Significant interactions were further analyzed using T-tests for Pre- and Post-Cigarettes.

Results

Alveolar Carbon Monoxide (COa)

To determine the extent to which nicotine dose may have been a factor in the results, COa Session Data were analyzed using a Session X Cigarette

ANOVA. No significant differences were found suggesting that Session did not influence these data.

For Condition Data, an analysis identical to that for Session Data was conducted for the carbon monoxide boost for each cigarette (post-cigarette COa minus pre-cigarette COa). Data were analyzed using a Condition X Cigarette ANOVA. No significant differences were found. These results suggest that nicotine dose did not significantly influence the findings when data were analyzed for Condition.

Session Data

Hedonic Ratings. Hedonic ratings were analyzed using a Session (3) X Cigarette (2) MANOVA to assess the extent to which order of the sessions influenced the findings for Condition Data. No significant effects were found.

Heart Rate. Heart rate was analyzed using a Session X Cigarette ANOVA. No significant effects were found. Based on the findings for hedonic ratings and heart rate, session number was not a factor in the study, and Condition Data were analyzed.

Condition Data

Hedonic Ratings. Analyses were conducted to determine the effects of Eating, Tooth Brushing, and Resting conditions for the hedonic rating data. The MANOVA indicated a significant Condition X Cigarette interaction, $F(2,34) = 6.31$, $p < .005$, which allowed for additional Condition X Cigarette ANOVAs to be conducted independently for each of the hedonic ratings.

Satisfaction, Enjoyment, and Taste ratings were each subjected to a Condition X Cigarette ANOVA. Analyses indicated significant interactions for Satisfaction, $F(2,34) = 3.80$, $p < .03$, Enjoyment, $F(2,34) = 7.09$, $p < .003$, and Taste, $F(2,34) = 7.54$, $p < .002$.

For Satisfaction, an ANOVA for each cigarette indicated no differences for the Pre-Cigarette; however, there was a significant effect for Condition for the Post-Cigarette, $F(2,34) = 6.11$, $p < .005$ (see Figure 1). T-tests for the Post-Cigarette data indicated a significant difference between Eating and Brushing Conditions, $t(17) = 2.76$, $p < .01$, and between Eating and Resting Conditions, $t(17) = 2.19$, $p < .04$. There was no significant difference between Brushing and Resting Conditions.

As with Satisfaction, no differences were found for Enjoyment ratings at the Pre-Cigarette, but a significant effect was found for the Post-Cigarette, $F(2,34) = 8.08$, $p < .001$ (see Figure 2). T-tests for condition pairs indicated a significant difference between Eating and Brushing Conditions, $t(17) = 3.26$, $p < .01$; Eating and Resting Conditions, $t(17) = 2.44$, $p < .03$; and Brushing and Resting Conditions, $t(17) = -2.32$, $p < .03$.

As with the previous two hedonic ratings, Taste ratings for Condition at the Pre-Cigarette were not significant; however, a significant effect for Condition was found for the Post-Cigarette, $F(2,34) = 9.73$, $p < .001$ (see Figure 3). T-tests indicated significant differences for all condition pairs: Eating and Brushing, $t(17) = 3.49$, $p < .003$; Eating and Resting, $t(17) = 3.61$, $p < .002$; and Brushing and Resting, $t(17) = -2.33$, $p < .03$. As shown in Table 1, the Post-Cigarette means for each of the three hedonic ratings are representative of the significant differences found.

Insert Table 1 about here

Heart Rate. A Condition x Cigarette analysis of variance was used to determine differences in heart rate among conditions for each cigarette. No significant differences were found.

Study 2

Method

Procedure

Ten smokers were randomly selected from the pool of 18 subjects used in Study 1 (High Risk Eating Group) to be compared with 10 smokers who reported smoking after a snack to be a low risk change condition (Low Risk Eating Group). The ten smokers for the latter group were recruited using the same methods and inclusion criteria as found in the original study with the exception being that they rated the frequency of smoking immediately following eating a snack as 1 (Never), 2 (Seldom), or 3 (Sometimes). All subjects participated in the eating condition paradigm used in Study 1. The data for the two groups were compared.

Analyses

To test the hypothesis that the two eating groups would differ, hedonic ratings were analyzed using a Group (2) X Cigarette (2) mixed design multivariate analysis of variance (MANOVA). This analysis was followed by a Group (2) X Cigarette (2) mixed design univariate analyses of variance (ANOVA) for each dependent variable. Significant interactions were further analyzed using T-tests for Pre- and Post-Cigarettes. As with the Session Data and Condition Data, heart rate was analyzed separately from hedonic ratings using a Group X Cigarette ANOVA. Alveolar carbon monoxide boost was subjected to an ANOVA to assess if nicotine dose was a factor in the results.

Results

Demographic Characteristics

To determine if the two eating groups differed significantly for demographic characteristics, ANOVAs were conducted. Results showed that the two groups did not differ significantly with regard to age, $F(1,18) = 1.66$, $p < .21$; number

of cigarettes smoked per day, $F(1,18) = 2.70$, $p < .12$; length of time smoked, $F(1,18) = .01$, $p < .93$; or initial COa rating (at time of interview), $F(1,18) = .57$, $p < .46$. Appropriately, the two groups differed significantly with regard to the Snack rating (how often they smoked immediately following a snack), $F(1,18) = 97.20$, $p < .001$.

Alveolar Carbon Monoxide (COa)

Carbon monoxide boost was calculated for the Pre-Cigarette and for the Post-Cigarette. Analyses were conducted to determine the extent to which nicotine dose contributed to the differences found. No significant effects were found, suggesting that dose did not influence the obtained results.

Hedonic Ratings

Results of the MANOVA indicated a significant Group X Cigarette interaction, $F(1,18) = 6.57$, $p < .02$. Follow-up ANOVAs were conducted for each dependent measure. Findings showed significant Group X Cigarette interactions for Satisfaction, $F(1,18) = 4.30$, $p < .05$, Enjoyment, $F(1,18) = 6.37$, $p < .02$, and Taste, $F(1, 18) = 8.02$, $p < .01$.

For Satisfaction, no significant effect was found for the Pre-Cigarette, and analysis for the Post-Cigarette approached significance, $F(1,18) = 3.17$, $p < .09$. When means for each cigarette were graphed, it was notable that the Low Risk Eating group found the Post-Cigarette to be less satisfying than the High Risk Eating group (see Figure 4).

Enjoyment ratings indicated no significant effect for the Pre-Cigarette. A significant effect was found, however, for Group and the Post-Cigarette, $F(1,18) = 4.66$, $p < .05$. As with Satisfaction ratings, the Low Risk Eating group reported less enjoyment for the Post-Cigarette than the High Risk Eating group (see Figure 5).

Analysis for Taste ratings indicated no significant results for either the Pre- or Post-Cigarettes, although the difference between Groups at the Post-Cigarette approached significance, $F(1,18) = 4.05$, $p < .06$. The lower hedonic ratings for the Low Risk Eating group found for both Satisfaction and Enjoyment were also found for Taste ratings (see Figure 6). As shown in Table 2, the mean hedonic ratings for the Post-Cigarette indicate the Low Risk Eating Group to have experienced less smoking pleasure than the High Risk Eating Group.

Insert Table 2 about here

Heart Rate

Filtered heart rate means were analyzed using a Group X Cigarette ANOVA. No significant differences were noted for the two groups.

Discussion

The results of this investigation suggest that situations which are more or less associated with smoking differ in the degree to which they affect pleasure ratings of a cigarette immediately following the situation. The results do not, however, suggest that this difference is indicative of tolerance reduction as was hypothesized. Hypotheses predicted that the High Risk Change (Eating) condition would exhibit a greater increase in hedonic ratings as opposed to the Low Risk Change (Tooth Brushing) condition, and that both of these conditions would exhibit a greater increase in ratings than the No Change (Resting) condition. Only the Eating condition was found to increase hedonic ratings at the Post-Cigarette, whereas, the Brushing condition resulted in a decrease in mean hedonic ratings at the Post-Cigarette. This finding is not consistent with what would be expected based on previous studies suggesting that a situational

change reduces tolerance (Baker & Tiffany, 1985; Epstein et al., 1989). This finding is also not consistent with the increase in mean hedonic ratings that would be predicted by the opponent-process model (Solomon & Corbit, 1973).

A finding that was unexpected was that resting resulted in more pleasure for the Post-Cigarette than tooth brushing. According to the opponent-process model of tolerance, the predicted outcome for the Resting condition at the Post-Cigarette would have been a continuation of the decrease in hedonic ratings from the Pre-Cigarette, and the expected outcome for the Brushing condition would have been an increase in hedonic ratings. That these results were not found suggests that tolerance most likely did not influence the findings and that the Eating condition results, which appear to be consistent with tolerance, should not be assumed to represent tolerance. This statement is also supported by the fact that no differences were found for nicotine dose across conditions (as measured by COa boost), indicating that smokers did not inhale greater amounts of nicotine in order to reduce tolerance.

Given that the opponent-process model does not explain the findings, an alternative explanation is that the extent to which a cigarette following a snack or following tooth brushing is pleasurable is associated with the person's smoking history (i.e., the likelihood that the person engages in the behavior). It would appear that when a situational cue is consistently paired with smoking, pleasure ratings increase, and if the cue is not paired with smoking, pleasure ratings decrease. As a result, if a smoker engages in a situation traditionally paired with smoking, the activity will serve to make the following cigarette more reinforcing.

Furthermore, a factor that appears to have contributed to the contradiction of the hypothesis for the Resting condition is the self-report made by the subjects. Subjects exhibited findings that were consistent with their initially self-reported

frequency of smoking following a snack and tooth brushing. For example, if subjects reported that eating was an activity that frequently or always resulted in smoking, the Eating condition resulted in an increase in hedonic ratings. Tooth brushing, an activity that was reported to never, seldom, or sometimes elicit smoking, resulted in the lowest hedonic ratings. It is interesting, however, that the Resting condition exhibited hedonic ratings that were greater than the Brushing condition but less than the Eating condition.

An initial concern for Study 1 was that if the Eating condition resulted in a greater increase in hedonic ratings for the Post-Cigarette than did the Brushing condition, then metabolic factors associated with eating might be present. Study 2 compared eating as both High Risk Change and Low Risk Change groups. The findings did not appear to show metabolism to be a factor in the results, as might have been indicated had no differences between groups been found. Instead, the results for Study 2 were consistent with the self-report by the subjects regarding smoking frequency following eating. Participants who reported that they typically smoked following a snack exhibited a greater increase in hedonic ratings (more pleasure) compared with the subjects who did not report eating to be a high risk situational cue for smoking. The findings of Studies 1 and 2 suggest a possible correlation between the frequency with which a person smokes following a particular activity and how pleasurable smoking is reported to be.

A second concern for Study 1 was that the session number (1, 2, or 3) may have affected the results and the interpretability of the Condition data. Findings for analyses of the Session data yielded no significant results thus providing greater confidence in the results for condition differences, specifically those differences noted for the Post-Cigarette.

The results of Studies 1 and 2 argue for a more refined view of the subjectivity of self-report by smokers. These studies suggest that there may be an association between the frequency with which situational cues are paired with smoking and the degree to which a cigarette is pleasurable following the activity. This explanation would account for previous findings suggesting that some situations are more associated with smoking than others (Epstein & Collins, 1977) and that smokers report the cigarette after a meal to be the most preferable (F. L. Collins et al., 1991; Jarvik et al., 1989). It would appear that smokers identify situations which are likely to elicit greater pleasure from a cigarette. Although tolerance reduction does not appear to have been the catalyst for the increase in hedonic ratings following eating, a stronger argument for an improved degree of reliability for self-report among smokers has been identified.

There are several clinical implications for this investigation. Ideally, it would be beneficial for smokers to not engage in the High Risk Change behaviors at all. However, this alternative is not realistic for all High Risk Change behaviors (e.g., smokers must eat). As a result, in order to help a smoker to quit smoking, he or she needs to be instructed to not smoke following those situations which most commonly elicit smoking. The smoker may need to engage in self-monitoring of situations in order to identify those situations which elicit smoking. Many smoking cessation programs utilize these techniques; however, the findings of the current study would suggest that an alternative method would be to instruct the smokers to engage more in behaviors which do not typically elicit smoking (e.g., using a breath spray when experiencing the urge to smoke).

More research is needed, however, before instructing smokers to engage in situations that do not typically elicit smoking. The findings of the current study

suggest that it is possible that certain situations may elicit smoking pleasure due to a learning history resulting from the repeated pairing of a situation with smoking. As a result, it may also be possible for a smoker to learn to obtain pleasure from currently "low risk" situations by repeatedly pairing them with smoking: Low risk situations might become high risk situations due to learning.

Additionally, it is important to note the specific strengths and weaknesses of the current study. Heart rate measures for subjects did not yield significant results. One methodological implication for this result was identified in the latter part of the study. Subjects were asked to make their hedonic ratings during a 30 s period. In addition, heart rate was recorded during this 30 s period. As a result, movement artifact may have contributed to the lack of heart rate results. A more appropriate way to measure heart rate might have been to have the subject make hedonic ratings for 15 s and then to rest for a 30 s heart rate period. This methodological change may have resulted in a better representation of heart rate measurement during the procedure.

Also, the PPG module was used to measure heart rate. While the module was an effective recording device, at times it was very sensitive to smokers' changes in skin temperature. Psychophysiological equipment incorporating electrodes may result in a more accurate assessment of heart rate effects to smoking.

A strength of the study was its attempt to identify a more subjective measure of tolerance. Even though results did not suggest tolerance to be a factor in smoking pleasure, significant findings indicate that other important situational factors exist that are associated with smoking that need to be identified. Future research might focus on the development of better definition of these factors. One might choose to expand the paradigm in this study to include a wide range of situations that vary in the extent to which they are

reported to elicit smoking. This expansion of situations used might assist in the identification of multiple situational cues that are commonly associated with smoking.

Also, more research is needed to determine how a person's smoking history influences the hedonics associated with drug use. Although ethical considerations would need to be addressed, it might be beneficial to determine if a previously "low risk" situational cue (e.g., tooth brushing) could become a "high risk" situational cue if repeatedly paired with smoking. Findings from studies such as these would help to provide a better understanding of the factors which influence the maintenance of smoking, to personalize smoking cessation programs, and to provide alternative means of instructing smokers in their cessation efforts.

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Appendix

Hedonic Ratings Scale

Rate how satisfying and enjoyable the cigarette was and how good it tasted using the following scales. Please select 1 number for each scale:

0 1 2 3 4 5 6 7 8 9

+------+-------+-------+------+-------+-------+------+-------+------+

Not at all satisfying Extremely satisfying

0 1 2 3 4 5 6 7 8 9

+------+-------+-------+------+-------+-------+------+-------+------+

Not at all enjoyable Extremely enjoyable

0 1 2 3 4 5 6 7 8 9

+------+-------+-------+------+-------+-------+------+-------+------+

Did not taste good at all Tasted extremely good

Table 1

Mean Hedonic Ratings for Each Condition at Pre- and Post-Cigarettes

		Experimental Cigarette	
Hedonic Rating	Condition	Pre	Post
Satisfaction			
	Eating	6.83 (1.48)	7.42 (1.41)
	Brushing	6.62 (1.56)	5.85 (2.16)
	Resting	6.89 (1.72)	6.73 (1.18)
Enjoyment			
	Eating	6.63 (1.50)	7.34 (1.43)
	Brushing	6.60 (1.55)	5.42 (2.25)
	Resting	6.85 (1.65)	6.60 (1.25)
Taste			
	Eating	6.25 (1.28)	7.00 (1.49)
	Brushing	6.04 (1.63)	4.83 (2.15)
	Resting	6.25 (1.57)	6.05 (1.13)

n = 18 for each condition.

Standard deviations in parentheses.

Table 2

Mean Hedonic Ratings for High and Low Risk Eating Groups at Pre- and Post-Cigarettes

		Experimental Cigarette	
Hedonic Rating	Group	Pre	Post
Satisfaction			
	High Risk	6.56 (1.33)	7.56 (1.08)
	Low Risk	6.76 (.96)	6.70 (1.08)
Enjoyment			
	High Risk	6.31 (1.33)	7.45 (1.07)
	Low Risk	6.44 (.84)	6.39 (1.13)
Taste			
	High Risk	5.99 (1.26)	7.04 (1.35)
	Low Risk	6.28 (.73)	5.91 (1.14)

n = 10 for each group.

Standard deviations in parentheses.

Figure Captions

Figure 1. Mean Satisfaction ratings for pre- and post-experimental cigarettes by condition.

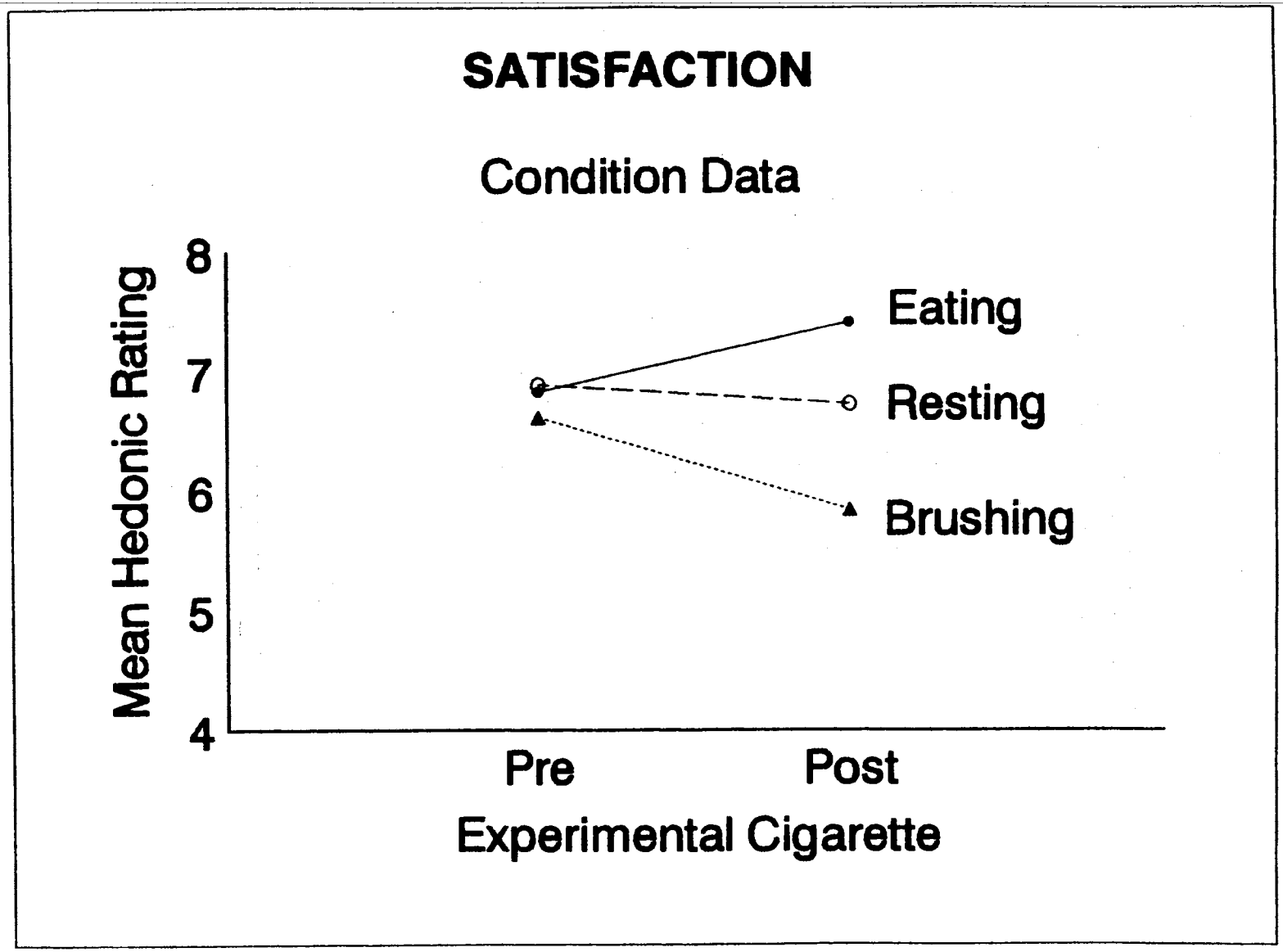
Figure 2. Mean Enjoyment ratings for pre- and post-experimental cigarettes by condition.

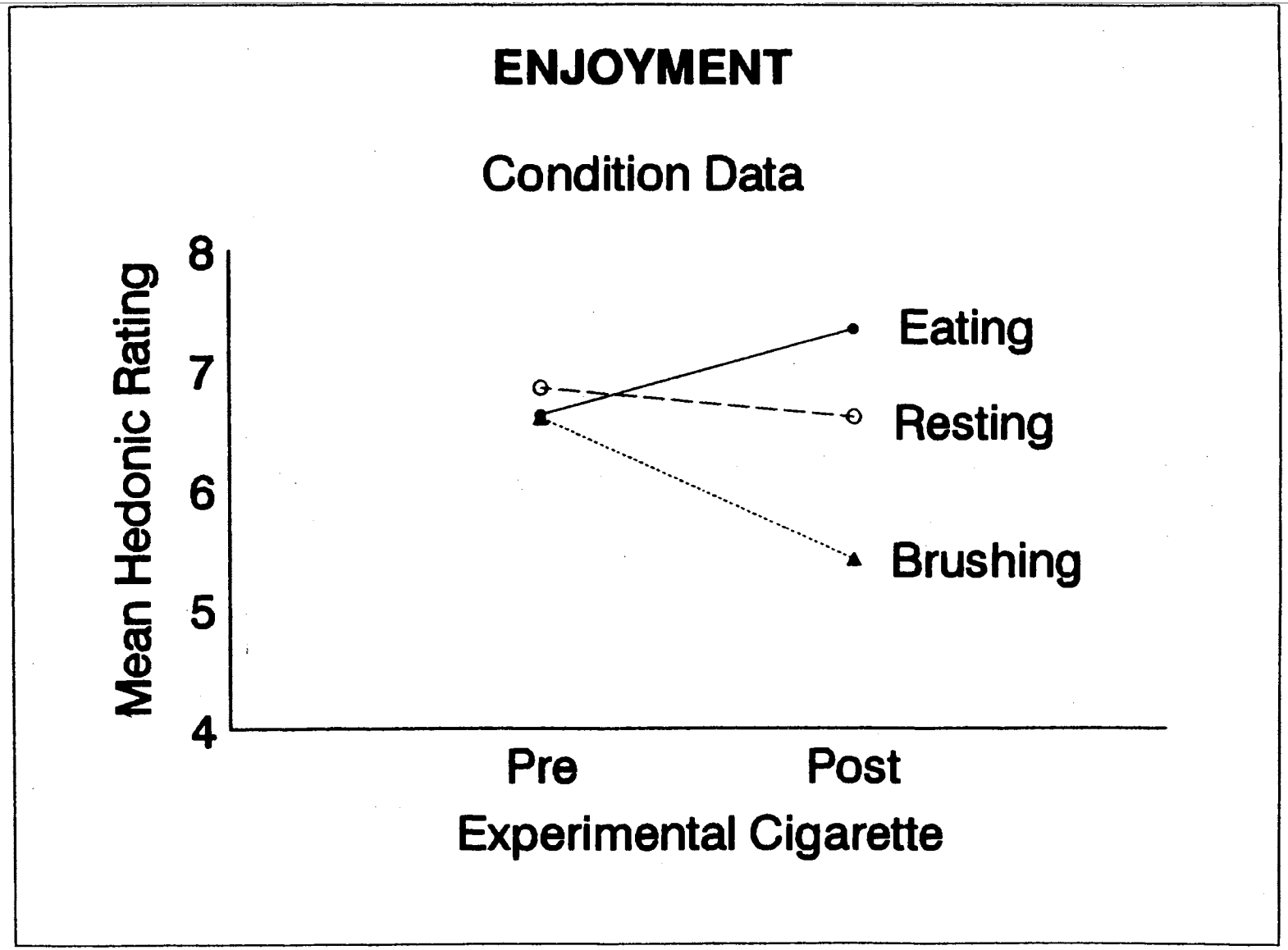
Figure 3. Mean Taste ratings for pre- and post-experimental cigarettes by condition.

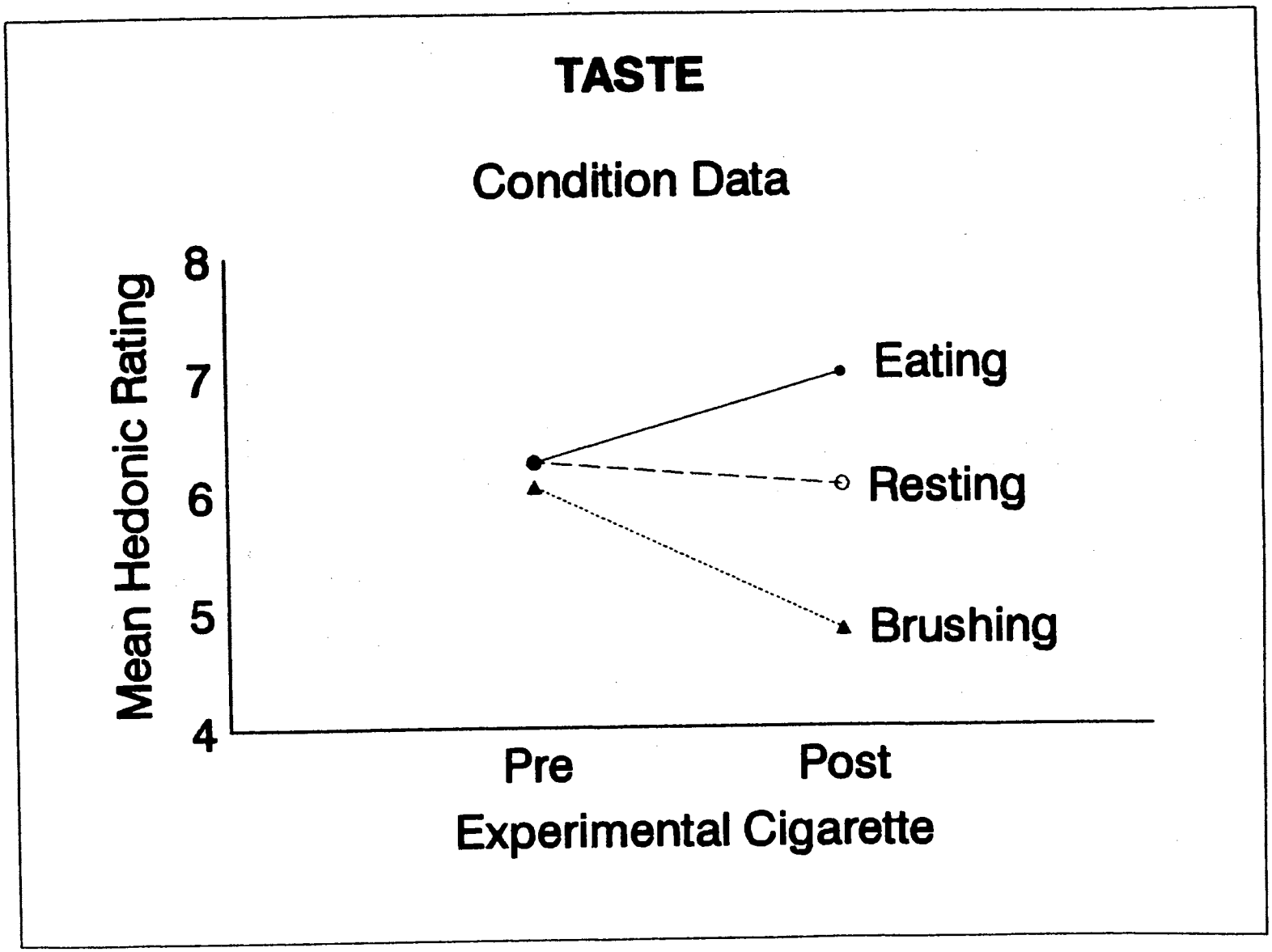
Figure 4. Mean Satisfaction ratings for pre- and post-experimental cigarettes by group.

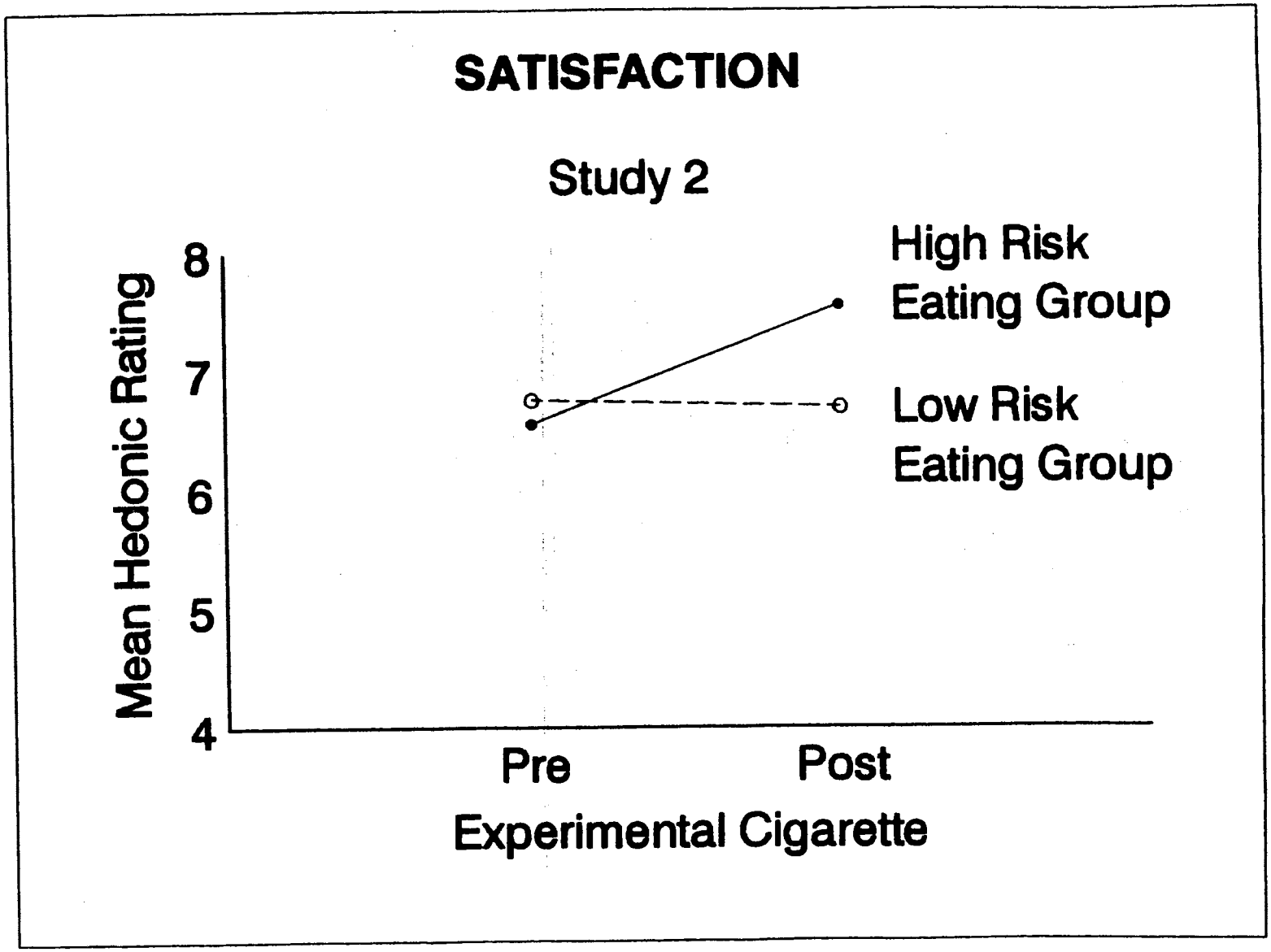
Figure 5. Mean Enjoyment ratings for pre- and post-experimental cigarettes by group.

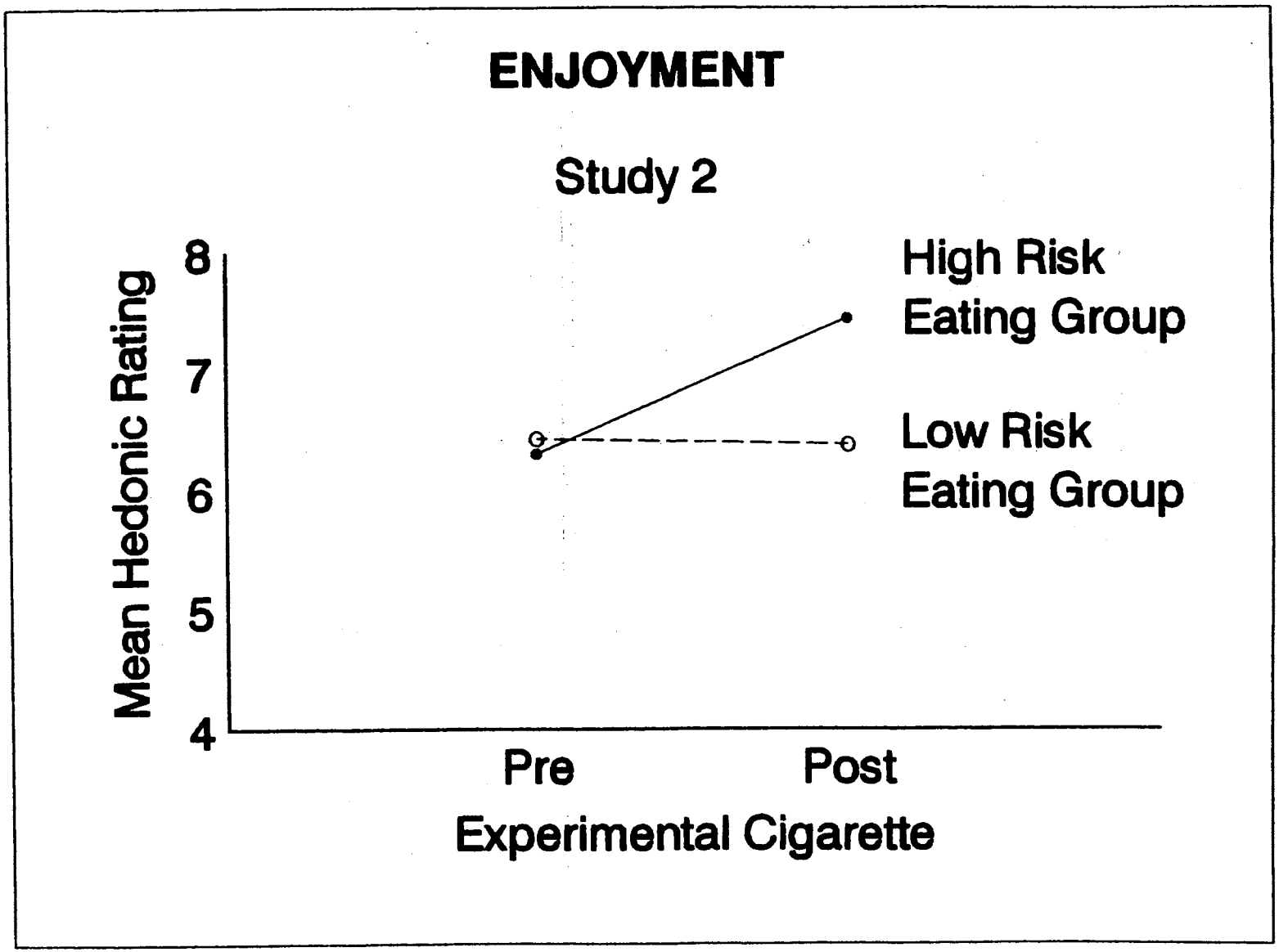
Figure 6. Mean Taste ratings for pre- and post-experimental cigarettes by group.

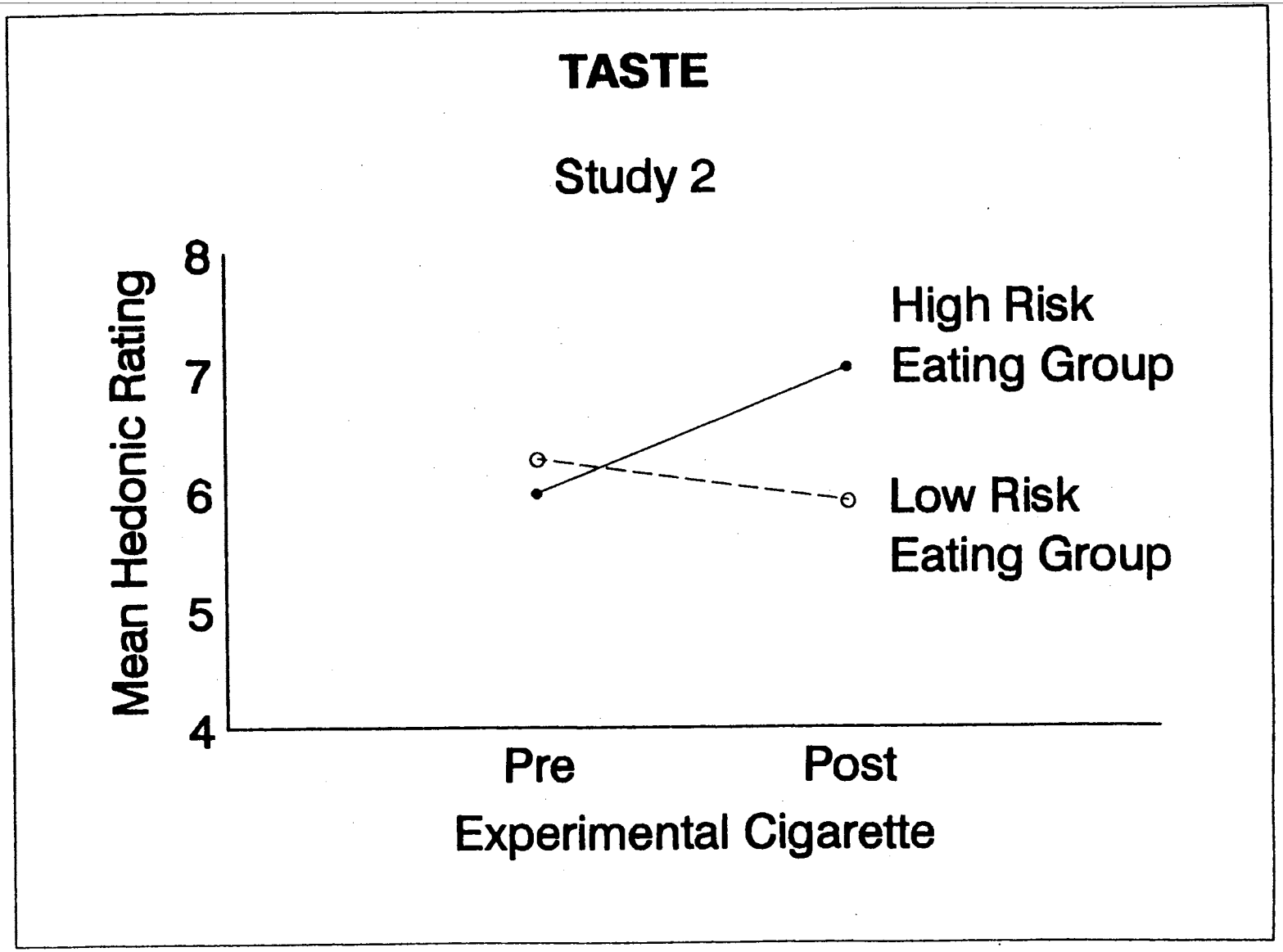

SATISFACTION
Condition Data
Mean Hedonic Rating
8
7
6
5
4
Eating
Resting
Brushing
Pre
Post
Experimental Cigarette


ENJOYMENT
Condition Data
Mean Hedonic Rating
8
7
6
5
4
Eating
Resting
Brushing
Pre
Post
Experimental Cigarette


TASTE
Condition Data
Mean Hedonic Rating
8
7
6
5
4
Eating
Resting
Brushing
Pre
Post
Experimental Cigarette


SATISFACTION
Study 2
High Risk
Eating Group
Low Risk
Eating Group
Mean Hedonic Rating
8
7
6
5
4
Pre
Post
Experimental Cigarette


ENJOYMENT
Study 2
Mean Hedonic Rating
8
7
6
5
4
High Risk Eating Group
Low Risk Eating Group
Pre
Post
Experimental Cigarette


TASTE
Study 2
Mean Hedonic Rating
8
7
6
5
4
High Risk
Eating Group
Low Risk
Eating Group
Pre
Post
Experimental Cigarette

VITA

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Doctor of Philosophy

Thesis: THE EFFECTS OF SITUATIONAL CUES ON THE CHANGE OF NICOTINE TOLERANCE

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OKLAHOMA STATE UNIVERSITY
INSTITUTIONAL REVIEW BOARD
FOR HUMAN SUBJECTS RESEARCH

Proposal Title: FACTORS THAT INFLUENCE NICOTINE TOLERANCE

Principal Investigator: FRANK COLLINS / STEPHANIE CORZATT

Date: 8-7-92 IRB # AS-93-006

This application has been reviewed by the IRB and

Processed as: Exempt [ ] Expedite [XX] Full Board Review [ ]

Renewal or Continuation [ ]

Approval Status Recommended by Reviewer(s):

Approved [XX] Deferred for Revision [ ]

Approved with Provision [ ] Disapproved [ ]

Approval status subject to review by full Institutional Review Board at next meeting, 2nd and 4th Thursday of each month.

Comments, Modifications/Conditions for Approval or Reason for Deferral or Disapproval:

Signature: Marcia L. Tilley Date: 9-2-92

Chair of Institutional Review Board