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Nicotine Self-Regultion in Heavy and Light Smokers

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NICOTINE SELF-REGULATION IN HEAVY AND LIGHT SMOKERS

BY

GWENDOLYN A. UNDERHILL

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE

REQUIREMENTS FOR THE DEGREE OF

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Abstract

The purpose of the present study was to provide a further test of the nicotine addiction theory. It was designed to determine the extent to which smokers regulate plasma nicotine levels and smoking behavior in response to varying nicotine yields. More specifically, it was designed to assess differences between heavy and light smokers in nicotine regulation. Age differences were also explored. The effects of varying nicotine yield (high and low nicotine dose) was measured in 19 male smokers (10 heavy smokers and 9 light smokers) on the following dependent variables: smoking behavior (puff frequency, intensity, duration and volume), ANS physiological measures (heart rate and peripheral skin temperature), subjective states (nicotine craving and withdrawal), plasma nicotine and carboxyhemoglobin levels. Urinary pH was also measured. Subjects attended two one-hour smoking sessions in which an opportunity to smoke a cigarette was provided every 10 minutes. Statistical analyses on all dependent variables were performed using an Analysis of Variance with Repeated Measures Design. Results showed no evidence for nicotine regulation at the pharmacological level, however, there was strong support for behavioral regulation. Heavy and light smokers responded in a similar fashion on most all of the dependent variables. There were some age differences in smoking style characterized by a greater puff frequency for older smokers. It was concluded that nicotine regulation at the plasma

nicotine level may be a long-term process which is not amenable to short-term study.

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Nicotine Self-Regulation in Heavy and Light Smokers

Perhaps the most widely occurring, frequently engaged in, publicly permissible, physically harmful behavior in the history of mankind is cigarette smoking. If it were not for the growing awareness of the health hazards of cigarette smoking, the mysteriously powerful nature of this behavior might never be questioned. Since the alarm sounded by the Surgeon General's Report (1964) alerting the public to the significant health risks associated with smoking, a host of various intervention strategies have been developed. However, in an exhaustive review of 89 treatment studies, Hunt and Besspalac (1974) conclude that most treatment programs produce less than a 50% abstinence rate at the end of treatment. This abstinence rate is reduced to 20% to 30% at one year to 18 month follow-ups. These findings lead to one conclusion: we do not know enough about why people smoke in order to help them stop smoking.

Cigarette smoking is a multidimensional behavior, involving psychological, behavioral and physiological levels of functioning. Consequently, any theory which addresses one or all of these components will provide further understanding of smoking behavior. However, the following question presents itself: which theoretical viewpoint is the most promising, given our present state of knowledge regarding the maintenance and cessation of smoking behavior? Since the primary objective of understanding smoking behavior is to develop effective treatment strategies, this question can

be answered, in part, by the following evidence. The majority of the present treatment techniques, which as stated, provide disappointing results, focus on the psychological and behavioral aspects of smoking behavior, largely neglecting the physiological components of smoking and their implications for treatment. Consequently, it appears to be a worthwhile endeavor to broaden our understanding of the physiological factors which underlie the maintenance of smoking behavior in order to develop treatment approaches complimented by this understanding.

The most promising and widely researched physiological model of smoking behavior to date is the nicotine addiction theory, developed by Schachter and his associates (1978). This paper will review the literature concerning the nicotine addiction theory and finally present a study designed to further delineate its boundary conditions. A brief excursion into the major alternative theories of smoking behavior will open this presentation.

Maintenance of Smoking Behavior: Theoretical Views

Tomkins' Smoking Topology. Tomkins (1966) developed a psychological model of smoking behavior which proposes that smoking is maintained by its regulation of affective states. He distinguished four types of smoking behavior: (1) habitual smoking, in which the individual would miss a cigarette if one was not available, though it may no longer provide a positive experience; (2) positive affect smoking, in which smoking is a stimulant to experience the positive affect of

excitement and a relaxant to experience the positive affect of enjoyment; (3) negative affect smoking or sedative smoking, in which the individual smokes to reduce feelings of distress, fear or shame. This type of smoker smokes only when troubled; (4) addictive smoking, in which the individual smokes both to produce positive affect and to reduce negative affect. The addicted smoker is always aware when he is not smoking and suffers whenever he is without a cigarette. He believes only smoking will reduce his suffering and confirms his expectations.

The validity of Tomkins' smoking topology was assessed by Leventhal and Avis (1976) by a factor analysis of responses to a "Reasons for Smoking" questionnaire. Using four separate samples of subjects and varying the composition of items for each sample, highly similar factor structures appeared. The factor composition was as follows: (a) Fiddle; (b) Habit; (c) Anxiety (smoking to reduce tension); (d) Addiction; (e) Stimulation; (f) Social Reward; (g) Pleasure-Taste. Further support for the validity of these factors was derived by agreement between subjects' self-perception and actual behavior. Subjects who scored high on the Pleasure-Taste factor smoked less cigarettes adulterated with vinegar than low Pleasure-Taste subjects. Habit smokers reduced smoking rates when subject to self-monitoring. Addictive smokers reported greater distress following 18 hours of nicotine deprivation, however, they did not increase their smoking rates following deprivation as predicted.

In another series of validity studies, Ikard and Tomkins (1973) found negative affect smokers smoked more in a negative affect situation than did positive affect smokers. Among positive affect, negative affect, preaddictive and addictive smokers, the greatest degree of discomfort following a three hour deprivation period was experienced by the addictive smokers.

Support for Tomkins' topology is conflicting. Adesso and Glad (1978) found no relationship between Tomkins' smoking types and actual smoking behavior in various experimental conditions. Nor do Tomkins' types of smokers respond in a predicted fashion to tailored treatment procedures. Kreidler, Shahar and Kreidler (1976) hypothesized that desensitization therapy would be more effective for negative affect smokers and that saturation therapy would be more effective for positive affect smokers. However, their results did not support this. Best and Hakstian (1978) argue for a more varied and differentiated model of smoking behavior than offered by Tomkins' affective smoking types. In a factor analysis of ratings to common cigarette smoking situations, they found a wide variety of specific environmental, cognitive, affective, pharmacological and sensorimotor events serve as discriminative cues for smoking.

In general, Tomkins' model of affective smoking types appears quite limited, particularly from a treatment point of view. Affective states are complex, unique, multidimensional and unstable. It appears artificial to hypothesize

a simple and direct relationship between a particular affective state and incidence of smoking that is consistency and unvarying within individual smokers.

Behavioral Approaches. Learning theory approaches to multiple problem behaviors flourished in the early 1970s, with smoking behavior being no exception. From a learning theory conceptualization, smoking is viewed as an overlearned behavior, initially acquired through social reinforcement (i.e., peer pressure). After repeated smoking trials it becomes intrinsically rewarding, conditioned to a wide variety of stimulus situations which, in turn, become discriminative stimuli, setting the occasion for smoking to occur. Maintained under a partial reinforcement schedule, smoking becomes highly resistant to extinction.

A wide variety of behavioral treatment techniques have been applied to smoking behavior including systematic desensitization (Wolpe, 1969), aversive conditioning, using stimuli such as electric shock, warm smoky air, and rapid smoking (Lichtenstein and Rodrigues, 1977; Lichtenstein, Harris, Birchler, Wahl and Schmahl, 1973), covert sensitization (Cautela, 1970), stimulus control procedures (Levinson, Shapiro, Schwartz and Tursky, 1971), behavioral contracting (O'Banion, Armstrong and Ellis, 1980), habit reversal and self-reinforcement techniques (Katz, Heiman and Gordon, 1977). These behavioral interventions have provided initially impressive, though short-term results. However, multi-component social-learning programs, which combine aversive procedures

with self-control techniques have resulted in greater success (Chapman, Smith & Layden, 1971). A behavioral conceptualization of smoking behavior is useful for understanding and treating the habitual aspects of smoking, however, it fails to take into account the physiologically rewarding nature of nicotine.

Opponent-Process Theory. The opponent-process theory, developed by Solomon and Corbit (1973), is a theory of acquired motivation which has been applied to addictive processes, including nicotine addiction. This model argues that many hedonic and emotional states are accompanied by opposing central nervous system mechanisms which reduce the intensity of the hedonic state, maintaining hedonic neutrality. Thus, any departures from affective equilibrium, both positive and negative, arouse opponent-process mechanisms which minimize affect intensity. Applied to cigarette smoking, this model maintains that the initially pleasurable state (A process) of smoking is followed by a dysphoric state (B process) of withdrawal. With repeated usage, the opponent withdrawal state becomes stronger and increasing dosages of nicotine are required to offset the negative effects of withdrawal. Thus, cigarette smoking is both positively reinforced in producing the pleasurable A state and negatively reinforced in avoiding the unpleasant B state. Hence, the addictive cycle is set in motion. Both A and B states are subject to classical conditioning, further strengthening the addictive process.

Though the opponent-process model is theoretically appealing, proposed treatment strategies derived from the model are complicated by the dual processes involved. One suggested treatment procedure is that of gradually fading out the intensity and frequency of the A process (i.e., cut down on smoking) in order to reduce the B process of withdrawal. However, to do this, the length of anticipated withdrawal must be known in advance in order to estimate the length and rate of the fade out period. Another technique suggested by this model is the use of antagonistic drugs. Again, the conceptualization of a biphasic process calls for a dual approach. Two drugs are recommended; one for eliminating the withdrawal B state, the other for reducing the residual reinforcing state produced by the summation of the A and B processes. This would necessitate a short-acting drug for the A state and a longer acting drug for the B state. The difficulty in applying the opponent-process theory to the treatment of cigarette smoking is obvious. Perhaps this is why there has been no research to date which utilizes this model for intervention strategies. However, the opponent-process model brings to light the very real complexity and difficulty in treating cigarette smoking.

Multidimensional Models. Since cigarette smoking is a complex behavior, involving several distinct and interacting levels of functioning, a multidimensional model of smoking is most appropriate. Glad, Tyre & Adesso (1976) propose a multidimensional model of smoking which encompasses three

main components: (1) a cognitive component, which includes attitudes and beliefs related to the effects of smoking; (2) a behavioral component, which focuses on the act of smoking as it is acquired through respondent, operant and modeling forms of learning; (3) an affective component, which is derived from the perception of feelings associated with smoking based on physiological stimulation and sensory pleasure. This model proposes a treatment approach in which separate techniques for each of the components are applied. These techniques include hypnotic suggestion, behavioral techniques and procedures for changing attitudes (i.e., strengthening cognitive dissonance). Though this model appreciates the multicomponents of smoking, it does little to integrate the various proposed components into a functional, interactive system. Such a system, rather than treating each component in isolation, would provide an understanding of the dynamic interdependency of forces that determine smoking behavior. A systematic, multidimensional model of smoking would also provide greater accuracy and prediction for individualized treatment approaches.

Russell (1974) proposes a tentative multidimensional model of smoking behavior which offers a promising foundation for an integrative theory. This model classifies smokers according to the predominant pattern of reinforcement for smoking. The classification scheme was derived from responses by 175 normal smokers to a 34-item self-completion

questionnaire of various motives for smoking. Factor analysis of the data revealed six oblique factors, representing six types of smoking: psychosocial, indulgent, sensorimotor, stimulation, addictive and automatic smoking. The most impressive finding was a major "pharmacological addiction" dimension which completely separated stimulation, automatic, and addictive factors from the remaining factors. These three factors were highly correlated with daily cigarette consumption and differentiated a sample of "normal" smokers from a criterion sample of addicted heavy smokers attending a smoking withdrawal clinic. There was a small negative correlation ($r = -.23$) between age and psychosocial smoking, with younger smokers tending to score higher on this factor. The authors suggest a progression from psychosocial to indulgent and/or sensorimotor smoking to addictive smoking, maintained primarily by pharmacological rewards (i.e., avoidance of withdrawal). Since, aside from psychosocial smoking, there was no strong association with age, the authors conclude that the progression to addictive smoking is not inevitable and occurs in only a small proportion of smokers. Furthermore, if there is a progression to addictive smoking, it occurs rather quickly in the individual's smoking history. Recently, Bosse, Garvey and Glynn (1980) investigated the hypothesis that smokers gravitate with age towards greater psychological and pharmacological addiction to cigarettes. Psychological addiction was measured in

381 smokers by responses to the Horn-Waingrow Smoker Survey. A pharmacological addiction index was derived by multiplying milligrams of tar and nicotine in the subjects' usual brand of cigarettes times the number of cigarettes smoked per day times the fraction of each cigarette smoked. Five age groups were studied: less than 39, 40 - 44, 45 - 49, 50 - 54, and 55+ years of age. The authors found a significant, though weak correlation ($r = .20$) between age and psychological addiction. Older subjects tended to score higher on this factor. However, no correlation was found between psychological addiction and pharmacological addiction. Although older smokers report stronger motives for smoking, they do not differ from younger smokers in amounts of tar and nicotine consumed. The authors proposed that two distinct concepts of psychological and pharmacological addiction exist. More rigorous research is needed in this area to further understand the pharmacological aspects of nicotine addiction, using physiological measures, and its interaction with nonpharmacological dimensions of smoking.

Nicotine Addiction Theory. The most widely known and perhaps most controversial model of smoking behavior is the nicotine addiction theory, a physiological model developed by Schachter and his associates (1978). This model makes two basic assumptions: (1) nicotine is the primary reinforcing element of tobacco smoke and (2) nicotine is an addictive substance. As is characteristic of other addictive substances,

the model predicts smokers will regulate nicotine intake in order to maintain a nicotine blood level which will prevent the aversive effects of withdrawal. Some internal mechanism reacts to low nicotine blood levels by causing the smoker to increase nicotine intake, while the same mechanism causes the smoker to decrease nicotine intake when nicotine blood levels are high.

Schachter's nicotine addiction theory evolved out of a series of studies which initially addressed the issue of the psychological utility afforded by cigarette smoking. One often cited reason given by smokers for their habit is that smoking calms their nerves or reduces anxiety. Consequently, Schachter, Silverstein, Herman and Liebling (1977) first set out to determine if smoking increases with stress. In manipulating stress, by varying intensity of electric shock, it was found that subjects did, indeed, smoke more in the high than in the low stress condition. The next question to be answered was whether smoking reduced anxiety as often purported by smokers. Silverstein (1976) approached this question by comparing smoking behavior in nonsmokers, smokers who were allowed to smoke either high or low nicotine cigarettes and deprived smokers under varying levels of shock-induced anxiety. It was found that smokers who smoked high nicotine cigarettes endured more shocks (i.e., evidenced less anxiety) than when they smoked low nicotine cigarettes. This is consistent with previous findings of higher pain

endurance thresholds for smokers while smoking, than while nicotine deprived (Nesbitt, 1973). However, smokers who smoked high nicotine cigarettes showed the same degree of tolerance for shocks as did nonsmokers. Therefore, it was concluded that smoking does not reduce anxiety, but rather not smoking increases anxiety. That is, deprived smokers are more anxious than nonsmokers. It was proposed that the anxiety-reducing effects of nicotine are due to the alleviation of the anxiety produced by withdrawal symptoms.

Since it was found that smoking increases with stress, (Schachter et al, 1977) but that it does not reduce stress (Silverstein, 1976), attention was focused on the biochemical fate of nicotine as effected by stress. Previous pharmacological findings indicated that the rate at which nicotine is excreted unchanged in the urine is effected by the urine pH, such that the more acidic the urine, the faster the nicotine excretion rate (Beckett, Rowland & Triggs, 1965; Haag & Larson, 1942). Schachter, Kozlowski and Silverstein (1977) took these findings one step further to determine if smoking rate varies with urine acidity. By manipulating urine pH, they found that smokers do, indeed, smoke more when the urine is acidified than when it is uncontrolled or alkalized.

To determine if urine pH was the biochemical mediator between stress and smoking, Schachter et al.(1977) examined the effects of stress on both cigarette smoking and urine pH

and found that commonly stressful events such as Ph.D. orals, party-going etc. do increase smoking rate, as well as increasing urine acidification. In order to determine if urine pH was the necessary and sufficient condition for the stress-smoking relationship, Schachter, Silverstein and Perlick (1977) independently manipulated stress and urine pH. They hypothesized that if urine pH is the necessary condition, then subjects should smoke more in a high than in a low stress condition or when urine pH is uncontrolled. However, subjects should not alter their smoking behavior in the two stress conditions if urine pH is experimentally stabilized. If urine pH is not the necessary condition for mediating the stress-smoking relationship, then manipulated urine pH should have no effect on smoking under the two conditions. The first hypothesis was confirmed and it was concluded that stress affects smoking only in that it changes urine pH. The latter directly influences the rate at which nicotine is excreted and, therefore, the nicotine intake of the smoker. The psychological reason for smoking under stress to reduce anxiety was replaced with the physiological explanation of smoking to replenish depleted nicotine supplies induced by stress. This implies that smokers regulate nicotine blood levels in order to avoid the aversive effects of withdrawal, rather than to regulate internal affective states. Evidence supporting the nicotine regulation model will be reviewed later in this paper.

One of the major implications of the nicotine addiction model for treatment is the danger this model detects in the current trend towards low-tar, low-nicotine cigarettes. If smokers do, indeed, regulate nicotine intake to maintain a characteristic nicotine blood level, then it is expected that they will smoke more low-tar, low-nicotine cigarettes to maintain their usual nicotine plasma levels. In doing so, they will end up taking in greater amounts of the physically hazardous elements of cigarette smoke (i.e., carbon monoxide) than if they had continued to smoke their usual brand of cigarettes. The nicotine addiction model suggests the development of a low-tar, high-nicotine cigarette as a means of reducing the hazards of cigarette smoking.

As previously stated, the nicotine addiction theory rests on two major assumptions: (1) nicotine is the primary reinforcing element of tobacco smoke and (2) nicotine is an addictive substance. These assumptions will be examined in a brief review of the pharmacological aspects of nicotine.

Pharmacological Aspects of Nicotine

Nicotine: Stimulant or Depressant? The primary pharmacological effect of nicotine is that of autonomic arousal resulting in increased heart rate (Armitage, 1973; Frankenhaeuser, Myrsten, Wazak, Neri & Post, 1968; Myrsten, Post Frankenhaeuser & Johansson, 1972; Gilbert & Hagan, 1980), blood pressure (Frankenhaeuser et al., 1968; Myrsten et al., 1972) and adrenalin excretion (Frankenhaeuser et al., 1968; Ek, Froberg, Kagan, Karlsson, Levi & Palmblad, 1977) and

decreases in skin temperature (Frakenhaeuser et al., 1968; Myrsten et al., 1973; Wood, 1960) and in skin conductance magnitude (Gilbert & Hagan, 1980). Central nervous system activation is evidenced in EEG arousal in man (Knott & Venables, 1977) and in cats (Armitage, Hall & Morrison, 1968) and is accompanied by increased speed of habituation of the EEG alpha desynchronization orienting response (Freidman, Horvath & Mears, 1974). Nicotine is also reported to increase mental efficiency (Myrsten et al., 1972; Mangan & Golding, 1978).

One would expect that the physiological activating effects of nicotine would result in correspondingly heightened emotional arousal. This does not appear to be true. Smokers report that smoking has a relaxing and calming effect. In exploring this paradox, Nesbitt (1973) found smokers were less "emotional" (i.e., showed greater tolerance to pain) when smoking than when not smoking and with high-nicotine cigarettes more so than with low-nicotine cigarettes. The decrease in emotional response was correlated with a simultaneous increase in physiological arousal, measured by pulse rate. This reduced emotionality was also found by Hutchinson and Emley (1973). They found nicotine had a similar effect to the major and minor tranquilizers in producing a calming effect (i.e., reducing irritability and aggression) in both monkeys and man in stressful and noxious environments.

It has been suggested that the effects of nicotine are biphasic, acting as a stimulant or depressant, depending on dosage (Armitage et al., 1968), as well as, rate of dosage. Morrison and Stephenson (1977) report an initially depressant effect of nicotine on behavior in rats, followed by a stimulant effect once tolerance develops. It also appears that the arousal state of the individual prior to nicotine administration interacts with the arousal-producing properties of drug. Murphee, Pfeiffer and Price (1967) found both stimulant and depressant effects of nicotine on EEG in different subjects. They suggest the effects of nicotine on the central nervous system is dependent to some degree on the state of the subject before nicotine administration.

Numerous theories have been developed to explain the paradoxical effects of nicotine though, as Gilbert (1979) points out, these theories lack convincing data to support them. He also notes that it is not known whether all types and intensities of emotion are reduced by nicotine. It is likely that the emotion-reducing effects of nicotine vary with different emotions and a variety of other factors. Gilbert suggests that the mechanism by which nicotine reduces emotion is influenced by a host of different variables including behavioral activity level, type of emotion, time since administration of the drug, and rate and dose of nicotine administration.

Nicotine: The Primary Reinforcer? The nicotine addiction theory assumes that nicotine is the primary reinforcing agent of cigarette smoke and that smokers avoid nicotine withdrawal by regulating nicotine blood levels. It is quite likely that nicotine is the primary reinforcing substance maintaining smoking behavior, though definitive evidence is lacking.

Next to nicotine, the two most probable reinforcing substances of tobacco smoke are carbon monoxide and tar. Jarvik (1979) notes that although carbon monoxide has the most pronounced acute pharmacological action next to nicotine, it is an unlikely candidate. He points out that cigarettes low in nicotine (and also tar) yield amounts of carbon monoxide similar to those of high nicotine cigarettes, but are not popular. Since nicotine and tar yields covary, it is difficult to study their independent effects. However, Goldfarb, Gritz, Jarvik and Stolerman (1976) independently manipulated tar and nicotine content of cigarettes and found that the number of cigarettes smoked was related to the nicotine content, but not to the tar content. This supports the hypothesis that nicotine is the primary reinforcing agent. It is also worthy of note that nicotine-free cigarettes (i.e., lettuce cigarettes) enjoyed only brief popularity and the two companies marketing these cigarettes went bankrupt (Jarvik, 1977).

Other lines of evidence supporting nicotine as the primary reinforcing constituent come from findings that

nicotine is self-administered by rats and monkeys (Deneau & Inoki, 1967) and that monkeys will choose to smoke with no extrinsic rewards to do so (Jarvik, 1967). Intravenous administration of nicotine usually decreases the frequency of subsequent smoking (Johnson, 1942; Lucchessi, Schuster & Emly, 1967) though not always (Kumar, Cooke, Lader & Russell, 1977). In the latter study, intravenous nicotine had no effect on subsequent smoking behavior, though cigarettes smoked immediately preceding the test session markedly reduced smoking. It was suggested that nicotine delivered to the blood and brain via the intravenous route had a less potent effect than inhaled nicotine. A more conclusive test of nicotine's reinforcing potential would be to extend this study to include measurements of plasma nicotine.

Jarvik (1977) proposes that though nicotine plays a vital role in the pleasure derived from cigarette smoking, its effects are potentiated by some as yet unknown substance in tobacco smoke. However, it appears that the necessary, though perhaps not sufficiently reinforcing properties of nicotine are well enough established to support the nicotine addiction model.

Nicotine: An Addictive Substance? Prior to discussing nicotine as an addictive drug, it may be useful to review the basic criteria of drug addiction. Swonger and Constantine (1976, pp.235) define drug addiction as "a periodic or chronic abuse of a drug, characterized by psychological

dependence, generally physical dependence, and a compulsion to continue use of the drug." Psychological dependence can be said to occur when the individual considers the drug necessary for maintaining a state of well-being. While physical dependence involves both (1) tolerance to the drug in which physiological adjustments occur which increase the body's ability to metabolize the drug. Therefore, increasing dosages of the drug are required to produce the initial desirable effects of the drug and (2) withdrawal symptoms following termination of the drug (Swonger & Constantine, 1967). Though there is still some question as to whether or not nicotine is an addictive substance, current evidence strongly suggests that it is.

Since nicotine causes an increase in physiological arousal, one would expect a decrease in arousal following abstinence from nicotine. Nicotine withdrawal symptoms include decreases in heart rate, blood pressure (Murphee & Schultz, 1968; Knapp, Bliss & Wells, 1963), skin temperature (Myrsten, Elgerot & Edgren, 1977), ~~adrenalin and noradrenalin~~ excretion (Myrsten et al., 1977; Elgerot, 1978), cortical alpha activity (Knott & Venables, 1977), increases in slow-wave EEG activity (Ulett & Itil, 1969) and improved hand steadiness (Myrsten et al., 1977). Affective changes following nicotine abstinence include irritability, anxiety, hostility, tension, restlessness, poor concentration, sleep disturbances (Myrsten et al., 1977; Morrison & Stephenson, 1972; Elgerot, 1978) and craving for cigarettes (Gritz & Jarvik, 1973;

Shiffman & Jarvik, 1976).

Jarvik (1979) points out that in order to classify the physiological effects following smoking cessation as withdrawal symptoms it is necessary to demonstrate a rebound effect, rather than merely a return to normal levels. Knott and Venables (1977) demonstrated a rebound effect in a study of cortical alpha activity. Alpha activity of deprived smokers was found to be significantly lower than that of active smokers and nonsmokers. After smoking two cigarettes, deprived smokers showed increases in alpha activity to levels similar to that of nonsmokers and smoker controls. Hence, the withdrawal symptoms from nicotine appear to be genuine.

Shiffman and Jarvik (1976) studied the time course of withdrawal symptoms over a 12 day abstinence period. Withdrawal symptoms were assessed daily by responses to a withdrawal questionnaire composed of four factors: (1) Stimulation (i.e., arousal), (2) desire to smoke, (3) physical symptoms and (4) psychological symptoms. All symptom groups, except stimulation, showed significant U-shaped trends as a function of days in abstinence. These symptoms decrease in severity in the first few days of abstinence and then increase in the second week. Psychological symptoms and craving also show a linear decrease as a function of abstinence. However, when viewed on a daily basis, craving is linearly related to hours in the day, with craving being lowest in the morning and increasing gradually during the day (Myrsten et al., 1977).

Though Shiffman and Jarvik (1976) expected that heavy smokers (i.e., subjects who smoked more than 20 cigarettes a day) would differ from light smokers (i.e., subjects who smoked 20 cigarettes or less a day) in reported withdrawal symptoms, they did so only on one factor. Heavy smokers showed increases in stimulation as abstinence proceeded, while light smokers showed decreases. Gritz and Jarvik (1973) also found no differences between heavy and light smokers in reports of craving following 48 hours of abstinence. This is a surprising finding since one would expect degree of withdrawal to be a positive linear function of degree of addiction. Eisenger (1971) found a positive correlation between daily nicotine intake and psychological addiction scores, while physical dependence, measured by questionnaire items, is reported to be highly correlated with physical withdrawal symptoms (Fagerstrom, 1978). It may be that the relationship between addiction and withdrawal is best viewed on a continuum of addiction, rather than as a dichotomy. This relationship clearly requires further exploration.

Thus far, nicotine appears to fulfill the criteria for an addictive substance in that psychological dependence, as well as, withdrawal symptoms have been demonstrated.

The second criteria for physical dependence, that is, tolerance, has also been found. Morrison and Stephenson (1972) report that the effect of nicotine on activity in rats is to act as a stimulant or depressant, depending upon the animals'.

previous experience with nicotine. For naive rats, the initial effects of nicotine on activity is to decrease it. These investigators found a tolerance to the initially depressing effect of nicotine on rat activity, evidenced by an increase in activity following the first few trials. Stolerman, Bunker and Jarvik (1974) also found nicotine tolerance in rats. Spontaneous locomotor activity was reduced in a dose-related fashion. Acute tolerance developed after a single pretreatment with nicotine. The dose of nicotine required to produce a decrement in activity was multiplied by a factor of 2.4.

The physiological changes resulting in tolerance to nicotine are evident in urinary excretion studies in humans. For a given dose of nicotine, nonsmokers excrete a greater portion of unchanged nicotine than smokers (Beckett & Triggs, 1967). This suggests that smokers have developed an increased ability to metabolize nicotine.

The present evidence strongly suggests that nicotine is, in fact, an addictive substance and, therefore, a valid assumption for the nicotine addiction theory. The addictive properties of nicotine are further supported by nicotine regulation studies.

A Closer Look at the Nicotine Addiction Theory: Nicotine Regulation Studies

The nicotine addiction theory maintains smokers will regulate their smoking behavior in order to maintain characteristic nicotine blood levels which will prevent the

discomfort of withdrawal symptoms. The overwhelming majority of studies which have tested the nicotine addiction theory have manipulated nicotine yield to observe the consequent changes in smoking behavior. However, there are reports of varying nicotine intake by intravenous administration and in nicotine chewing gum. These latter manipulations have the advantage of avoiding the possible intervening effects of tar and other tobacco constituents. However, these unnatural routes of nicotine distribution can only approximate the effects of inhaled nicotine. The effects of nicotine manipulations have been assessed by changes in smoking behavior, including total cigarette consumption, nicotine trapped in cigarette filters, puff analysis etc. However, changes in smoking behavior are only an estimate for the amount of nicotine inhaled and, therefore, entering the blood. More sophisticated nicotine regulation studies have assessed changes in COHB, plasma and urinary nicotine in addition to changes in smoking behavior. Nicotine regulation studies incorporating these smoking variables will be discussed.

Nicotine Yield and Smoking Behavior. One of the earliest nicotine regulation studies, performed by Finnegan, Larson and Haag (1945), provided mixed support for the nicotine addiction theory. These investigators varied nicotine yield by adding nicotine to low nicotine cigarettes and, therefore, controlling for differences in tar content. After two weeks

of smoking their usual brand of cigarettes, subjects smoked high nicotine cigarettes (1.96mg.nicotine) for two weeks, followed by two weeks of smoking low nicotine cigarettes (.34mg. nicotine). Daily cigarette consumption increased for only half of the subjects when smoking the low nicotine brand. However, subjects who did not regulate nicotine intake, by increasing cigarette consumption, reported considerably more withdrawal symptoms. No statistical analyses were performed, however. This study suggests that while not all smokers regulate nicotine intake, the consequence of not doing so is withdrawal symptoms.

Goldfarb and Jarvik (1972) also found some smokers regulate nicotine more than others. Following a control week of smoking their usual brand of cigarettes, subjects smoked cigarettes cut to half their normal length (proximal end) for one week and cigarettes marked with a red line at the half-way point (distal end) for another week. Though there was a tendency for subjects to smoke more half-length than normal length cigarettes, the difference was not statistically significant. However, 12 of the 18 subjects increased the number of distal end cigarettes smoked per day by an average of five and the number of proximal end cigarettes by an average of seven. This suggests an attempt to compensate for reduced nicotine yield by some subjects.

In another shorter term study in which total cigarette consumption was measured, Frith (1971) found a linear relationship between nicotine content and number of cigarettes

smoked in a eight hour period. The greater the nicotine content among the three nicotine yields (1.02mg., 1.37mg., and 2.11mg.), the fewer the number of cigarettes smoked. This study also found a linear relationship between nicotine content and time taken to smoke a single cigarette. The greater the nicotine content, the longer it took to smoke the cigarette. Consequently, an approximately equal number of puffs were taken from both the high and lower nicotine cigarettes.

It appears that the amount of nicotine available to a smoker will effect the way in which the smoker regulates smoking behavior. When number of cigarettes available is restricted, smokers will regulate nicotine intake by taking more frequent puffs on low nicotine than on high nicotine cigarettes (Ashton & Watson, 1971), as well as increasing the duration of puffs and puff volume (Adams, 1978). In fact, Henningfield and Griffiths (1979) experimentally manipulated the effects of number of cigarettes available on smoking behavior and found that decreasing number of cigarettes during a session resulted in increased number of puffs per cigarette. When the nicotine content of low nicotine cigarettes is quite low (i.e., 2mg.) smokers will not only smoke more low nicotine cigarettes given ad libitum, but also take more frequent puffs from them (Jarvik, Pope, Scheider, Baer-Weiss & Gritz, 1978). The latter types of behavioral regulation also occur when nicotine yield is varied by reducing the size of the smoker's usual brand of

cigarette to half and quarter lengths (Jarvik et al., 1978).

The time period allotted to smoking cigarettes of varying nicotine yields may also alter the ways in which a smoker adjusts smoking behavior. Creighton and Lewis (1978) conducted a study extending over a three month period in which subjects smoked medium, high, and low nicotine cigarettes. They found subjects increased the intensity with which they smoked the lower nicotine brand and decreased the intensity of smoking the high nicotine brand when compared with the control (medium nicotine) brand. However, the total number of cigarettes smoked per day did not differ between the three brands. It is possible that a subject's usual number of cigarettes smoked a day, and consequent self-attribution as a "pack-a-day smoker" for example, may have overridden regulation by increasing number of cigarettes smoked. Therefore, regulation occurred through varying puff intensity.

Smokers appear less sensitive to small differences in nicotine yields. Forbes, Robinson, Hanley and Colburn (1976) provided nicotine yields with decrements of .25mg., .25-.50mg. and .70mg. of nicotine from subjects' usual nicotine yield. Subjects showed no tendency to compensate for the reduced nicotine yield by extracting greater amounts of nicotine, which was measured by the amount of nicotine trapped in the cigarette filters.

All of the nicotine regulation studies thus far mentioned are limited in providing support for the nicotine addiction

theory. In restricting measures of nicotine regulation to total cigarette consumption and puff parameters such as volume, intensity, duration, frequency etc., estimates of mouth-level intake only can be made. Since actual nicotine regulation depends on the amount of nicotine inhaled, measures of the latter are essential.

Measurements of Nicotine Intake: Plasma Nicotine and Carboxyhemoglobin (COHb). Given the importance of measuring actual nicotine intake for testing the nicotine addiction theory, changes in plasma and urinary nicotine, breath carbon monoxide and COHb have been assessed in relation to varying nicotine yields. The relationship among these variables has received considerable attention.

One of the first studies to assess the relationship between nicotine intake and plasma nicotine was conducted by Issac and Rand (1972). Following an overnight eight hour deprivation period, six male habitual smokers smoked their preferred brand of cigarette ad libitum for 6.5 hours. A blood sample was taken 30 minutes following the last cigarette. The results indicated plasma nicotine levels rose significantly during the smoking period from a pre-session mean of 2.7ng./ml. to a post-session mean of 20.7ng./ml. There was wide variation in post-session plasma nicotine levels (range = 12-44ng./ml.). In a second experiment, following an eight hour deprivation period, four subjects smoked a cigarette of their preferred brand at the rate of one puff per minute. Blood samples were taken during smoking

and at fixed intervals for two hours following the last cigarette. The results showed plasma nicotine levels rose rapidly during smoking and declined slowly during the post-session period. Wide individual differences in plasma nicotine levels were again observed. There was a high correlation ($r = .88$) between plasma nicotine peak levels and amount of nicotine abstracted. The latter was estimated by calculating the difference between the nicotine content of exhaled and inhaled smoke. Though subjects varied in the rate of decline in plasma nicotine levels, the plasma nicotine half-life was less than 30 minutes for all subjects. It was found that the decay curve of plasma nicotine includes two components; an initial phase reflecting nicotine uptake and tissue distribution and a second slower phase suggested to represent nicotine's metabolism and excretion.

Ashton, Stepney and Thompson (1981) studied the relationship between COHb and plasma nicotine to determine the extent to which they are correlated and whether measuring exposure to CO provides a reliable estimate of exposure to nicotine. In a crossover design, subjects smoked high nicotine cigarettes for one week and low nicotine cigarettes for another week. They attended laboratory sessions twice a week in which pattern of puffing was measured for one cigarette. Blood samples were taken pre and post sessions. The pre-session samples provided baseline trough levels, reflecting previous nicotine exposure during the day. The results indicated a high correlation between plasma nicotine

and COHb concentrations pre sessions for high nicotine cigarettes ($r=.96$) and low nicotine cigarettes ($r=.93$). These correlations fell to $r=.75$ and $r=.70$ respectively for post session measurements. The investigators attributed the difference between the pre and post session correlations to differences in the pharmacokinetics of the two substances. They concluded that the CO intake of a single laboratory smoked cigarette is a poor estimate of nicotine uptake. However, there was a strong association between long-term exposure to nicotine and carbon monoxide.

Russell, Jarvis, Iyer and Feyerabend (1980) studied the relationship between nicotine yield, plasma nicotine and COHb. They found that though the correlation between plasma nicotine concentration and nicotine yield of cigarettes was significant, nicotine yield accounted for only 4.4% of the variation in plasma nicotine concentration. They also found a low correlation between COHb and cigarette consumption, with the latter accounting for only 9% of the variation in amount of smoke inhaled. These findings suggest that nicotine regulation occurs by changes in individual patterns of puffing and inhalation, rather than by changes in cigarette consumption and nicotine yield. Similar results are reported using alveolar carbon monoxide estimates of nicotine absorption (Rawborne, Murphy, Tate & Kane, 1978; Frederiksen & Martin, 1979). These findings further document the necessity of using physiological measures of nicotine regulation.

Nicotine Yield: Plasma Nicotine and COHb. The following two studies provide good examples of how misleading reliance on changes in smoking behavior alone can be in assessing nicotine regulation. Ashton, Stepney and Thompson (1979) conducted an 11 week crossover study of nicotine regulation in which changes in plasma nicotine, COHb and smoking behavior were measured. Subjects smoked medium nicotine (1.4mg.nicotine), high nicotine (1.84mg. nicotine) and low nicotine (.6mg. nicotine) cigarettes in three different phases and attended weekly lab sessions. Changes in plasma nicotine and COHb levels revealed that smokers compensated for about two-thirds of the difference in nicotine yields when switching from the medium nicotine to either the high or low nicotine cigarettes. The extent to which actual nicotine intake was maintained on the three brands of cigarettes varied greatly between subjects. Changes in puffing behavior and 24 hour cigarette consumption was not significant. Regulation was achieved through changes in inhalation, rather than changes in smoking behavior reflecting mouth-level intake.

Turner, Sillett and Ball (1974), on the other hand, found positive evidence for behavioral regulation of nicotine which was not reflected at the physiological level. Subjects smoked medium nicotine (1.4mg.), low nicotine (.8mg.) and very low nicotine (.3mg.) cigarettes for a period of one week each. Though cigarette consumption increased significantly during the low and very low nicotine

periods, compared with the medium period, mean COHb levels fell from 6.6% in the medium period to 6.25% in the low period and 3.80% in the very low period. Therefore, while mouth-level intake increased, inhalation did not. The investigators noted that this may have been due to the low nicotine content of the very low nicotine cigarettes which subjects rated as too weak and unsatisfying.

Smokers appear to be more responsive to excessively high levels of nicotine than they are to plasma nicotine levels which are lower than their usual levels. Russell, Wilson, Patel, Feyerabend and Cole (1975) measured nicotine plasma levels after subjects smoked cigarettes with high nicotine (3.2mg.), medium nicotine (mean= 1.3mg.) and low nicotine (.14mg.) yields. Midmorning and afternoon nicotine blood levels were measured in 10 subjects on each of four days. Midmorning samples were taken after subjects had smoked their usual brand of cigarettes ad libitum, while the afternoon sample was taken five hours later after subjects continued to smoke their usual brand or switched to a high or low nicotine cigarette during the course of the day. After switching to a high nicotine brand, number of cigarettes smoked decreased significantly though plasma nicotine levels were not significantly different from morning levels (mean = 29.2ng./ml. and 30.1ng./ml. respectively). However, after switching to low nicotine cigarettes, plasma nicotine levels dropped significantly (mean = 8.5ng./ml.), while there was a slight,

but nonsignificant, increase in number of cigarettes smoked. The actual plasma nicotine level bore no relation to the subject's usual cigarette consumption, to the number of cigarettes smoked in the preceeding hours, or even to the nicotine yield of the cigarette smoked (except for the low nicotine cigarettes). The authors suggest that the plasma nicotine levels just after a cigarette depends more on the way the cigarette is smoked than on its nicotine yield or the number that have been smoked in the preceeding hours. Though there was a great deal of individual variation in plasma nicotine levels, individual patterns could not be identified due to the small number of subjects, the limited number of samples taken, and the lack of urinary pH control. Furthermore, it was suggested that the nicotine yield of the low nicotine cigarettes used in this study was too low to permit nicotine regulation.

In another study of nicotine regulation, Russell, Sutton, Feyerabend and Saloojee (1980) varied nicotine yield by using shortened cigarettes, thereby reducing nicotine dosage without affecting concentration. Following 48 hours of ad libitum smoking of full (1.5 mg. nicotine, 14.2 mg. CO), three-quarters (.79 mg. nicotine, 10.1 mg.CO), and half-length (.47 mg. nicotine, 6.1 mg. CO) cigarettes in 10 subjects, the following measures were taken: smoking behavior (i.e., cigarette consumption and puff rate), mouth-level intake (calculated from butt content), and intake to the lungs (plasma nicotine and COHb). Results indicated

that mouth-level intake was maintained on the shortened cigarettes due to increase in puff intensity and total cigarette consumption. However, there was only partial maintenance of amount of smoke inhaled, as measured by COHb compensation (58%) which was achieved by half of the subjects. The COHb% for the full, three-quarters and half-length cigarettes were 7.3%, 6.3% and 5.3% respectively. The latter two values represent a corresponding COHb% reduction from the full-length cigarettes of 13.7% and 27.4% respectively. The authors speculate that smoke irritancy may have prevented subjects from compensation by inhaling more from the shortened cigarettes. Degree of compensation, measured by plasma nicotine levels, was not significant. It was suggested that COHb is a more accurate measure of overall daily nicotine intake into the lungs due to its longer half-life than plasma nicotine. The latter is a valid estimate of nicotine intake immediately preceeding blood sampling. Since partial regulation was achieved by half of the subjects, measured by COHb, while not at all by others would suggest some smokers regulate nicotine intake, while others do not.

Gritz, Baer-Weiss and Jarvik (1976) assessed physiological regulation of nicotine by measuring changes in urinary nicotine following variations in nicotine yield. Subjects smoked full-length and half-length cigarettes limited to either the proximal or distal end. For each subject, the number of cigarettes administered was held

constant to his daily average. Therefore, any regulation of nicotine intake would have to occur through adjustment of smoking style, rather than total cigarette consumption. Subjects smoked each of the three brands of nicotine for one day with each smoking day followed by one abstinence day. Results of the urinary nicotine analysis indicated subjects extracted proportionately more nicotine from the half-length than from the whole cigarettes.

In summary, nicotine regulation studies which have manipulated nicotine yield are inconsistently supportive of the nicotine addiction theory. It appears that the strength of nicotine regulation is influenced by variables such as length of exposure to varying nicotine yields, dosage of nicotine, time at which measurements such as plasma nicotine and COHb are made in relation to prior smoking and perhaps even the type of smoker, as suggested by Russell et al.(1980).

Intravenous Nicotine and Smoking Behavior. The effects of administering nicotine intravenously on regulation of subsequent smoking behavior have provided mixed results. Lucchessi, Schuster and Emley (1967) administered intravenous nicotine to subjects unaware of the nature of the drug in nine six-hour sessions. Smoking behavior was not altered significantly when nicotine was administered in a dose of 1mg. per hour for six hours. However, cigarette consumption decreased significantly when nicotine was

administered at the rate of 2 - 4 mg. per hour. There was a 27% reduction in the number of cigarettes smoked from an average of 10 to 7.3 cigarettes. Given the large dosages of nicotine administered, a greater reduction in smoking was expected.

Kumar, Cooke, Lader and Russell (1977) suggested that the weak results found by Lucchessi et al. (1967) may have been due to the method of nicotine administration, which was a poor simulation for inhaled nicotine due to the slow infusion. When nicotine is inhaled it is absorbed and circulated in a series of puff-by-puff boli of high nicotine concentrations. In an effort to mimic inhaled nicotine more closely, these investigators administered nicotine intravenously as ten rapid doses at the rate of one per minute, simulating 10 puffs from a cigarette. In Experiment I subjects were preloaded with inhaled nicotine from three different cigarettes varying in nicotine yield (12 deep puffs on each cigarette held for 3 to 5 seconds). Subsequent ad libitum smoking behavior was reduced in a dose related way. In Experiment 2 subjects were given three varying doses of nicotine intravenously, roughly equivalent to the doses of inhaled nicotine preloads. However, subsequent smoking was unaffected. Since no measure of inhalation was taken, it is possible subjects were inhaling less from the cigarettes following intravenous administration. Clearly, further nicotine regulation studies are needed in which nicotine is administered intravenously with particular

attention to dosage and method of nicotine administration in relation to post session nicotine concentrations.

Nicotine Chewing Gum and Smoking Behavior. Though it might be expected that buccal absorption of nicotine through nicotine chewing gum would be less effective than intravenous and inhaled nicotine in effecting nicotine blood levels and therefore, nicotine regulation, this does not appear to be so. Russell, Feyerabend and Cole (1976) compared plasma nicotine levels in a single subject after smoking 1.2 mg. nicotine cigarettes and after chewing gum containing either 2 mg. or 4 mg. of nicotine. Administration of 4 mg. nicotine chewing gum resulted in plasma nicotine levels comparable to those following smoking, which was not obtained with 2 mg. nicotine gum. However, it took considerably longer for plasma nicotine levels to rise with the chewing gum. Though nicotine in nicotine gum is absorbed slowly, it appears to be effective in altering smoking behavior. It has been found that high nicotine gum preloads significantly reduce frequency of puffing on subsequent cigarettes, while low nicotine gum preloads do not (Kozlowski, Jarvik & Gritz, 1975). In addition, nicotine chewing gum has been found to significantly improve smoking abstinence rates. Raw, Jarvis, Feyerabend and Russell (1980) conducted a one year follow-up of smokers attending a smoking withdrawal clinic. They found 38% of 69 smokers receiving nicotine chewing gum were still abstinent, compared with only 14% abstinence among smokers receiving psychological treatment. Similar

results were found by Puska, Bjorkqvist and Kosela (1979).

Nicotine Regulation in Heavy and Light Smokers. Degree of nicotine regulation appears to vary considerably depending upon the nature of the independent and dependent measures used. However, a consistent feature of nicotine regulation, regardless of design parameters, is the finding of wide individual variation in degree of compensation (i.e., Finnegan et al., 1945; Goldfarb & Jarvik, 1972; Ashton et al., 1979; Russell et al., 1975; 1980). This is most strikingly seen in the Russell et al. (1980) study in which it was found that approximately half of the subjects were clearcut compensators of nicotine intake, measured by COHb levels (mean = 102% compensation), while half were not regulators. These two groups did not differ in baseline smoking habits, plasma nicotine and COHb levels, or subjective mood and "satisfaction" ratings when smoking shortened cigarettes. This finding was in agreement with a previous smoke dilution study (Sutton, Feyerabend, Cole & Russell, 1978) and suggests that some smokers smoke in response to changes in nicotine blood levels, while others do not. Precisely what stimuli control smoking behavior in the latter group is open to question. Schachter (1978) asserts that all heavy smokers are addicted and suggests that smokers who do not track nicotine content are consciously imposing restraints on their cigarette consumption such as self-control for health reasons. He indicates that the extent to which such concerns are prominent, the smoker

inhibits his smoking in various ways to lower consumption, thus masking nicotine addiction. Furthermore, he contends that such "restrained" smokers pay the price of physiological and psychological withdrawal for their self-control.

Russell et al. (1980) found no differences in usual cigarette consumption between smokers who regulated nicotine intake and those who did not (mean daily cigarette consumption for all subjects = 26.7 cigarettes). However, there is some evidence to suggest that light smokers are less likely to regulate nicotine intake than heavy smokers. Schachter (1977) studied nicotine regulation in seven heavy smokers (minimum of 20 cigarettes per day) and four light smokers (maximum of 15 cigarettes per day). Subjects smoked low or high nicotine cigarettes on alternating weeks. The results revealed partial regulation for heavy smokers, reflected in a 25% increase in low nicotine cigarette consumption, while light smokers showed no consistent indications of regulation. Contrary to Schachter's (1977) speculation, these nonregulating light smokers do not appear to suffer from withdrawal symptoms (Perlick, 1977). Schachter (1979) concludes that these nonregulating smokers are nonaddicted "freaks" who provide a new window onto the understanding of the addiction process.

On closer observation, it appears likely that light smokers who do not regulate nicotine intake are, in fact, addicted, however, in a more subtle manner than heavy smokers. Since one feature of withdrawal syndromes is that

their severity is dose-dependent (Jarvik, 1979), one would expect heavy smokers to report more severe withdrawal symptoms than light smokers (Jarvik, 1979). However, with total abstinence from cigarettes, heavy and light smokers do not differ significantly in severity of reported withdrawal symptoms (Gritz & Jarvik, 1973; Shiffman & Jarvik, 1976). What appears to be emerging is that light smokers do not experience nicotine withdrawal to a lesser extent than heavy smokers, but rather, light smokers require less nicotine to avoid withdrawal. According to the nicotine addiction theory, escape from withdrawal is the impetus for nicotine regulation. One might speculate that light smokers, having a higher withdrawal threshold and, therefore, able to withstand greater variability in plasma nicotine levels, would regulate less completely than heavy smokers. This explanation would account for Schachter's (1977) apparent anomaly of nonregulating light smokers who report no withdrawal symptoms.

There is recent evidence which suggests that highly dependent smokers regulate more completely than less dependent smokers. Fagerstrom and Bates (1981) studied the relationship between physical dependence to nicotine, measured by the Tolerance Questionnaire and variations in nicotine regulation. Fourteen subjects smoked high nicotine (1.5 mg.) and low nicotine (.5 mg.) cigarettes in the laboratory on two separate days in a counterbalanced design. Subjects' responses to the Tolerance Questionnaire were

correlated with a composite "Smoking Score" derived from number of puffs, interpuff intervals and puff duration. The results showed that the low nicotine cigarettes were smoked more effectively than the high nicotine cigarettes and that the more dependent smokers smoked significantly more effectively than the less dependent smokers, regardless of nicotine content. Nicotine dependence was significantly correlated with degree of cigarette consumption. The authors conclude that "more highly dependent smokers are more skillful and/or have a stronger desire to regulate the level of nicotine." Though not always the case, the more dependent smokers in this study tended to have a higher daily cigarette consumption than the less dependent smokers. Unfortunately, the investigators of this study did not measure nicotine inhalation. It would be interesting to see if the more dependent smokers regulate nicotine more completely at the physiological level, in addition to greater regulation at the behavioral level.

Statement of the Problem

Testing the nicotine addiction theory by exploring differences among heavy and light smokers is an intriguing and important challenge in that it begins to outline the boundary conditions of this theory. Schachter's (1977) study of nicotine regulation in heavy and light smokers is severely limited on several accounts: (1) there was no measure of plasma nicotine, a critical measure for testing nicotine regulation; (2) nor was there a measure of smoking

behavior (e.g. puff frequency, intensity, duration) other than total cigarette consumption; (3) the small number of subjects used in this study (i.e., 11) alerts caution to conclusions drawn. Although the studies by Ashton et al. (1979) and Russell et al. (1975; 1980) provide more substantial tests of the nicotine addiction theory, they too provide inconclusive evidence due to the following methodological limitations: (1) Nicotine regulation, following reduction in nicotine yield, was not measured continuously and directly under laboratory conditions. Nicotine blood levels were sampled before and after a considerable period of ad libitum smoking outside of the laboratory. Consequently, compensation, reflected in nicotine blood levels could not be assessed during the ad lib smoking period, given the short half-life of serum nicotine (i.e., less than 30 minutes, Russell, 1979). Smoking behavior (e.g., puff frequency, duration, intensity and volume) also was not measured during the ad lib smoking period outside the lab. Rather, it was inferred from the sample of smoking behavior in the post smoking session in the lab. It is known that the way in which a cigarette is smoked is a more important determinant of nicotine intake than total cigarette consumption (Russell et al., 1975). In the Russell studies the latter was the only measure available, aside from butt analysis of nicotine, for determining nicotine compensation during the ad libitum smoking period outside of the lab. In order to avert these pitfalls in assessing nicotine regulation

it is necessary to measure smoking behavior and nicotine blood levels continuously and directly under laboratory conditions. (2) Russell et al. (1980) found partial compensation for reduced nicotine yield measured by COHb levels, while there was no compensation reflected in plasma nicotine levels. COHb levels reflect total daily nicotine intake, while plasma nicotine levels only reflect nicotine intake for cigarettes smoked within a short period prior to sampling. Therefore, it is not surprising that Russell et al. (1980) did not find compensation of total daily nicotine intake measured by plasma nicotine. By measuring plasma nicotine continuously and directly in the lab, the apparent inconsistency between the two plasma measures of nicotine could be further explored. (3) Providing satisfactory nicotine yield is problematic, though crucial, in nicotine regulation studies. In both of the Russell et al. studies (1975, 1980), the authors suggest nicotine regulation was inhibited by (a) high draw on the low nicotine cigarettes, as well as the excessively low nicotine content, making nicotine regulation impossible (Russell et al., 1975) and (b) the high irritancy of the shortened cigarettes (Russell et al., 1980). Therefore, it is necessary to measure nicotine regulation using cigarettes with low irritancy and sufficient nicotine yield to make complete compensation possible. (4) Russell et al. (1975) found a high degree of individual variation in plasma nicotine levels, however, urinary pH was not controlled. Nicotine excretion rate

is influenced by urine pH , while nicotine intake covaries with manipulated urine pH (Schachter, Kozlowski & Silverstein, 1977). Therefore, it becomes important to assess the extent to which individual variations in nicotine plasma levels are correlated with variations in baseline urine pH levels.

Hypotheses

The purpose of the present study was to provide a more definitive test of the nicotine addiction theory than previous studies by investigating nicotine regulation in the laboratory and, therefore, avoiding the methodological limitations of previous studies. It was specifically designed to test the nicotine addiction theory using heavy and light smokers by measuring changes in smoking behavior and plasma nicotine levels directly under laboratory conditions in response to changes in nicotine yield. It was hypothesized that a significant proportion of the previously reported individual variation in nicotine regulation, both behaviorally and physiologically, could be systematized by separating smokers into heavy and light categories.

Nicotine regulation in this study can be said to occur if plasma nicotine levels in the low nicotine condition are not significantly different from plasma nicotine levels in the high nicotine condition. If nicotine regulation occurs, the following changes in the remaining dependent variables are expected: (a) smoking behavior should be significantly greater under the low nicotine condition,

reflecting behavioral compensation; (b) COHb values should be significantly greater under the low nicotine condition, reflecting greater depth of inhalation on the low nicotine cigarettes, necessary for maintaining constant plasma nicotine levels; (c) physiological measures of heart rate and peripheral skin temperature should not be significantly different under the high and low nicotine conditions; (d) subjective measurements should reflect no differences in craving or withdrawal between the high and low conditions. In regard to differences among heavy and light smokers, the following hypotheses were tested: if, according to the nicotine addiction theory, escape from withdrawal is the impetus for nicotine regulation, and light smokers require less nicotine to avoid withdrawal than heavy smokers, then they should also withstand greater variability in plasma nicotine levels. This should be reflected in less complete nicotine regulation in light smokers than in heavy smokers, without the consequences of withdrawal. Conversely, heavy smokers, having a lower withdrawal threshold, should report greater withdrawal following the low nicotine session if they do not regulate plasma nicotine levels. The effects of age on nicotine regulation were also explored. The existing research which focuses on age and smoking behavior, suggests older smokers, regardless of usual nicotine consumption, report somewhat greater psychological addiction than younger smokers (Bosse et al., 1980). Consequently, the present study looked at the effects of age on smoking behavior from

an exploratory point of view. In addition, the present study assessed the degree to which urine pH was related to plasma nicotine levels, thereby effecting nicotine regulation. Self-imposed restraint of nicotine intake and nicotine tolerance were also determined.

II. Method

Subjects. Subjects were 20 males recruited from the local community through newspaper advertisements. Subjects were within the age range of 20 to 56 years of age. One subject was eliminated from the study due to noncompliance with the experimental procedure (i.e., plasma nicotine levels revealed that he did not comply with the request to abstain from smoking during the deprivation period). Consequently, 19 subjects participated in the study. All subjects were in good general health including absence of serious cardiac, vascular, pulmonary, or renal disease and medication which might affect CNS function.

Table 1 presents the age distribution of subjects. Within each group of heavy and light smokers, subjects were equally divided by a median split into two age-matched groups; 20 to 29 years of age and 30 to 56 years of age. Number of years which subjects had been smoking was as follows: Light-Young = 8 years, Heavy-Young = 9 years, Light-Old = 20 years, Heavy-Old = 27 years.

Table 2 presents the distribution of reported daily nicotine intake. Light smokers were defined as smoking 5 - 20 cigarettes a day, while heavy smokers were defined

Table 1
Age Distribution of Subjects

Young

<u>Subject#</u>	<u>Light</u>	<u>Subject#</u>	<u>Heavy</u>
1	21	5	22
2	20	6	22
3	22	7	25
4	24	8	27
	$\bar{X} = 21.75$	9	
	S.D. = 1.48		$\bar{X} = 24.8$
			S.D. = 2.48

Old

<u>Subject#</u>	<u>Light</u>	<u>Subject#</u>	<u>Heavy</u>
10	33	15	32
11	35	16	33
12	36	17	41
13	46	18	48
14	56	19	55
	$\bar{X} = 41.2$		$\bar{X} = 41.8$
	S.D. = 8.66		S.D. = 8.8

Young Smokers $\bar{X}$ Age = 23.44 S.D. = 2.59

Old Smokers $\bar{X}$ Age = 41.5 S.D. = 8.73

Table 2

Reported Daily Nicotine Intake

<u>S#</u>	<u>Total No. Cigarettes</u> <u>Smoked per Day</u>	<u>X</u>	<u>Mg. Nicotine</u> <u>of usual</u> <u>Brand</u>	<u>=</u>	<u>Total mg.</u> <u>Nicotine</u> <u>Available</u> <u>Per Day</u>
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Light - Young

1	7.5	X	.816	=	6.12
4*	10.0	X	1.020	=	10.20
2	15.0	X	.612	=	9.18
3	17.5	X	.816	=	14.28
	$\bar{X} = 12.5$				$\bar{X} = 9.95$
	S.D. = 3.95				S.D. = 2.92

Light - Old

10	16.0	X	1.330	=	21.28
12*	17.5	X	1.120	=	19.60
14	20.0	X	.816	=	16.32
11*	20.0	X	.816	=	16.32
13*	20.0	X	1.430	=	28.60
	$\bar{X} = 18.7$				$\bar{X} = 20.42$
	S.D. = 1.66				S.D. = 4.52

Heavy - Young

5	25.0	X	1.22	=	30.50
8	27.5	X	1.33	=	36.58
7	27.5	X	1.33	=	36.58
6	35.0	X	.714	=	24.99
9	40.0	X	1.02	=	40.80
	$\bar{X} = 31.0$				$\bar{X} = 33.89$
	S.D. = 5.6				S.D. = 5.53

Heavy - Old

16	35.0	X	.714	=	24.99
15	35.0	X	1.02	=	35.70
18	35.0	X	1.33	=	46.55
19	40.0	X	.612	=	24.99
17	50.0	X	1.12	=	56.00
	$\bar{X} = 39.0$				$\bar{X} = 37.65$
	S.D. = 5.8				S.D. = 12.16

*Subjects who reported to inhale only "sometimes"

as smoking 25 - 50 cigarettes per day. The nicotine yield of subjects' usual brand of cigarettes was multiplied by the number of cigarettes smoked per day to get an estimate of total milligrams of nicotine available per day. It is important to note that three subjects in the Light-Old group reported to inhale "sometimes", while all other subjects, except one subject in the Light-Young group, reported to inhale "always". Consequently, the total milligrams of nicotine available per day in the Light-Old group that is actually inhaled, should be considerably lower than the estimated value which is shown in Table 2. It is also worthy to note that the total milligrams of nicotine available per day is an approximation of mouth-level intake and provides less information regarding the amount of smoke that is actually inhaled by the subject.

Subjects signed an Informed Consent Form (see Appendix A) before the experimental procedure and after the hazards of venipuncture were described. Subjects were paid 25\$ for full participation in the study.

Apparatus. The smoking laboratory was divided into two rooms consisting of a subject room and an experimenter room. The subject room was controlled for temperature and humidity. Continual smoke ventilation was provided through a commercially available air filter. A television, cushioned chair and smoking console were present in the subject room. The subject was seated next to the smoking console which dispensed cigarettes automatically, presented

experimental stimuli and measured behavioral, subjective and physiological responses. All stimuli presented to the subject and behavioral and physiological measures obtained were controlled and recorded in the experimenter room. The two laboratory rooms were divided by a wall in the center of which was a two-way mirror for observing the subject. This laboratory model is similar to that used by Henningfield and Griffiths (1979).

Dependent Measures

Urine Samples. Prior to experimental sessions, 20 cc. urine samples were taken to determine urine pH values.

Smoking Topography. Puff frequency, duration (seconds), intensity (liters/sec.) and volume (liters) were measured by a vacuum switch (Model 505-3, Micro Pneumatic Logic, Inc.) which was connected to an air-tight flexible Teflon tube which carried smoke from the subject's mouthpiece (commercially available plastic cigarette holder). Pressure changes from inhalation were transmitted to the pressure sensor where they were converted to a digital output on a remote computer terminal (Texas Instruments Silent 700) with magnetic cassette storage (Data Compactor).

Carbon Monoxide Estimates. Cigarette smoke contains 1 to 5 percent carbon monoxide (CO) (Jarvik, 1979) which is present in the lungs two to four hours following smoking. Carbon monoxide intake can be assessed using either measures of breath carbon monoxide or measuring percent of carboxy-hemoglobin (COHb) in the blood. Both measures of CO estimate

overall depth of inhalation of cigarette smoke and are highly correlated with each other ($r = .97$) (Wald, Idle, & Boreham, 1981). Due to equipment failure, breath CO values were obtained on only six subjects. COHb values, obtained from venous blood samples were taken on the remainder of subjects. Breath CO values were converted to estimated COHb values using Smith's (1977) regression equation: $\text{COHb } \% = 0.181 \text{ CO ppm (parts per million)}$. Both CO estimates were measured pre and post each experimental session. Using the breath CO procedure, subjects inhaled for 20 seconds and then exhaled into two polyvinl bags attached to a Y-shaped tube filled in sequence, so that the first 75ml. of breath was discarded. Breath samples were analyzed by an ecolyser (Model 2000) within one hour after they were obtained. COHb samples were analyzed for COHb% using an CO-Oximeter 282 (Instrumentation Laboratory).

Physiological Measures. Heart rate (BPM) and peripheral skin temperature ($^{\circ}\text{C}$) were measured using sensors placed at standard locations on the body (Venables & Martin, 1967). The monitoring equipment was custom manufactured by Med Associates (East Fairfield, VT.). Visual monitoring of physiological responses was provided by a 4-channel polygraph. Analog signals (integrated over time where appropriate) were digitized for data storage and processing.

Subjective States. Nicotine craving was measured using a potentiometer with a calibrated scale located on the experimental console. Voltage levels from the various resistance

settings chosen by the subject were converted from analog to digital form for data processing. A light above the potentiometer was labeled "What is your desire to smoke?". The potentiometer was calibrated on an 11-point scale with "0" as "not at all", "5" as "moderate", and "10" as "very great". Nicotine withdrawal was measured using the Shiffman Nicotine Withdrawal Scale (Shiffman & Jarvik, 1976) (see Appendix B). This scale was abstracted from the 43 item questionnaire used by Gritz and Jarvik (1973) to assess the nicotine withdrawal syndrome. It consists of 25 items, each scored on a 7-point scale ranging from "very definitely" to "very definitely not". The scale is comprised of the following four subscales: (1) stimulation subscale (measuring level of stimulation and alertness relative to their norm for that time of day); (2) craving subscale (items measuring craving or desire to smoke); (3) psychological symptoms subscale (e.g., anxiety, contentment); (4) physical symptoms subscale (e.g., tachycardia, tremor).

Plasma Nicotine. Venipuncture was performed by a certified laboratory technician and supervised by a licensed physician. The venipuncture involved taking successive 10 ml. blood samples. An 18 guage butterfly infusion set (Abbott Laboratories) with a three-way stopcock was used. A dextrose-water (D $\frac{5}{10}$ W) sterile solution was employed using a microdrop infusion to prevent clotting between samples. The venipuncture catheter was kept in place on the subject's

left arm throughout the blood monitoring session. A 2 foot long plastic tube was connected to the venipuncture catheter which was passed through a small opening in the wall to the experimenter room where blood samples were drawn. Blood samples were analyzed for nicotine content using standard radioimmunoassay procedure. All samples were analyzed at the American Health Foundation, Valhalla, N.Y.

Procedure.

Subjects were scheduled for 3 sessions for 3 consecutive days of the week. Throughout the experiment subjects smoked only research cigarettes which were standardized for high nicotine (2.87 mg.) and low nicotine (.48 mg.) yields and which were provided by the Tobacco and Health Research Institute (University of Kentucky, Lexington, KY.). Day 1 was a Preparatory Period for the two experimental sessions on Day 2 and Day 3. The procedure for Day 2 and Day 3 was identical except that subjects smoked a different nicotine yield cigarette during each of the two sessions. Within each of the four groups of Heavy, Light, Young and Old smokers the order of presentation for nicotine yield was counterbalanced with half the subjects in each group smoking High nicotine cigarettes during Session 1 and Low nicotine cigarettes during Session 2, while the other half received the reverse order. On Day 1 subjects attended a 30 minute Preparation Period during which they were given a supply of research cigarettes (High or Low nicotine) and instructed

to smoke only these cigarettes for the remainder of the day and evening. They were instructed to stop smoking at 9:00 P.M. that evening until the start of the experimental session the following day. They were asked to bring the cigarettes butts and unsmoked cigarettes back to the lab the following day (see Appendix C). A baseline measure of nicotine withdrawal (Shiffman Nicotine Withdrawal Scale) was obtained during the Preparatory Period. Subjects were given a Smoking History (see Appendix D) which included the Fagerstrom Tolerance Questionnaire and an assessment of smoking restraint, to take home and return completed the following day.

Prior to the first experimental session on Day 2, a urine sample was taken to assess urine pH. During the first half of the session subjects were acclimated to the experimental apparatus and environment. After sensors were attached, the subject completed the Shiffman Withdrawal Scale and read the instructions for the experimental session (see Appendix E). Breath CO and COHb estimates were then taken.

During experimental sessions 1 and 2 subjects were provided the opportunity to smoke a cigarette every 10 minutes if they chose to do so. Cigarette availability was indicated by illuminating a signal light ("Want a cigarette?"). The subject self-administered a cigarette by pressing a button ("yes"). Subjects had five opportunities to smoke a cigarette during each session.

Throughout the experimental session subjects watched a pre-recorded movie on a videotape recording machine. The film was a commercially available cassette featuring a two-part (60 minutes each) movie ("The Sound of Music"). Part 1 was shown during the first experimental session, while Part 2 was shown during the second session.

Following completion of Session 1, CO estimates were taken and subjects completed the Shiffman Withdrawal Scale. They were provided with a supply of cigarettes (High or Low nicotine) to be smoked ad libitum for the remainder of the day and evening. Again, they were instructed to return the cigarette butts and unsmoked cigarettes. Subjects were provided with the same nicotine yield cigarettes that they would be smoking during the session the following day. This procedure allowed subjects to become accustomed to the experimental cigarettes prior to the session.

The procedure for Session 2 was the same as for Session 1, except that subjects smoked the alternate nicotine yield cigarette to that smoked during Session 1. All subjects were tested at the same time of the day (i.e., 10:00 a.m.).

Dependent Measure: Preparation for Statistical Analyses
Smoking Behavior.

(a) Total number of cigarettes: This was a measure of the total number of cigarettes each subject chose to smoke in each experimental session.

(b) Frequency of puffs: This was the average number of puffs taken per cigarette, per session. The total number of puffs taken in each session was divided by the number of cigarettes smoked in that session.

(c) Intensity (mean liters per second): This was the average intensity per puff, per session. This value was derived by obtaining the total intensity for all puffs on each cigarette, which was then divided by the frequency of puffs taken on that cigarette. These values were summed across all cigarettes smoked in each session and divided by the number of cigarettes smoked in that session.

(d) Duration (mean seconds): This was the average duration per puff, per session. This value was derived in the same manner as was Intensity.

(e) Total puff Volume (liters): This was the total volume of smoke drawn through the cigarette holder in each session. The intensity of each puff was multiplied by the duration of the puff and summed across all cigarettes in each session.

(f) Average puff Volume (liters): This was the average volume of smoke per puff, per session. The intensity of each puff was multiplied by the duration of the puff and summed across all puffs for each cigarette to get the total volume of smoke per cigarette. This value was then divided by the frequency of puffs per cigarette to obtain the average volume of smoke per puff, per cigarette. These

values were summed across all cigarettes per session and divided by the number of cigarettes smoked in each session.

Plasma Nicotine (ng./ml.) and Urine pH. 12 10 ml. blood samples were taken during each session. Samples were drawn pre (0 minutes) and post (55 minutes) each session and pre-post each of the five opportunities to smoke a cigarette. However, due to the costly expense of radio-immunoassay for estimating plasma nicotine content and financial constraints, analyses were performed on the following samples: pre and post the first cigarette smoked in each session and post the last cigarette smoked in each session. Since subjects had been nicotine deprived for 13 hours prior to each session, depth of inhalation and consequent plasma nicotine levels were expected to be higher for the first cigarette smoked. Differences between smokers in achieving initial plasma nicotine levels could therefore, be assessed. The plasma nicotine values obtained following the last cigarette smoked during the session provided an indication of the final adjustment smokers made in their plasma nicotine levels and, therefore, were most representative of optimal plasma nicotine levels. Urine pH values were obtained pre and post each session and analyzed as such.

Carbon Monoxide Estimates. Breath CO (ppm) and COHb (%) measures were taken pre and post each session. All breath CO values were converted to % COHb using

Smith's (1977) regression formula $\% \text{COHb} = 0.181 \text{ CO (ppm)}$. Statistical analyses were based on the pre-post session values.

Physiological Measures.

Heart Rate (BMP). Heart rate was measured continuously throughout each session. Statistical analyses were performed on heart rate values obtained pre-post the first cigarette smoked in each session and post the last cigarette smoked in each session. Since the greatest increase in heart rate occurs following the first cigarette smoked after a period of nicotine deprivation (Frankenhaeuser et al., 1968), the heart rate measure taken pre and post the first cigarette provided an estimate of the acute effects of varying nicotine yield on heart rate. The heart rate measure taken pre the first cigarette and post the last cigarette smoked provided an estimate of the longer term effects of varying nicotine yield on heart rate following a period of habituation to the nicotine yield.

Peripheral Skin Temperature (°C). Peripheral skin temperature was measured continuously throughout each session. Final analyses were performed on skin temperature values obtained pre the first cigarette smoked and post the last cigarette smoked in each session. Since the effects of nicotine on peripheral skin temperature are somewhat sluggish compared to the effects on heart rate (Frankenhaeuser et al., 1968), separate analyses were not

performed after the first cigarette smoked. This measure provided an overall index of reduction in skin temperature during each session.

Subjective Measures.

Craving. Craving was measured according to the subject's self-monitoring of subjective changes in craving throughout each session. Statistical analyses were confined to the pre and post session craving scores recorded at 0 and 55 minutes in each session. This provided an overall measure of reduction in craving over the entire session.

Shiffman Withdrawal Scale. Shiffman Withdrawal Scale scores were obtained pre and post sessions, as previously described, and analyzed as such.

Smoking History Questionnaire.

Fagerstrom Tolerance Questionnaire. Scores on the Fagerstrom Tolerance Questionnaire provided an overall self-report estimate of physical dependency on nicotine. Subjects' self-report of nicotine intake (i.e., total number of cigarettes smoked per day) and, therefore, classification as a heavy or light smoker, was compared with their nicotine dependency score on the Tolerance Questionnaire. This comparison provided an assessment of agreement between the two classification measures. Statistical analyses were not performed on the Tolerance Questionnaire scores, as its purpose was to provide descriptive information for guiding future research.

Smoking Restraint Question. Responses to the smoking restraint question were used to provide descriptive information for further understanding any differences between smokers in nicotine regulation (see Appendix D, p. 143). This data was not statistically analyzed.

III. Results

Statistical analysis of each dependent variable was performed using Analysis of Variance with Repeated Measures. The between-subject variables for each analysis were Type of Smoker (heavy, light) and Age (young, old). The within-subject variable was Nicotine Dose (high, low). Depending upon the dependent variable, total scores, difference scores, or pre and post scores were used in the analysis. All smoking behavior dependent variables were measured using total (or mean) scores for the high and low Nicotine Dose. Plasma nicotine and COHb values were measured using difference scores in which the pre score was used as a baseline and subtracted from the post score. Pre and post scores entered the analyses for the physiological and subjective measures. The repeated measure for these analyses included pre high, post high, pre low, and post low scores. Consequently, the analyses for smoking behavior, plasma nicotine and COHb were 2 x 2 x 2 ANOVAs with Repeated Measures, while the analyses for the physiological and subjective measures were 2 x 2 x 4 ANOVAs with Repeated Measures. The effects of order of presentation of Nicotine Dose (high, low) were

controlled for by counterbalancing the order within each group of the between-subject variables (i.e., heavy, light, young, old). Half of the subjects in each of the four groups received high nicotine cigarettes in the first session and low nicotine cigarettes in the second session, while the other half of the subjects in the group received the reverse order of presentation. Since order of Nicotine Dose presentation was controlled for by counterbalancing, it was not entered into the statistical analyses as a separate factor. All analyses were performed using the BMDP2V computer package. The assumption of homogeneity of variance for Analysis of Variance was tested using the Cochran Test, which was hand calculated. All tests for homogeneity of variance were nonsignificant, except for the analysis for plasma nicotine (pre first cigarette and post first cigarette). The Cochran critical value was .6287, $df = 4, 4$ (.6841, $df = 3, 4$ using the harmonic mean). The obtained value was .70. However, since the F test is robust with respect to minor violations of the homogeneity of variance assumption (Winer, 1962), transformation of the data was not deemed necessary. All post hoc analyses including Simple Effects tests and Newman-Keuls Tests were calculated by hand. The group means and respective standard deviations for all dependent variables are presented in Appendices F through I.

Statistical Analyses

Urine pH and Plasma Nicotine. Prior to analyzing plasma nicotine levels, urine pH values were examined to assess the relationship between the two measures. Since urine pH is inversely related to plasma nicotine excretion rate (Beckett & Triggs, 1966) a correlation analysis was performed on the two measures to determine degree of correlation. Four Pearson r correlation analyses were performed in which the pre session (high, low) urine pH values were correlated with the plasma nicotine values post the first and last cigarette smoked in each session. These latter values were difference scores in which the baseline plasma nicotine values (pre first cigarette) were subtracted out. The following results were obtained for each of the four analyses: (1) pre high urine pH and post high plasma nicotine-first cigarette, $r = .18$; (2) pre high urine pH and post high plasma nicotine-last cigarette, $r = .01$; (3) pre low urine pH and post low plasma nicotine-first cigarette, $r = -.16$; (4) pre low urine pH and post low plasma nicotine-last cigarette, $r = .03$. These correlations are quite low, none of which reached statistical significance. One reason for the low correlations was due to the small degree of variability in urine pH values. The urine pH values for all groups were within the neutral range of urine pH, with little within group variability. Urine pH significantly effects plasma nicotine excretion rate when it is either very acidic or very alkaline. This finding has been reported

in the literature through experimental manipulation of urine pH. Therefore, it was concluded that urine pH, as it naturally occurred, had negligible effect on the plasma nicotine values obtained. Plasma nicotine values were, therefore, statistically analyzed without adjustment for urine pH.

Plasma Nicotine. Table 3 presents the results of the plasma nicotine analysis for the session. There was a significant main effect for Nicotine Dose ($F = 12.45$, $df = 1.13$, $p < .01$). Plasma nicotine levels were significantly lower when subjects smoked low nicotine cigarettes (mean = 5.12 ng./ml.) than when smoking high nicotine cigarettes (mean = 22.64 ng./ml.). This indicates that the major hypothesis of this study was not confirmed. That is, nicotine regulation, at the pharmacological level did not occur. Hypotheses regarding differences between heavy and light smokers in nicotine regulation were not supported. There were also no differences between young and older smokers in nicotine regulation. The average reduction in plasma nicotine levels (i.e., decrease in the low nicotine session compared with the high nicotine session) for all subjects on the low nicotine cigarettes was 77.7%. Table 4 presents changes in plasma nicotine levels from the high to low nicotine sessions following the first and last cigarette for each group. All groups show relatively large reductions in plasma nicotine. The smallest reductions in plasma nicotine levels were obtained by the heavy-young smokers (pre-post first cigarette) and the heavy-old smokers

Table 3

Analysis of Variance for Plasma Nicotine
(Pre First Cigarette - Post Last Cigarette)

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	8.70	1	8.71	.03
Age (A)	633.69	1	663.69	2.59
S x A	8.59	1	8.59	.03
Error	3326.00	13	255.85	
Within Subjects				
Nicotine Dose (N)	2443.00	1	2443.00	12.48*
N x S	47.20	1	47.20	.24
N x A	660.26	1	660.26	3.37
N x S x A	14.36	1	14.36	.07
Error	2545.18	13	195.78	

*p < .01

Table 4

Percent Reduction in Plasma Nicotine Levels

Pre First Cigarette - Post Last Cigarette
(mg. plasma nicotine)

	<u>$\bar{X}$ High</u>	<u>$\bar{X}$ Low</u>	<u>% Reduction</u>
Light-Old	13.73	4.33	64.46%
Light-Young	32.08	2.00	93.96%
Heavy-Old	12.66	5.42	57.19%
Heavy-Young	30.40	7.80	74.34%

Pre-Post First Cigarette

	<u>$\bar{X}$ High</u>	<u>$\bar{X}$ Low</u>	<u>% Reduction</u>
Light-Old	7.58	2.78	63.32%
Light-Young	10.22	3.00	70.65%
Heavy-Old	14.56	3.96	72.80%
Heavy-Young	18.84	8.42	55.21%

(pre first - post last cigarette). However, neither of these groups were significantly different from the other groups, since the Type of Smoker x Nicotine Dose interactions were not significant for these two analyses. There was a high degree of variability in plasma nicotine levels within groups (see Appendix F). Consequently, there was a high degree of variability in percent of plasma nicotine reduction within groups. There was only one subject whose percent reduction in plasma nicotine level was less than 50% (i.e., subject #2, light-young smoker = 34%).

The results of the plasma nicotine analysis for the first cigarette are shown in Table 5. There was a significant main effect for Nicotine Dose ($F = 19.62$, $df = 1,14$, $p < .001$). Again, plasma nicotine levels were significantly lower for the low nicotine cigarette (mean = 4.72 ng./ml.) compared to the high nicotine cigarette (mean = 13.22 ng./ml.) resulting in a 64.3% reduction. There was also a significant main effect for Type of Smoker ($F = 6.84$, $df = 1,14$, $p < .05$). Heavy smokers had significantly higher plasma nicotine values (mean = 11.43 ng./ml.) than light smokers (mean = 5.89 ng./ml.) for the first cigarette. Consequently, while heavy and light smokers do not differ in plasma nicotine levels over the entire session, heavy smokers attain higher plasma nicotine levels on the first cigarette smoked during the session. This finding occurs for both the high and low nicotine cigarettes since the Type of

Table 5

Analysis of Variance for Plasma Nicotine
(Pre-Post First Cigarette)

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	272.93	1	272.93	6.84*
Age (A)	74.43	1	74.43	1.87
S x A	18.85	1	18.85	.47
Error	558.55	14	39.89	
Within Subjects				
Nicotine Dose (D)	605.18	1		19.62*
N x S	44.55	1		1.44
N x A	2.70	1		.09
N x S x A	3.88	1		.13
Error	431.81	14		

*p < .01

Smoker x Nicotine Dose interaction was not significant. Therefore, while heavy smokers achieve higher plasma nicotine levels than light smokers on the first cigarette, they do not regulate plasma nicotine levels by attaining equivalent nicotine levels for the high and low cigarette. COHb. The results of the COHb analysis are shown in Table 6. The results revealed a significant main effect for Nicotine Dose ($F = 6.60$, $df = 1,15$, $p < .05$). COHb values were significantly higher following the low nicotine session (mean = 1.86% COHb) compared to the high nicotine session (mean = 1.23% COHb). Though the exact CO yield of the low nicotine cigarettes has not been determined by the Tobacco and Health Research Institute, it is estimated to be 16.5 mg.¹ The CO yield of the high nicotine cigarettes is known to be 18.4 mg.. Consequently, the higher COHb values obtained following the low nicotine session indicate that subjects attempted nicotine regulation by inhaling more smoke from the low nicotine cigarettes than from the high nicotine cigarettes. However, this increased inhalation was not sufficient for nicotine regulation to occur, as reflected in the plasma nicotine analysis.

Smoking Behavior

Total number of cigarettes. Table 7 presents the results of the analysis for total number of cigarettes smoked during the session. There was a significant main effect for Nicotine Dose ($F = 13.49$, $df = 1,15$, $p < .01$). Subjects

Table 6

Analysis of Variance for COHb

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	1.07	1	1.07	.61
Age (A)	.65	1	.65	.37
S x A	.41	1	.41	.23
Error	26.51	15	1.77	
Within Subjects				
Nicotine Dose (N)	3.55	1	3.55	6.60*
N x S	.26	1	.26	.49
N x A	.07	1	.07	.14
N x S x A	.004	1	.004	.01
Error	8.07	15	.53	

*p < .05

Table 7

Analysis of Variance for Total Number of Cigarettes

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	5.84	1	5.83	2.07
Age (A)	3.24	1	3.24	1.15
S x A	.001	1	.001	.00
Error	42.37	15	2.82	
Within Subjects				
Nicotine Dose (N)	1.23	1	1.23	13.49*
N x S	.25	1	.24	2.71
N x A	.53	1	.53	5.79
N x S x A	.01	1	.01	.14
Error	1.37	15	.09	

*p < .01

smoked significantly more low nicotine cigarettes (mean = 3.53) than high nicotine cigarettes (mean = 3.16). There was also a significant Nicotine Dose x Age interaction ($F = 5.79$, $df = 1,15$, $p < .05$). The results of the Simple Effects test, presented in Table 8, show that older subjects smoked significantly more low nicotine cigarettes (mean = 3.9) than high nicotine cigarettes (mean = 3.3) ($F = 19.65$, $df = 1,15$, $p < .001$). There were no significant differences in total number of cigarettes smoked by young subjects in the high and low nicotine sessions. No other effects were significant.

Puff Frequency. The results of the analysis on puff frequency are shown in Table 9. There was a significant main effect for Age ($F = 11.22$, $df = 1,15$, $p < .01$). Older subjects took a significantly greater number of puffs on cigarettes (mean = 13.06) than younger subjects (mean = 7.73).

Puff Intensity. There were no significant effects for puff intensity as seen in Table 10. Therefore, all groups of subjects smoked the high and low nicotine cigarettes with equal intensity.

Puff Duration. There were also no significant effects for puff duration as seen in Table 11.

Total Puff Volume. Table 12 shows the results of the analysis for total puff volume. There was a significant main effect for Nicotine Dose ($F = 21.95$, $df = 1,15$, $p < .001$). The volume of smoke reaching mouth-level intake was signi-

Table 8

Simple Effects Test for Nicotine Dose X Age
Interaction (Total Number of Cigarettes)

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
a at b ₁	.43	1	.43	.295
a at b ₂	2.95	1	2.95	2.02
Error	43.75	30	1.458	
b at a ₁	1.8	1	1.80	19.65*
b at a ₂	.05	1	.05	.54
Error	1.37	15	.0916	

a₁ = Older Smokers

a₂ = Younger Smokers

b₁ = High Nicotine Session

b₂ = Low Nicotine Session

*p < .001

Table 9

Analysis of Variance for Puff Frequency

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	9.37	1	9.37	.40
Age (A)	265.86	1	265.86	11.22*
S X A	4.64	1	4.63	.20
Error	355.53	15	23.70	
Within Subjects				
Nicotine Dose (N)	.035	1	.035	.03
N X S	5.01	1	5.01	3.81
N X A	.745	1	.745	.57
N X S X A	.872	1	.872	.66
Error	19.73	15	1.31	

*p < .01

Table 10

Analysis of Variance for Puff Intensity

<u>Source</u>	<u>SS</u>	<u>.DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	7126.77	1	7126.77	3.95
Age (A)	924.19	1	924.19	.51
S X A	268.62	1	268.62	.15
Error	27134.44	15	1808.96	
Within Subjects				
Nicotine Dose (N)	485.99	1	485.99	2.13
N X S	114.58	1	114.58	.50
N X A	116.47	1	116.47	.51
N X S X A	127.26	1	127.26	.56
Error	3428.18	15	228.55	

Table 11

Analysis of Variance for Puff Duration

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	2.55	1	2.55	1.65
Age (A)	3.86	1	3.86	2.51
S X A	2.82	1	2.82	1.83
Error	23.10	15	1.54	
Within Subjects				
Nicotine Dose (N)	.436	1	.436	2.11
N X S	.029	1	.029	.14
N X A	.068	1	.068	.33
N X S X A	.637	1	.637	3.09
Error	3.094	15	.206	

Table 12

Analysis of Variance for Total Puff Volume

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	452222	1	452222	.03
Age (A)	69059740	1	69059570	4.52*
S X A	8659431	1	8659431	.57
Error	229413871	15	15294258	
Within Subjects				
Nicotine Dose (N)	18458260	1	18458260	21.95**
N X S	1695003	1	1695003	2.02
N X A	1457894	1	1457894	1.73
N X S X A	30605	1	30605	.04
Error	12615866	15	841057	

**p < .01

*p < .05

ificantly greater for the low nicotine cigarettes (mean = 5523.63 liters) than for the high nicotine cigarettes (mean = 4083.16 liters). Subjects are showing a significant degree of compensation at the behavioral level of smoking. However, this compensation is not sufficiently complete for plasma nicotine regulation to occur. Behavioral compensation, reflected in puff volume, also does not represent the amount of smoke actually inhaled, necessary for plasma nicotine regulation. There was a significant main effect for Age ($F = 4.52$, $df = 1,15$, $p < .05$). Older subjects drew significantly greater volume of smoke (mean = 6055.5 liters) than younger subjects (mean = 3412.17 liters).

Average Puff Volume. Table 13 shows the results of the analysis for average puff volume. There was a significant main effect for Nicotine Dose ($F = 15.89$, $df = 1,15$, $p < .01$). Average puff volume was significantly greater for low nicotine cigarettes (mean = 151.49 liters) as compared to high nicotine cigarettes (mean = 126.18 liters).

Physiological Measures

Heart Rate. The results of heart rate change pre the first cigarette and post the last cigarette are shown in Table 14. There was a significant main effect for Nicotine Dose ($F = 8.33$, $df = 3,43$, $p < .001$). The results of the Newman-Keuls test on Nicotine Dose are shown in Table 15. The following meaningful comparisons were

Table 13

Analysis of Variance for Average Puff Volume

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	15135.71	1	15135.71	1.74
Age (A)	210.83	1	210.83	.02
S X A	1145.25	1	1145.25	.13
Error	130302.36	15	8686.82	
Within Subjects				
Nicotine Dose (N)	5736.21	1	5736.21	15.89*
N X S	529.19	1	529.19	1.47
N X A	158.56	1	158.56	.44
N X S X A	672.58	1	672.58	1.86
Error	5414.59	15	360.97	

*p < .01

Table 14

Analysis of Variance for Heart Rate
(Pre First Cigarette - Post Last Cigarette)

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	1216.02	1	1216.02	2.54
Age (A)	413.60	1	413.60	.86
S X A	50.47	1	50.47	.11
Error	7194.95	15	479.66	
Within Subjects				
Nicotine Dose (N)	1699.49	3	566.49	8.33*
N X S	91.51	3	30.50	.45
N X A	126.03	3	42.01	.62
N X S X A	165.49	3	55.16	.81
Error	3059.25	45	67.98	

*p < .001

Table 15

Newman-Keuls Test for Nicotine Dose

Heart Rate: Pre First Cigarette - Post Last Cigarette

	Pre-Low <u>72.211</u>	Pre-High <u>72.579</u>	Post-Low <u>77.474</u>	Post-High <u>83.474</u>	
Pre-Low		.368	5.263	11.263**	
Pre-High			4.895	10.895**	
Post-Low				6.000*	
Post-High					
$S_B = 1.90$	**q.99 (r,45)	$r =$	$\frac{2}{7.23}$	$\frac{3}{8.30}$	$\frac{4}{8.93}$
	*q.95 (r,45)		5.43	6.54	7.20

significant: pre high (mean = 72.58 BPM) - post high (mean = 83.47 BPM), pre low (mean = 72.21 BPM) - post low (mean = 77.47 BPM), post high - post low. All subjects showed significant increases in heart rate following the last cigarette smoked in both the high and low sessions. However, this increase was significantly greater after smoking high nicotine cigarettes.

Table 16 presents the results of the analysis for heart rate change following the first cigarette smoked in each session. There was a significant main effect for Nicotine Dose ($F = 12.46$, $df = 3,45$, $p < .001$). The results of the Newman-Keuls test, shown in Table 17, revealed the following meaningful significant comparisons: pre high (mean = 72.58 BPM) - post high (mean = 84.79 BPM), pre low (mean = 72.21 BPM) - post low (mean = 82.00 BPM). Heart rate increase was not significantly greater following the first high nicotine cigarette compared with the first low nicotine cigarette.

Peripheral Skin Temperature. Table 18 shows the results of the analysis for peripheral skin temperature. There was a significant main effect for Nicotine Dose ($F = 2.81$, $df = 3,42$, $p < .05$). However, results of the Newman-Keuls test were not significant (see Table 19). There was also a significant Nicotine Dose x Type of Smoker interaction ($F = 2.97$, $df = 3,42$, $p < .05$). Results of the Simple Effects test, shown in Table 20, revealed significant

Table 16

Analysis of Variance for Heart Rate
(Pre-Post First Cigarette)

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	2170.23	1	2170.23	3.98
Age (A)	370.66	1	370.66	.68
S X A	111.83	1	111.83	.20
Error	8189.15	15	545.94	
Within Subjects				
Nicotine Dose (N)	2415.79	3	805.26	12.46*
N X S	97.21	3	32.40	.50
N X A	156.46	3	52.15	.81
N X S X A	62.99	3	20.99	.33
Error	2907.45	45	64.61	

*p < .0001

Table 17

Newman-Keuls Test for Nicotine Dose

Heart Rate: Pre-Post First Cigarette

	Pre-Low <u>72.21</u>	Pre-High <u>72.579</u>	Post-Low <u>82.000</u>	Post-High <u>84.789</u>
Pre-Low		.368	9.789*	12.580*
Pre-High			9.420*	12.210*
Post-Low				2.789
Post-High				

$$S_B = 1.85 \quad *q.99 (r, 45) \quad r = \quad \frac{2}{7.07} \quad \frac{3}{8.08} \quad \frac{4}{8.70}$$

Table 18

Analysis of Variance for Peripheral Skin Temperature

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	57.30	1	57.30	2.41
Age (A)	39.62	1	39.62	1.66
S X A	2.15	1	2.15	.09
Error	333.18	14	23.79	
Within Subjects				
Nicotine Dose (N)	36.31	3	12.10	2.81*
N X S	38.40	3	12.80	2.97*
N X A	16.98	3	5.66	1.31
N X S X A	24.82	3	8.27	1.92
Error	181.13	42	4.31	

*p < .05

Table 19

Newman-Keuls Test for Nicotine Dose

Peripheral Skin Temperature

	Post-High <u>31.34</u>	Post-Low <u>32.05</u>	Pre-High <u>32.92</u>	Pre-Low <u>32.95</u>
Post-High		.71	1.58	1.61
Post-Low			.87	.90
Pre-High				.03
Pre-Low				
$S_B = .4926$	$q_{.95}(r, 42) \quad r =$			
			$\frac{2}{1.41}$	$\frac{3}{1.69}$
				$\frac{4}{1.87}$

Table 20

Simple Effects Test for Nicotine Dose X Type of Smoker
Interaction (Peripheral Skin Temperature)

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
a at b ₁	.66	1	.66	.07
a at b ₂	7.26	1	7.26	.79
a at b ₃	20.41	1	20.41	2.22
a at b ₄	35.28	1	35.28	3.84
Error	514.32	56	9.13	
b at a ₁	40.54	1	40.54	9.41**
b at a ₂	18.81	1	18.81	4.36*
Error	181.13	42	4.31	

**p < .01

*p < .05

a₁ = Light Smokersa₂ = Heavy Smokersb₁ = Pre High Nicotine Sessionb₂ = Post High Nicotine Sessionb₃ = Pre Low Nicotine Sessionb₄ = Post Low Nicotine Session

differences in skin temperature due to Nicotine Dose within both the light group ($F = 9.41$, $df = 1,42$, $p < .01$) and heavy group ($F = 4.36$, $df = 1,42$, $p .05$). The results of the Newman-Keuls test performed on these differences are shown in Tables 21 and 22. Heavy smokers do not show a significant reduction in skin temperature over the high or low nicotine sessions. However, their skin temperature was significantly lower following the high nicotine session compared with the low nicotine session post value. Light smokers showed a significant reduction in skin temperature over the high nicotine session, while skin temperature was not significantly lower over the low nicotine session.

Subjective Measures. The results of the analysis on the Shiffman Withdrawal Scale are shown in Table 23. This analysis was performed on the baseline, pre and post scores of the total Shiffman Withdrawal Scale score. There was a significant main effect for Nicotine Dose ($F = 9.76$, $df = 4,56$, $p < .001$). The Newman-Keuls test revealed the following significant comparisons: baseline - pre high, baseline - pre low, pre low - post low, and pre high - post high. The significant differences between the baseline measure taken on Day 1 of the experiment and the pre high and pre low session measures indicate that subjects were experiencing a significant degree of withdrawal following the 13 hour deprivation period. Within both the high and low nicotine sessions, subjects reported a significant reduction in

Table 21

Newman-Keuls Test for Effects of Nicotine Dose
on Heavy Smokers (Peripheral Skin Temperature)

	Post-Low <u>30.22</u>	Post-High <u>30.71</u>	Pre-Low <u>31.89</u>	Pre-High <u>32.95</u>
Post-Low		.49	1.67	2.73**
Post-High			1.18	2.24*
Pre-Low				1.06
Pre-High				

Table 22

Newman-Keuls Test For Effects of Nicotine Dose
on Light Smokers (Peripheral Skin Temperature)

	Post-High <u>31.98</u>	Pre-High <u>32.89</u>	Post-Low <u>33.85</u>	Pre-Low <u>34.02</u>
Post-High		.91	1.87*	2.04*
Pre-High			.96	1.13
Post-Low				.17
Pre-Low				

$S_B = .489$	*q.95 (r,42)	r=	$\frac{2}{1.39}$	$\frac{3}{1.68}$	$\frac{4}{1.85}$
	**q.99 (r,42)		1.86	2.14	2.29

Table 23

Analysis of Variance for Shiffman Withdrawal Scale

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	1897.28	1	1897.28	4.16
Age (A)	462.08	1	462.08	1.01
S X A	3.04	1	3.04	.01
Error	6391.50	14	456.63	
Within Subjects				
Nicotine Dose (N)	2848.69	4	712.17	9.76*
N X S	606.14	4	151.17	2.08
N X A	61.79	4	15.53	.21
N X S X A	289.85	4	72.46	.99
Error	4086.40	56	72.97	

*p < .0001

Table 24
Newman-Keuls Test for Nicotine Dose
Shiffman Withdrawal Scale

	Post-Low <u>61.22</u>	Post-High <u>63.56</u>	Baseline <u>66.33</u>	Pre-Low <u>74.56</u>	Pre-High <u>75.06</u>
Post-Low		2.34	5.11	13.34*	13.84*
Post-High			2.77	11.00*	11.50*
Baseline				8.23*	8.73*
Pre-Low					.50
Pre-High					
$S\bar{B} = 2.03$	*q.99 (r,56)	r =	$\frac{2}{7.63}$	$\frac{3}{8.69}$	$\frac{4}{9.34}$
				$\frac{5}{9.78}$	

Table 25
Total Shiffman Withdrawal Scale Scores
Converted to Mean Scores

(25 items, range = 25 - 175)

	<u>Total Scores</u>	<u>Mean Scores</u>
Baseline	66.33	2.65
Pre-High	75.06	3.00
Post-High	63.56	2.54
Pre-Low	74.56	2.98
Post-Low	61.22	2.45

withdrawal symptoms. However, the degree of withdrawal reduction did not differ for the high and low sessions. Table 25 shows the group mean for total Shiffman scores and their conversion to mean Shiffman scores. The Shiffman items were scored on a 7-point scale with 4 representing a neutral degree of withdrawal. All mean scores were below the neutral point. This suggests that even though there were significant differences in withdrawal ratings pre and post sessions, subjects did not report strong withdrawal symptoms following the deprivation period.

Tables 26 through 29 present the results of the analyses for the four Shiffman Withdrawal subscales. There was no significant effects for the physical symptoms, stimulation, or psychological symptoms subscales. However, there was a significant main effect for Nicotine Dose on the craving subscale ($F = 30.67$, $df = 3,45$, $p < .001$). The results of the Newman-Keuls test, shown in Table 30, reveals significant comparisons within sessions for pre low - post low and pre high - post high, indicating a significant reduction in reported craving over both sessions. However, this reduction was not significantly different for the high and low sessions. Table 31 shows a breakdown of the group means for total scores to mean scores. Subjects are reporting craving levels slightly above neutral prior to each session.

The results of the craving scale, measured by the potentiometer, are shown in Table 32. There was a main

Table 26

Analysis of Variance for Shiffman Withdrawal Scale
Physical Symptoms Subscale

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	17.66	1	17.66	.79
Age (A)	26.26	1	26.26	1.17
S X A	.00	1	.00	.00
Error	337.48	15	22.49	
Within Subjects				
Nicotine Dose (N)	22.33	3	7.44	1.38
N X S	31.48	3	10.49	1.94
N X A	28.81	3	9.60	1.78
N X S X A	24.15	3	8.05	1.49
Error	242.96	45	5.39	

Table 27

Analysis of Variance for Shiffman Withdrawal Scale
Stimulation Subscale

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	142.35	1	142.35	2.69
Age (A)	4.70	1	4.70	.09
S X A	20.75	1	20.75	.39
Error	793.40	15	52.89	
Within Subjects				
Nicotine Dose (N)	56.19	3	18.73	1.23
N X S	38.45	3	12.81	.84
N X A	45.55	3	15.18	1.00
N X S X A	16.80	3	5.60	.37
Error	683.30	45	15.18	

Table 28

Analysis of Variance for Shiffman Withdrawal Scale
Psychological Symptoms Subscale

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	183.08	1	183.08	3.49
Age (A)	21.50	1	21.50	.41
S X A	135.32	1	135.32	2.58
Error	787.88	15	52.52	
Within Subjects				
Nicotine Dose (N)	10.95	3	3.65	.20
N X S	58.75	3	19.58	1.06
N X A	23.21	3	7.73	.42
N X S X A	39.27	3	13.09	.71
Error	829.96	45	18.44	

Table 29

Analysis of Variance for Shiffman Withdrawal Scale
Craving Subscale

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	415.81	1	415.81	4.12
Age (A)	132.18	1	132.18	1.31
S X A	99.57	1	99.57	.99
Error	1514.00	15	100.93	
Within Subjects				
Nicotine Dose (N)	2885.55	3	961.85	30.67*
N X S	122.45	3	40.81	1.30
N X A	80.10	3	26.70	.85
N X S X A	46.97	3	15.66	.50
Error	1411.10	45	31.35	

*p < .001

Table 30
Newman-Keuls Test for Nicotine Dose
Shiffman Craving Subscale

	Post-Low <u>18.26</u>	Post-High <u>19.32</u>	Pre-Low <u>30.74</u>	Pre-High <u>32.00</u>
Post-Low		1.06	12.48*	13.74*
Post-High			11.42*	12.68*
Pre-Low				1.26
Pre-High				
$\bar{S}_B = 1.66$	*q.99 (r, 45)	$r =$	$6.\overset{2}{\underset{4}{3}}$	$7.\overset{3}{\underset{25}{2}}$ $7.\overset{4}{\underset{8}{8}}$

Table 31
Total Shiffman Craving Scores
Converted to Mean Scores

(7 items, range = 7-49)

	<u>Total Scores</u>	<u>Mean Scores</u>
Pre-High	32.00	4.57
Post-High	19.32	2.76
Pre-Low	30.74	4.39
Post-Low	18.26	2.61

Table 32

Analysis of Variance for Craving

<u>Source</u>	<u>SS</u>	<u>DF</u>	<u>MS</u>	<u>F</u>
Between Subjects				
Type of Smoker (S)	17.21	1	17.21	1.33
Age (A)	6.63	1	6.63	.51
S X A	5.56	1	5.56	.43
Error	193.88	15	12.92	
Within Subjects				
Nicotine Dose (N)	333.31	3	111.10	27.22*
N X S	29.82	3	9.94	2.44
N X A	1.81	3	.60	.15
N X S X A	5.75	3	1.91	.47
Error	183.66	45	4.08	

*p < .001

effect for Nicotine Dose ($F = 27.22$, $df = 3,45$, $p < .001$). The Newman-Keuls analysis in Table 33 shows the following significant comparisons: pre low - post low and pre high - post high, indicating significant reduction in reported craving over both sessions. Table 34 shows the mean craving scores, based on an 11-point scale with a neutral rating of 5. On this measure of craving, subjects reported very high pre session craving scores, reflecting a high desire to smoke following the deprivation period.

Fagerstrom Tolerance Questionnaire. Table 35 presents the Tolerance Questionnaire scores for all subjects. All but two of the heavy smokers achieved scores placing them in the high end of the physical dependency range. Two heavy smokers are classified as moderately dependent. Among the light smokers, five subjects are classified as moderately dependent, while four light smokers fall in the low range of physical dependency. There appears to be a high level of agreement between subjects' self-report, based on total number of cigarettes smoked a day, and nicotine physical dependency scores for heavy smokers. While there were no light smokers who had scores in the high dependency range, old and young light smokers appeared to differ in degree of physical dependency. Light old smokers scored primarily in the moderately dependent range, while most all light young smokers scored in the low dependency range. When considering dependency scores on the basis of

Table 33

Newman-Keuls Test for Nicotine Dose
Craving

	Post-High <u>3.631</u>	Post-Low <u>3.789</u>	Pre-High <u>7.737</u>	Pre-Low <u>8.211</u>
Post-High		.158	4.106*	4.580*
Post-Low			3.948*	4.422*
Pre-High				.474
Pre-Low				
$S_B = .465$	*q.99 (r,45)	r =	$\frac{2}{1.78}$	$\frac{3}{2.03}$
				$\frac{4}{2.19}$

Table 34

Average Craving Scores

Range = 0 - 10

Pre-High = 7.74

Post-High = 3.63

Pre-Low = 8.21

Post-Low = 3.79

Table 35

Fagerstrom Tolerance Questionnaire Scores

<u>Light-Old</u>	<u>Total Score</u>
S#	
10	5
14	6
13	5
11	6
12	3
	$\bar{X} = 5$

<u>Light-Young</u>	
2	3
3	5
4	2
1	3
	$\bar{X} = 3.25$

<u>Heavy-Old</u>	
17	8
15	8
19	8
16	8
18	2
	$\bar{X} = 8.2$

<u>Heavy-Young</u>	
9	8
5	7
6	6
8	10
7	2
	$\bar{X} = 9$

Scale range = 0 - 11

0 - 3 = Low Dependency

4 - 7 = Moderate Dependency

8 - 11 = High Dependency

age alone, there was very little difference between young smokers (mean score = 7) and old smokers (mean = 6.6).

Both age groups report moderate physical dependency.

Smoking Restraint Question. Responses to the smoking restraint question revealed that two subjects in the light old group reported to be restraining their daily nicotine consumption by two and five cigarettes each, two light young subjects reported cutting back by 12 and 10 cigarettes each and two heavy young smokers reported reducing nicotine intake by five and five to seven cigarettes each. There were no heavy old smokers who reported smoking restraint. The latter finding is not surprising since a smoker with a long history of heavy nicotine addiction is more resistant to changing smoking habits. The equal distribution of restrained smokers in the other groups, suggest smoking restraint is not a significant factor in the present study in affecting nicotine regulation at either the pharmacological or behavioral level.

IV. Discussion

The major hypothesis of the present study that heavy and light smokers would differ in nicotine regulation at the pharmacological level was not confirmed. It was speculated that the high degree of individual variability reported in the nicotine regulation literature could be accounted for on the basis of varying degrees of nicotine addiction and, therefore, tendency to regulate nicotine.

Neither heavy or light smokers regulated plasma nicotine levels. The hypothesis that light smokers would not report increased withdrawal for failure to regulate plasma nicotine levels was confirmed. However, heavy smokers behaved in a similar fashion to light smokers on most all dependent variables with one important exception. Heavy smokers had significantly higher plasma nicotine levels following the first cigarette smoked in both the high and low nicotine sessions. This suggests that following a 13 hour nicotine deprivation period, heavy smokers have a greater urgency than light smokers to raise plasma nicotine levels on the first cigarette. However, by the end of the session both groups reached similar plasma nicotine levels. On the average, heavy and light smokers achieved higher plasma nicotine levels following the last cigarette smoked, compared with levels following the first cigarette. This suggests that during the course of the session, light smokers caught up to heavy smokers in plasma nicotine levels. Since plasma nicotine level was assessed at the beginning and end of sessions, changes in the rate of increase in plasma nicotine levels for the heavy and light smokers could not be determined. Therefore, it is not known exactly how heavy and light smokers end up with the same levels of plasma nicotine by the end of the last cigarette. One of the limitations of a one hour smoking session is that it prevents an understanding of how heavy and light smokers differ in

smoking patterns over the course of a day. It may well be that within any given hourly segment of the day heavy and light smokers do not differ in smoking behavior. However, differences may emerge only in the frequency of smoking periods throughout the day. These differences may be particularly minimized when subjects are given an opportunity to smoke freely following a 13 hour deprivation period.

The major unexpected finding of the present study was that heavy smokers did not regulate plasma nicotine levels. Though there was a high degree of individual variability in plasma nicotine levels, there was only one subject, a light young smoker, who showed a reduction in plasma nicotine level of less than 50% following the low nicotine session. The results of the Fagerstrom Tolerance Questionnaire suggest that the heavy smokers were highly dependent on nicotine. Consequently, the initial criterion for classifying heavy smokers as such appears valid. Schachter (1978) asserts that heavy smokers who do not regulate nicotine are intentionally limiting daily nicotine intake for health reasons etc.. However, only two of the 10 heavy smokers reported to be limiting daily nicotine intake on the Smoking Restraint question. Therefore, smoking restraint was not a reason for absence of regulation for the heavy smokers. It was hypothesized that if heavy smokers did not regulate plasma nicotine levels, they would report a greater degree of withdrawal symptoms following

the low nicotine session. It was also predicted that heavy smokers would report greater withdrawal than light smokers if they failed to regulate. Neither of these hypotheses were supported. Although heavy smokers reported greater withdrawal symptoms pre sessions than light smokers, the difference was not statistically significant. Since, according to the nicotine addiction theory, the impetus for nicotine regulation is avoidance of withdrawal symptoms, it is not surprising that heavy smokers did not regulate. Since they were not experiencing withdrawal at the end of the low nicotine session, there was no motivating stimulus for increasing plasma nicotine levels beyond the level reached. Again, the limitations of a one hour smoking session are strongly suggestive. Following a one hour ad libitum smoking period, after 13 hours of nicotine deprivation, smokers may well experience little withdrawal in comparison to what they experienced prior to the smoking period. It is noteworthy that all nicotine regulation studies reported thus far which have assessed changes in plasma nicotine levels have been over a period of a day at the minimum. Even over such a period, nicotine regulation at the plasma nicotine level has been very weak (Russell et al., 1975;1980). The strongest evidence for plasma nicotine regulation was reported in an 11 week regulation study (Ashton et al., 1979). Consequently, it is speculated that nicotine regulation at the plasma

nicotine level may not occur in a one hour laboratory smoking session. Smokers' adjustment to varying nicotine yield may require an extended period of time. Smokers may well experience withdrawal during this period of readjustment. However, smokers sensitivity to and awareness of withdrawal symptoms may depend upon the frequency and availability of nicotine intake prior to withdrawal inquiry.

Behavioral regulation, measured by changes in smoking topology, was strongly supported. All subjects extracted a significantly greater average and total puff volume of smoke from the low nicotine cigarettes, compared to the high nicotine cigarettes. The average puff volume is dependent upon the combined effect of puff intensity, duration and frequency. Since these latter variables, when considered individually, did not significantly effect smoking behavior for all subjects, it appears that an additive effect of these variables accounted for the greater average puff volume for the low nicotine cigarettes. This also appears to account for the greater total puff volume on the low nicotine cigarettes. In addition to puff intensity, duration and frequency, total number of cigarettes smoked determines total puff volume. Only half the subjects (older smokers) smoked more low than high nicotine cigarettes. It appears that the combined effect of at least two of the dependent smoking variables contributed to the

greater total puff volume on the low nicotine cigarettes. However, which combination of smoking variables resulted in a greater total puff volume for the low nicotine cigarettes can only be speculated. Jarvik et al. (1978) found that smokers compensate for reduced nicotine yield by increasing the total number of low nicotine cigarettes smoked, in addition to increasing the frequency of puffs taken on each cigarette in a two hour ad libitum smoking period. Over a long-term period (i.e., three months), smokers compensate for reduced nicotine yield by smoking low nicotine cigarettes with greater intensity than high nicotine cigarettes, without changes in total cigarette consumption (Creighton & Lewis, 1978). One hypothesis is that smokers have a characteristic style of smoking which is determined by puff intensity and duration. These smoking variables may be more resistant to change during a short-term period of reduced nicotine yield. Total number of cigarettes smoked and frequency of puffs may be more easily altered without changing the smoker's characteristic style of smoking. However, when given a long period of exposure to reduced nicotine yield, smokers may change their characteristic style more gradually. Consequently, the greater total puff volume on the low nicotine cigarettes found in the present study is most likely due to a combination of greater puff frequency and total number of low nicotine cigarettes smoked. The greater puff volume

on the low nicotine cigarettes was not limited to mouth-level intake since subjects had significantly higher COHb levels, reflecting inhalation, following the low nicotine session

Differences in smoking behavior, regardless of nicotine yield, were found as a function of age. Older smokers smoked more low than high nicotine cigarettes, though no more than younger subjects. Older smokers also had a greater puff frequency and total puff volume than younger smokers, regardless of nicotine yield. However, their average puff volume was not significantly greater than younger smokers. This set of findings suggest that the greater total puff volume achieved by older smokers was due to the greater frequency of puffs taken on each cigarette smoked. Consequently, older smokers appear to be distinguished from younger smokers in that they take more frequent puffs on cigarettes smoked. However, this greater puff frequency is offset by a reduction in the amount of smoke inhaled from each cigarette. Since the COHb levels, reflecting smoke inhalation, and plasma nicotine levels did not differ in young and old smokers, both groups inhaled similar amounts of cigarette smoke. On the basis of the Fagerstrom Tolerance Questionnaire, older smokers reported a similar degree of physical dependency to younger smokers. This is consistent with the findings of Bosse et al. (1980) that older smokers do not report greater physical addiction than younger smokers.

One hypothesis to account for smoking behavior in older smokers is the, as the number of years an individual smokes increases, the sensorimotor aspects of smoking become more reinforcing without necessarily increasing total cigarette consumption or physical dependency.

Physiological responses reflected nonregulation at the plasma nicotine level. Subjects had significantly higher heart rates following the high nicotine session as compared to the low nicotine session. Greater heart rate responses were due to the higher plasma nicotine levels following the high nicotine session. However, heart rate increase was not significantly greater following the first high nicotine cigarette compared with the first low nicotine cigarette. This finding was surprising since smokers had significantly higher plasma nicotine levels following the first high nicotine cigarette than for the first low nicotine cigarette. This suggests that following a 13 hour deprivation period, heart rate change is very sensitive to relatively small amounts of plasma nicotine. One hypothesis to account for this finding is that there is a ceiling effect for heart rate change in response to initial doses of nicotine. Plasma nicotine levels attained following the first high and low nicotine cigarettes may have been sufficient to bolster heart rate to its upper limit. Consequently, differences in heart rate did not occur between the first high and low nicotine cigarette. This

explanation could also account for the reason why heavy and light smokers did not differ in heart rate changes following the first cigarette smoked in each session. Heavy smokers had significantly higher plasma nicotine levels than light smokers following both the first high and low nicotine cigarette. This would suggest that heavy smokers should have greater heart rate increases following the first cigarette smoked. However, if an upper limit for heart rate increase was reached by both heavy and light smokers, no differences would occur.

Both heavy and light smokers had significantly greater skin temperature reduction over the high nicotine session. While heavy smokers had lower skin temperature at the end of the high nicotine session, compared with the end of the low nicotine session, light smokers did not. Light smokers, on the other hand, evidenced a significant drop in skin temperature within the high nicotine session. However, post session skin temperature values for light smokers were not significantly different for the high and low sessions. One explanation is that light smokers, in smoking less than heavy smokers, are more physiologically responsive than heavy smokers to small amounts of plasma nicotine. Consequently, light smokers showed equal degrees of skin temperature reduction over both the high and low nicotine sessions.

Responses to the Shiffman Withdrawal Scale indicate that all subjects experienced mild withdrawal following the nicotine deprivation period. This is consistent with the findings reported by Shiffman and Jarvik (1976) who found that smokers report only mild withdrawal following a one day period of abstinence. The present study also found no differences between heavy and light smokers in reported withdrawal following the overnight deprivation period. Shiffman and Jarvik (1976) also found no differences between heavy and light smokers on the Shiffman Withdrawal Scale, with the exception of the stimulation subscale. On this latter subscale heavy smokers reported greater stimulation than light smokers. Though heavy smokers in the present study reported greater stimulation than light smokers, this difference was not statistically significant. As previously discussed, the most striking finding from the Withdrawal Scale was that heavy smokers did not report greater withdrawal following the low nicotine session in which they did not regulate plasma nicotine levels.

Subjects reported significant reductions in craving, measured by the Schiffman Withdrawal craving subscale and the craving potentiometer. However, there was some discrepancy between the degree of craving reported by the two measures. Subjects reported greater craving using the potentiometer. The content of both craving measures is quite similar. In both measures subjects are asked

essentially how much they desire to smoke a cigarette. Subjects completed the Shiffman Withdrawal Scale approximately 10 minutes prior to the onset of the smoking session. Craving responses, using the potentiometer, were made at the onset of the smoking session, prior to actual smoking. Consequently, subjects may have reported greater craving using the latter measure due to the perceived availability of cigarettes. This hypothesis makes the assumption that reported craving for an addictive substance is correlated with the perceived availability of that substance. It may be physiologically adaptive to minimize perceived craving when the addictive substance is not available to reduce it. Another hypothesis regards the familiarity of the two craving measures. Subjects completed the Shiffman Withdrawal Scale on the day prior to the first smoking session. Consequently, responses to the Shiffman craving items prior to the smoking session may have been lowered due to previous responding to these items in a context of nonwithdrawal.

V. Conclusion

The present study was designed to test the boundary conditions of the nicotine addiction theory. Heavy and light smokers did not differ in nicotine regulation as was hypothesized. Neither heavy or light smokers regulated plasma nicotine levels, however, both groups demonstrated behavioral regulation. It was speculated that these results were due to the limitations of a one hour smoking

period in the laboratory. It is likely that smokers require an extended period of time, greater than a day, to make the necessary behavioral and physiological adjustments to reduced nicotine yield. Over such a period of readjustment, heavy smokers may well regulate plasma nicotine levels to a greater extent than light smokers. Consequently, the most limiting boundary condition of the nicotine regulation theory suggested by the present study is that nicotine regulation may be highly dependent upon the time period over which it is assessed. It is likely that the longer the period of readjustment, within limits, to reduced nicotine yield, the greater the degree of nicotine regulation. However, this study provides strong support for the consequences implied by the nicotine regulation theory. Subjects had significantly higher COHb levels following the low nicotine session, compared with the high nicotine session, reflecting greater carbon monoxide intake. Schachter's (1978) strongest defense in favor of acknowledging nicotine regulation is the dangerous health risk consequent to the recent trend towards low-tar, low-nicotine cigarettes. If smokers compensate for reduced nicotine yield by smoking more low nicotine cigarettes, they also increase carbon monoxide intake beyond that extracted from their usual brand of cigarettes. Since carbon monoxide is a major toxic element of cigarette smoke, posing serious health risks, the benefit of the low-tar, low-nicotine

cigarette trend becomes a hazard. Consequently, even though subjects did not regulate plasma nicotine levels, the dangerous consequences, implied in nicotine regulation, remain the same.

Further research is recommended in which nicotine regulation in heavy and light smokers is studied on a long-term basis. Such a study would eliminate the necessity of a pre smoking deprivation period to enhance nicotine regulation. In the present study, it was suggested that the 13 hour deprivation period reduced the likelihood of observing differences between heavy and light smokers, rather than increasing it. Should differences between heavy and light smokers in nicotine regulation occur in a long-term study, then differential treatment programs for smoking cessation would be warranted. Heavy smokers may require a more gradual reduction in nicotine intake for successful abstinence than light smokers.

There has been little research exploring the effects of age differences on smoking. The present study demonstrated clear differences between young and older smokers in smoking topology. These differences may break down over a longer period of time than was studied. Hence, a long-term study is also recommended to determine if differences in smoking style in young and older smokers is a robust phenomenon. If this finding is supported, it would suggest that the sensorimotor aspects of smoking

be given greater attention in smoking treatment programs for older smokers.

The major conclusion of the present study is that the underlying mechanisms which determine smoking behavior may not be amenable to short-term study. Smoking behavior is a multidimensional behavior determined by a wide variety of internal and external stimuli. Consequently, it may be best studied and understood in a molar, rather than a molecular context in which the patterns that constitute smoking behavior emerge.

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Appendix A

Consent Form

Behavioral Medicine Research Unit

I, _____, agree to participate as a subject in a research project on smoking conducted at the Behavioral Medicine Unit. I understand that various electrophysiological measurements of heart rate, skin temperature, muscle activity, etc. may be taken using electrodes or sensors placed on my skin. Urine samples will also determine nicotine levels at various times. The procedure consists of the presentation of lights or sounds at different times and involves smoking a few cigarettes in an attempt to learn about what happens when people smoke.

In some sessions, a small amount of blood will be taken over a few hours using a standard venipuncture procedure administered by a qualified medical technician. Other than possible bruises and temporary soreness in the arm, there are no special risks involved.

I have been assured that the procedures are harmless to me both physically and psychologically and do not increase the known risks of smoking. The testing procedure has been explained to my satisfaction. I understand that I may withdraw at any time without jeopardizing my right to treatment at the Behavioral Medicine Unit. I also understand that no information which reveals my identity will

be released without my permission.

I, the undersigned, have understood the above explanation and give consent to my voluntary participation in the forementioned research project.

Witnessed by

Signature of Subject

Date

This dissertation is numbered incorrectly, there is no page 130.

Appendix B

Shiffman Nicotine Withdrawal Scale

Description of Scale Scoring: This scale consists of 25 items which were scored on a 7-point scale with the following labeled points: "very definitely, definitely, probably, possibly, probably not, definitely not, very definitely not". The first and last labeled points corresponded to ratings of 1 and 7 respectively. The craving subscale consists of items 1, 8, 10, 14, 17, 20, and 22; the physical symptoms subscale consists of items 2, 12, 13, 23 and 25; the stimulation subscale consists of items 4, 6, 9, 11, 15, and 18; the psychological symptoms subscale consists of items 3, 5, 7, 16, 19, 21 and 24.

Directions: In response to each of the following items, please mark the appropriate box. We are interested in how you feel at the time you are filling out the questionnaire.

1. If you could smoke freely, would you like a cigarette this minute?
2. Is your heart beating faster than usual?
3. Do you feel more calm than usual?
4. Are you able to concentrate as well as usual?
5. Are you feeling very frustrated?
6. Do you feel wide awake?
7. Do you feel content?
8. If you had just eaten, would you want a cigarette?

(Shiffman Withdrawal Scale)

9. Do you feel more restless than usual?
10. Are you thinking of cigarettes more than usual?
11. Are you unusually sleepy for this time of day?
12. Do you have fluttery feelings in your chest right now?
13. Do you feel hungrier than usual for this time of day?
14. If you were permitted to smoke, would you refuse a cigarette right now?
15. Do you feel unusually tired?
16. Do you feel more tense than usual?
17. Do you miss a cigarette?
18. Do you feel alert?
19. Do you feel anxious?
20. Do you have an urge to smoke a cigarette right now?
21. Are you feeling irritable?
22. Would you find a cigarette unpleasant right now?
23. Are your hands shaky?
24. Are you less nervous than usual?
25. Is your appetite smaller than normal?

Appendix C

Subject Preparatory Instructions

You will be asked to come to this laboratory at the same time each day for three consecutive days. The first day you will be here for $\frac{1}{2}$ hour. On the second and third day you will be here for $1\frac{1}{2}$ hours each day. For your participation in the experiment you will be paid \$25.00. You will be paid this amount when it has been verified through urine analysis that you have followed the instructions.

On Day 1 you will be asked to come to the Behavioral Medicine Research Laboratory room 5E237, Building #5, V.A.M.C., 555 Willard Ave., Newington. At that time the experimenter will ask you for a urine sample. Your participation in the study will be explained and you will be given consent forms to sign and a questionnaire to take home and complete. You will be given cigarettes and asked to smoke these instead of your own brand for the rest of that day. You may smoke until 9:00 p.m., but YOU MUST NOT SMOKE ANY CIGARETTES AFTER THAT TIME. Please save all of your cigarette butts and unsmoked cigarettes and bring them with you to the experiment the next day.

On Day 2 you will return to the laboratory at 10:00 a.m. Please bring with you the completed questionnaire you were given on Day 1, butts and unsmoked cigarettes, and a

(Subject Preparatory Instructions)

Tee shirt to wear during the experiment. When you arrive the experimenter will ask you for a urine sample. Following this you will go through the actual experiment. After completion of the experiment, you will be given cigarettes to smoke for the rest of the day. Again, smoke only these cigarettes. DO NOT SMOKE AFTER 9:00 p.m.

On Day 3 you will return to the laboratory at 10:00 a.m. Remember to bring you cigarette butts and unsmoked cigarettes. After completion of the experiment, the experimenter will be glad to answer any questions you have.

It is most important that you follow these instructions exactly and especially that you do not smoke after 9:00 p.m. on Day 1 and Day 2. If our laboratory tests show that you have not followed these instructions you will not be paid until you come back and repeat the experimental session.

Appendix D
Smoking History

1. Name: _____ Date: _____
2. Address: _____
3. Social Security Number: _____
4. Telephone: Home: _____ 5. Business: _____
6. Age: _____ 7. Date of Birth: _____ 8. Birth Place _____
9. Married _____ Widowed _____ Divorced _____ Separated _____
Single _____
10. Occupation: _____
11. Education: Last year of education completed (circle)
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
MA PhD. Other
12. Name and phone number of person to contact in case of
emergency: Name: _____ Phone: _____
13. Which hand do you hold your cigarette with? _____
14. Number of cigarettes you smoked today? _____
15. Time since last cigarette _____
16. Number of cups of coffee you had today _____
17. Time since last cup of coffee _____
- (items 18-- 25: Fagerstrom Tolerance Questionnaire)
18. How many cigarettes a day do you smoke? _____
19. What brand do you smoke? _____
20. Do you inhale? (circle one) always sometimes never

(Smoking history)

21. Do you smoke more during the morning than during the rest of the day? _____
22. How soon after you wake up do you smoke your first cigarette? _____
23. Which cigarette would you hate to give up? _____
24. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., in church, at the library, cinema etc.)? _____
25. Do you smoke if you are so ill that you are in bed most of the day? _____

Personal Data

1. Health during childhood: List illnesses _____

2. Health during adolescence: List illnesses _____

3. What is your height? _____ Your weight? _____
4. What is your body build (check one)
Large _____ Medium _____ Small _____
5. Please list five of your favorite foods _____

6. Please list five of your least favorite foods _____

7. Estimate the number of cigarettes you smoke a day _____
a.) Type: 1. menthol non-filter 2. regular non-filter
3. menthol filter 4. filter (circle one)

(Smoking History)

8. If you smoke a pipe or cigars: How many pipes per day__
cigars per day _____
9. What is the maximum number of cigarettes you have
smoked per day for a period of at least one year_____
10. How many years have you been smoking? _____
11. How many times have you tried to stop smoking?_____
12. Which method has been more effective in stopping?
a.) gradual reduction_____
b.) stopping abruptly_____
c.) other (specify)_____
13. What was your longest interval of non-smoking in
days_____; months_____
14. Did you suffer changes in appetite when trying to stop
smoking? a.) yes_____ 1.) increased _____ 2.) decreased
b.) no _____
15. Did you suffer changes in mood? yes no
If "yes" rank below to indicate the changes you
experienced: (rank 1 = most frequent)
1. Happy_____	6. Energetic_____
2. Tired_____	7. Depressed_____
3. Angry_____	8. On edge_____
4. Tense_____	9. other (specify)_____
5. Shaky_____	
16. What made you resume smoking?_____

(Smoking History)

17. When did you first begin smoking? (year) _____

How old were you? _____

18. Where did you first begin smoking? (circle one)

1. Home

2. Junior High School

3. High School

4. With Friends

5. On Job

6. Other (specify) _____

19. Why did you first begin to smoke? _____

20. Is smoking a pleasure? Yes _____ No _____

If "yes" specify _____

Is smoking an escape from discomfort or displeasure?

yes no (circle one) If yes specify _____

21. What time of day do you smoke the most? (circle one)

a.) A.M. before noon

d.) Dinnertime

b.) Noon to 2 P.M.

e.) 7 P.M. to 9 P.M.

c.) 2 P.M. to 6 P.M.

f.) after 9 P.M.

22. List 5 places in rank order in which smoking is most likely to occur (e.g., kitchen, de, office, friend's house etc.; 1 = most likely)

1. _____

5. _____

2. _____

3. _____

4. _____

(Smoking History)

23. List 5 moods in rank order in which smoking is most likely to occur (e.g., relaxed, happy, anxious, angry, etc.; 1 = most likely)

1. _____
2. _____
3. _____
4. _____
5. _____

24. List 5 events in rank order in which smoking is most likely to occur (e.g., lunchtime, dinner, on arising, when driving, etc.; 1 = most likely)

1. _____
2. _____
3. _____
4. _____
5. _____

25. List 5 people with whom smoking is most likely to occur (e.g., spouse, friends, fellow workers, alone etc; 1 = most likely)

1. _____
2. _____
3. _____
4. _____
5. _____

(Smoking History)

26. Did you experience physical discomfort from smoking your first cigarette? Not at all_____ Slightly_____

Moderately_____ Extremely_____ I don'd recal_____

27. When you wake up in the morning, how long does it usually take you to light up your first ciagrette?

_____Hours _____Minutes

28. How many members of your immediate family smoke or have smoked? (circle)

mother smokes stopped smoking smoked when alive

father smokes stopped smoking smoked when alive

spouse smokes stopped smoking smoked when alive

sibling smokes stopped smoking smoked when alive

children smokes stopped smoking smoked when alive

29. Of the people you live with now, how many of them smoke?

30. What physical exercise do you get each week?_____

31. How active are you physically compared with other people of your age and occupation? (circle) more same less

32. Do you drink coffee regularly? yes no

If "yes"

a.) what brand_____

b.) on the average, how many cups/day_____

c.) at what time of day do you have your first cup_____

d.) under what circumstances_____

e.) in what places_____

(Smoking History)

f.) what is the longest time you go without coffee_____

g.) how do you feel when you skip your daily coffee_____

33. How do you feel before you drink coffee?_____

during _____

after _____

34. Does coffee drinking ever cause problems? yes no

If "yes", specify_____

35. Do you smoke while drinking coffee?_____

" " eat " " " _____

36. Do you take prescribed medications regularly? yes no

If "yes", specify_____

Frequency and reason for taking_____

37. Do you take recreational drugs regularly? yes no

If "yes", specify kind and amount_____

Frequency and reason for taking_____

38. List your five main fears:

1. _____

2. _____

3. _____

4. _____

5. _____

39. Underline any of the following that apply to you:

headaches

dizziness

fainting spells

(Smoking History)

palpitations	stomach trouble	no appetite
bowel disturbances	fatigue	insomnia
nightmares	take sedatives	alcoholism
feel tense	feel panicky	tremors
depressed	suicidal ideas	take drugs
unable to relax	sexual problems	shy with people
don't like weekends and vacations	over ambitious	can't make decisions
can't make friends	inferiority feel- ings	home conditions bad
can't keep a job	memory problems	unable to have a good time
financial problems		concentration diffi- culties
others		

33. Underline any of the following words which apply to you:

worthless, useless, a "nobody", "life is empty",
 inadequate, stupid, incompetent, naive, "can't do any-
 thing right", guilty, evil, morally wrong, hostile,
 horrible thoughts, full of hate, anxious, agitated,
 cowardly, unassertive, panicky, aggressive, ugly,
 deformed, unattractive, repulsive, depressed, lonely,
 unloved, misunderstood, bored, restless, confused,
 unconfident, in conflict, full of regrets, worthwhile,
 sympathetic, intelligent, attractive, confident,
 considerate, others: _____

(Smoking History)

(Smoking Restraint Question)

34. Are you presently trying to reduce the number of cigarettes you smoke daily for health reasons, financial reasons, etc.? a.) yes _____ b.) _____

If "yes", how many cigarettes a day have you cut out of your usual daily intake? _____

Appendix E

Subject Instructions for Experimental Sessions

This is a study to examine the effects of smoking on heart rate, skin temperature, muscle activity, and blood chemistry. The experiment will begin with the experimenter hooking up sensors to your fingers, face, and chest. A laboratory technician will then insert a small needle into your arm from which blood samples will be drawn. From that time on you must remain as still as possible.

The actual smoking session will begin when the black box to your right lights up and you hear a tone. From now on every time you hear a tone you should be alert to a change on the console to your right. After a few minutes you will again hear a tone and the window on the console to your right will light up and ask "Do you want a cigarette?" If you want a cigarette simply depress the lever next to the window. You will have 10 seconds to do this. The cigarette dispenser to your right will give you a cigarette if you have depressed the lever. You should put the cigarette in the cigarette holder, light the cigarette with the matches provided, and then smoke the cigarette in your normal fashion for the duration of the smoking trial. When the smoking period is over the green light will go off. Please put out your cigarette at this time. There will be 5 of these smoking trials, with 5 5-minute rest periods in between.

(Subject Instructions for Experimental Sessions)

between. If you choose not to smoke during any of these trials simply do not depress the lever.

Please adjust the dial at your right to reflect your desire for a cigarette. You should change this setting as often as your desire for a cigarette changes.

Appendix F

Group Means and Standard Deviations: Biochemical Measures

Urine pH

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X} =$	5.63	5.83	5.70	5.68
	S.D. =	.27	.41	.40	.55
Pre-Low	$\bar{X} =$	6.27	5.74	5.77	5.99
	S.D. =	.83	.30	.45	.54

*Plasma Nicotine: Pre First Cigarette - Post Last Cigarette

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	13.73	32.07	12.66	30.39
Nicotine	S.D. =	13.87	36.59	12.31	12.27
Low	$\bar{X} =$	4.33	2.00	5.42	7.80
Nicotine	S.D. =	3.97	2.78	4.09	5.85

*Plasma Nicotine: Pre-- Post First Cigarette

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	7.57	10.22	14.56	18.79
Nicotine	S.D. =	11.02	6.39	5.71	7.16
Low	$\bar{X} =$	2.77	3.00	3.96	8.42
Nicotine	S.D. =	2.70	4.06	4.60	1.56

* ng./ml.

(Appendix F Continued)

%COHb

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X}$ =	.86	1.44	1.26	1.38
Nicotine	S.D. =	.69	1.07	.86	.65
Low	$\bar{X}$ =	1.42	1.78	2.11	2.09
Nicotine	S.D. =	.86	1.40	1.83	.73

Appendix G

Group Means and Standard Deviations: Smoking Topology

Total Number of Cigarettes

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	2.80	2.50	3.80	3.40
Nicotine	S.D. =	1.64	1.00	1.30	.89
Low	$\bar{X} =$	3.69	2.75	4.20	3.40
Nicotine	S.D. =	1.34	.96	1.30	.89

Puff Frequency

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	14.54	7.93	11.80	7.21
Nicotine	S.D. =	3.65	4.19	4.63	1.47
Low	$\bar{X} =$	13.28	7.85	12.62	7.98
Nicotine	S.D. =	2.63	4.17	4.54	1.73

Puff Intensity*

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	44.62	60.03	77.67	75.04
Nicotine	S.D. =	15.53	18.98	45.64	33.17
Low	$\bar{X} =$	48.47	63.57	81.15	92.91
Nicotine	S.D. =	14.40	24.04	45.78	34.75

* liters per second

(Appendix G continued)

Puff Duration

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	3.73	2.20	2.35	2.43
Nicotine	S.D. =	.94	.71	.45	1.10
Low	$\bar{X} =$	3.54	2.70	2.79	2.52
Nicotine	S.D. =	1.09	.72	1.20	.89

Total Puff Volume*

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	5769.2	2437.7	4647.8	3248.8
Nicotine	S.D. =	2823.4	2359.7	1184.1	784.4
Low	$\bar{X} =$	7081.8	3077.3	6823.2	4623.0
Nicotine	S.D. =	4240.8	2766.1	2360.3	1324.6

Average Puff Volume*

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
High	$\bar{X} =$	109.94	107.99	139.96	143.17
Nicotine	S.D. =	62.18	32.89	96.99	55.58
Low	$\bar{X} =$	131.48	120.83	159.59	187.91
Nicotine	S.D. =	62.63	17.31	81.07	77.66

* liters

Appendix H

Group Means and Standard Deviations: Physiological Measures

*Heart Rate: Pre First Cigarette - Post Last Cigarette

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X}$ =	73.20	62.50	76.80	75.80
	S.D. =	10.26	1.91	10.63	24.74
Post-High	$\bar{X}$ =	80.40	82.00	88.00	83.20
	S.D. =	13.37	6.92	9.38	12.13
Pre-Low	$\bar{X}$ =	72.00	61.00	79.60	74.00
	S.D. =	10.19	7.74	20.70	8.12
Post-Low	$\bar{X}$ =	75.20	70.00	82.00	81.20
	S.D. =	10.82	17.28	12.57	11.71

*Heart Rate: Pre - Post First Cigarette

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X}$ =	73.20	62.50	76.80	75.80
	S.D. =	10.25	1.91	10.63	24.74
Post-High	$\bar{X}$ =	81.20	78.00	88.40	90.20
	S.D. =	12.93	16.24	10.13	17.41
Pre-Low	$\bar{X}$ =	72.00	61.00	79.60	74.00
	S.D. =	10.19	7.74	20.70	8.12
Post-Low	$\bar{X}$ =	75.60	73.00	90.40	87.20
	S.D. =	7.40	11.13	15.58	11.62

*BPM

(Appendix H continued)

Peripheral Skin Temperature (°C)

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X} =$	33.44	32.33	33.74	31.83
	S.D. =	1.81	2.47	.75	4.16
Post-High	$\bar{X} =$	31.52	29.68	33.68	29.86
	S.D. =	4.42	3.38	3.27	4.26
Pre-Low	$\bar{X} =$	32.21	31.47	33.75	34.34
	S.D. =	3.09	3.19	1.48	.81
Post-Low	$\bar{X} =$	31.84	28.17	33.64	34.19
	S.D. =	4.25	3.45	2.76	.29

Appendix I

Group Means and Standard Deviations: Subjective Measures

Shiffman Withdrawal Scale

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Baseline	$\bar{X}$ =	69.60	58.25	68.50	67.80
	S.D. =	9.76	8.22	11.35	5.58
Pre-High	$\bar{X}$ =	68.80	64.25	83.25	83.40
	S.D. =	9.62	11.92	21.57	6.65
Post-High	$\bar{X}$ =	61.00	61.00	69.50	63.40
	S.D. =	8.27	9.41	15.41	8.96
Pre-Low	$\bar{X}$ =	68.80	66.50	87.25	76.60
	S.D. =	10.91	23.61	16.15	9.31
Post-Low	$\bar{X}$ =	60.00	57.25	67.75	60.40
	S.D. =	14.58	11.61	12.44	10.45

Shiffman Physical Symptoms Subscale

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X}$ =	15.40	15.75	14.20	15.40
	S.D. =	1.67	2.21	.83	3.04
Post-High	$\bar{X}$ =	11.80	16.25	14.40	15.00
	S.D. =	6.14	2.06	2.07	3.00
Pre-Low	$\bar{X}$ =	13.40	14.75	13.80	16.60
	S.D. =	3.71	2.06	1.78	2.07
Post-Low	$\bar{X}$ =	13.00	11.50	15.00	15.20
	S.D. =	5.38	3.87	2.00	2.38

(Appendix I continued)

Shiffman Stimulation Subscale

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X}$ =	7.80	7.00	12.60	12.20
	S.D. =	1.92	2.16	5.27	4.32
Post-High	$\bar{X}$ =	11.80	10.00	14.60	11.60
	S.D. =	4.54	1.82	4.66	3.64
Pre-Low	$\bar{X}$ =	8.00	12.25	11.40	11.00
	S.D. =	4.84	7.71	8.67	4.30
Post-Low	$\bar{X}$ =	10.20	10.75	14.40	12.00
	S.D. =	3.27	5.56	5.94	5.09

Shiffman Psychological Symptoms Subscale

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X}$ =	15.20	16.00	21.00	20.40
	S.D. =	4.02	1.41	9.51	4.77
Post-High	$\bar{X}$ =	17.20	16.25	21.20	16.40
	S.D. =	5.67	2.50	5.71	3.84
Pre-Low	$\bar{X}$ =	14.00	17.75	22.80	18.00
	S.D. =	4.74	4.50	7.52	5.61
Post-Low	$\bar{X}$ =	15.40	18.25	20.00	15.20
	S.D. =	4.82	2.63	3.93	4.38

(Appendix I continued)

Shiffman Craving Subscale

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X}$ =	30.80	25.50	35.00	35.40
	S.D. =	9.73	7.93	9.69	3.57
Post-High	$\bar{X}$ =	18.20	18.50	20.40	20.00
	S.D. =	2.48	8.10	6.22	4.69
Pre-Low	$\bar{X}$ =	31.40	21.75	35.00	33.00
	S.D. =	7.36	12.44	3.53	3.67
Post-Low	$\bar{X}$ =	19.40	14.25	19.00	19.60
	S.D. =	6.80	4.71	8.06	6.46

Craving Measure

		<u>Light</u> <u>Old</u>	<u>Light</u> <u>Young</u>	<u>Heavy</u> <u>Old</u>	<u>Heavy</u> <u>Young</u>
Pre-High	$\bar{X}$ =	6.00	7.00	8.80	9.00
	S.D. =	4.06	2.16	1.64	1.41
Post-High	$\bar{X}$ =	3.00	5.50	3.40	3.00
	S.D. =	2.64	2.64	1.67	2.54
Pre-Low	$\bar{X}$ =	7.20	7.75	9.00	8.80
	S.D. =	4.38	1.50	1.41	1.30
Post-Low	$\bar{X}$ =	3.00	3.50	4.00	4.60
	S.D. =	2.64	3.10	1.41	2.70