EFFECTS OF NICOTINE PHARMACOLOGY AND STIMULUS EXPECTANCIES ON WITHDRAWAL AND ATTENTIONAL PROCESSING

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ABSTRACT

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Smoking is a major public health issue in the United States. People smoke for different reasons many of which go beyond the simple pharmacology of nicotine. The current study sought to clarify the independent and potentially interactive effects of nicotine pharmacology and smoking expectancies on self-reported withdrawal symptoms and sustained attention. To this end, the study employed a mixed design with a modified balanced placebo component, as well as repeated assessments (pre-smoking vs. post-smoking) of the Wisconsin Smoking Withdrawal Scale and the Rapid Visual

Information Processing task. This design created four groups of participants split by instructional set (told high-dose nicotine cigarette vs. told low-dose nicotine cigarette) and actual nicotine dose (low-dose vs. high-dose). For subjective measures of withdrawal, results indicated that expectancies, but not nicotine pharmacology, were associated with the alleviation of symptoms. Individuals expecting to receive a low-dose nicotine cigarette reported lower levels of withdrawal compared to those expecting to receive a high-dose nicotine cigarette. For sustained attention, nicotine pharmacology, but not expectancy, was associated with facilitated performance. Participants who received a high-dose nicotine cigarette exhibited decreased reaction times on the RVIP task. No interactions of expectancies and pharmacology were noted for withdrawal or sustained attention. The current findings underscore the importance of non-nicotinic factors in the maintenance of smoking behavior, particularly with regard to subjective perception of withdrawal symptoms. Though preliminary, these results suggest that modern smoking cessation techniques should take into account sensory factors that go beyond the pharmacological effects of nicotine addiction.

CHAPTER 1

INTRODUCTION AND RATIONALE

The literature is rich with examples of non-pharmacological reasons for engaging in addictive behaviors. For example, many studies have shown that individuals initiate and maintain their use of tobacco as a means of stress-relief (Parrott, 1998), and individuals frequently believe that smoking will enhance their thinking abilities (Spielberger, Reheiser, Carlos, & Foreyt, 2000; Spielberger & Reheiser, 2006). Other work suggests that some individuals may even smoke in order to have something to do with their hands (Jarvis, 2004). However, to date, research has not effectively separated the pharmacological effects of cigarettes, which contain many active substances in addition to nicotine, and smokers' expectancies about the effects of nicotine use. This gap in the literature exists partially because effective placebos for tobacco cigarettes have not been forthcoming (Robinson, Houtsmuller, Moolchan, & Pickworth, 2000).

Under ideal circumstances, the balanced placebo design (BPD) allows for the examination of independent and combined contributions of nicotine pharmacology and individual stimulus expectancies in the maintenance of smoking. However, this method is only as effective as the placebo that is chosen for the study. A new option, the partially de-nicotinized cigarette, may provide a satisfactory solution to this problem by providing the behavioral sensation of smoking while removing most of the pharmacological effects attributed to the addictive component of cigarettes, nicotine. Importantly, the presence of a small amount nicotine in the *partially* de-nicotinized cigarettes acts to prevent *severe*

nicotine withdrawal, which could otherwise lead participants to guess that they have been assigned to the placebo group.

Study Purpose and Experimental Design

The purpose of the current study was to expand upon the limited amount of tobacco research that has used a balanced placebo design to address the interaction between pharmacological and expectancy effects (Juliano & Brandon, 2002; Kelemen & Kaighobadi, 2007; Perkins et al., 2004, and Perkins et al., 2008) by comparing the effects of high-dose nicotine cigarettes and low-dose nicotine cigarettes on withdrawal and sustained attention after a smoking session. Thus, a 2 (actual nicotine content: high-dose vs. low-dose) X 2 (expectancy: expecting high-dose or expecting low-dose) design was utilized. This design resulted in the establishment of four experimental groups of participants split by instructional set (e.g., those who were told that they were given high-dose nicotine vs. those who were told that they were given low-dose nicotine) and actual nicotine dose (low-dose cigarette: 0.30 mg nicotine vs. high-dose cigarette: 0.60 mg nicotine). In statistical analyses, baseline measures of nicotine withdrawal (subjective measure: number of self-reported withdrawal symptoms) and sustained attention (objective measure: reaction time measures on a computerized task) were collected prior to the smoking session and were used as covariates in the analyses of data collected after the smoking session. This strategy allowed the researchers to examine main and interactive effects of pharmacology and expectancies while controlling for baseline levels of these measures.

Experimental Questions and Hypotheses

Two experimental questions were addressed: Question 1) will participants who are told that they have received a high dose of nicotine, and therefore are expecting a high dose of nicotine, report a lower level of withdrawal symptoms compared to those participants who are expecting a low dose of nicotine? Question 2) will participants who are expecting a high dose of nicotine exhibit better performance on a cognitive task after a smoking session compared to those expecting a low dose of nicotine?

For Question 1, based on previous research (Kelemen & Kaighobadi, 2007; Pickworth et al., 1999; Robinson et al., 2000; Shiffman et al., 2004), it was hypothesized that participants in the two groups expecting to receive a high dose of nicotine (that is, told high dose nicotine/received high dose nicotine and told high dose nicotine/received low dose nicotine) would report lower levels of withdrawal symptoms after smoking a cigarette compared to the other two conditions. Because self-reports of withdrawal symptoms are subjective in nature, it was predicted that expectancies (vs. pharmacology) would have a greater effect on withdrawal reports.

For Question 2, it was hypothesized that individuals who received a high-dose nicotine cigarette would perform more efficiently (e.g., exhibit quicker reaction times) on the computerized sustained attention task compared to individuals who received a low-dose nicotine cigarette (Heishman, Taylor & Henningfield, 1994; Levin, McClernon, & Rezvani, 2006; Wesnes & Warburton, 1983). Historically, studies have shown that the pharmacological effects of nicotine act to improve sustained attention, and for this reason, it was hypothesized that pharmacology would have a greater effect (vs. expectancies) on this objective measure of attention. Because no research to date has

documented the effects of nicotine expectancies on sustained attention, the potential role of instructional set on this variable remained an empirical question.

To summarize, the current study sought to fill a hole in the existing tobacco research literature by using a balanced placebo design to examine the separate and combined effects of smoking expectancies and nicotine pharmacology on subjective nicotine withdrawal and performance on a computerized sustained attention task. Such work provides valuable insight into the role that non-pharmacological factors play in the maintenance of smoking behavior and may ultimately contribute to the development of more successful smoking cessation strategies.

CHAPTER 2

NICOTINE

Cigarette smoking is the leading cause of preventable death in the United States. In fact, approximately 440,000 Americans die prematurely each year as a result of cigarette smoking (Julien, 2008). Nicotine, the primary pharmacological ingredient in cigarettes, plays a critical role in the reinforcement, and consequently, the maintenance of smoking behavior (Gross, Lee, & Stitzer, 1997; Juliano & Brandon, 2004; Julien 2008; Rose, 2006). However, nicotine is only one of the estimated 4,000 chemical constituents of the average cigarette (Gross, Lee, & Stitzer, 1997; Julien, 2008; Juliano & Brandon, 2004; Rose, 2006; US Department of Health and Human Services, 1998). Given the chemical complexity of cigarettes, any examination of the combined and independent effects of nicotine and non-nicotine factors in the role of smoking behavior must take into account an understanding of the psychopharmacology of tobacco use.

Nicotine Pharmacology

The amount of nicotine actually absorbed into the body as a result of smoking ranges from about 20% (Julien, 2008) to much as 90% (Armitage et al., 1975). When a cigarette is smoked, nicotine is suspended in the form of tar particles and quickly absorbed through the mouth, then through the small airways and alveoli of the lungs. Next, nicotine travels to the heart where the blood quickly becomes saturated with nicotine. This rapid absorption of nicotine into the bloodstream results in the perceived

"rush" that individuals feel after the first puff of a cigarette, and may partly explain the addictive nature of smoking. The nicotine-saturated blood then leaves the heart and is rapidly absorbed into the brain.

Once in the brain, nicotine activates the widely distributed nicotinic acetylcholine receptors. The activation of these receptors facilitates the release of dopamine, acetylcholine, and glutamate. The release of dopamine in the mesocorticolimbic system accounts for the behavioral reinforcement, stimulant, antidepressant, and addictive properties of nicotine (Julien, 2008). The activation of the acetylcholinergic systems of the brain produces cognitive arousal and facilitation of attentional functions, including sustained attention, defined as a fundamental component of attention characterized by one's readiness to detect rarely and unpredictably occurring signals over prolonged periods of time (Sarter, Givens, & Bruno, 2001).

After passing through the brain and stimulating the nicotinic acetylcholine receptors, which are distributed densely in the thalamus and frontal region of the human brain (Kimes et al., 2003), nicotine continues its journey through the blood stream and is distributed to other tissues in the body, such as the liver. Nicotine is both absorbed and eliminated rapidly from the body. Approximately 80 to 90 percent of the administered nicotine is metabolized by the liver. The lungs and kidneys eliminate the remaining 10 to 20 percent. The elimination half-life of nicotine is approximately 2 hours, but can vary between 1 and 4 hours (Benowitz, 1986). Because of nicotine's relatively short elimination half-life, chronic smokers must administer nicotine frequently in order to avoid withdrawal symptoms. Thus, in order to evaluate the effects of nicotine on

attention, a researcher must administer tasks or questionnaires fairly quickly after the nicotine is ingested.

Although the nicotine content of a cigarette is contingent on the manufacturer, as well as the strain (e.g. burley, cavendish, corojo, etc.) of tobacco used (Benowitz, 1986; US Department of Health and Human Services, 1998), the level of nicotine consumed by a given individual varies widely and depends on a number of different factors, such as puff volume, depth of inhalation, extent of dilution with room air, length of time the smoke is held in the lungs, puffing rate, intensity of puffing, and the total number of cigarettes consumed in one smoking episode (Benowitz, 1986; Julien, 2008). Studies have shown that a smoker will take larger puffs and smoke more quickly when given a low-yield nicotine cigarette (Herning, Jones, Bachman, & Mines, 1981) compared to a high-yield nicotine cigarette. Thus, a smoker has the ability to adjust his or her smoking behavior in order to regulate the level of nicotine in the bloodstream.

Accordingly, smokers may unconsciously adjust their technique in order to reach a steady-state level of nicotine in the brain, which produces the desired effects (e.g. cognitive arousal and facilitation of attention) while avoiding the unpleasant effects associated with very high (e.g. dizziness) or very low (e.g. withdrawal effects) nicotine concentrations. Thus, for tobacco research, it is critical to recognize smokers' manipulations of smoking conditions, as similar blood levels may be obtained from both low-yield and high-yield cigarettes, depending on smoking technique. In addition to the pharmacological actions of nicotine, researchers must also understand the cognitive and behavioral effects of withdrawal associated with the ceasing of smoking behavior.

Nicotine Withdrawal

For many smokers, nicotine administration induces stimulation and pleasure, while simultaneously reducing stress and anxiety (Benowitz, 2008). Therefore, smoking behavior may act as a means to control mood and modulate arousal. Importantly, among chronic smokers, the termination of nicotine administration results in withdrawal effects, including irritability, depressed mood, craving for nicotine, anxiety, restless, and an inability to concentrate (Benowitz, 2008; Jorenby et al., 1996). Withdrawal can be defined as, "a syndrome of behavioral, affective, cognitive, and physiological symptoms, typically transient, emerging upon cessation or reduction of tobacco use, and causing distress or impairment" (Shiffman, West, & Gilbert, 2004, p. 600). Thus, nicotine addiction can be described as a combination of positive (i.e., enhanced mood and cognitive arousal) and negative (i.e., relief of withdrawal symptoms) reinforcements.

The stimulation of nicotinic acetylcholine receptors in the brain (as described above) facilitates the release of dopamine in the ventral tegmental area of the midbrain and the nucleus accumbens, areas that are associated with the "reward pathway" (Julien, 2008). Thus, when nicotine is administered, the nicotinic acetylcholine receptors are stimulated, which increases the release of dopamine, creating a pleasurable feeling. The reinforcement of smoking involves the repeated pairing of nicotine administrations with subsequent feelings of reward. However, prolonged nicotine administration can lead to a low steady-state concentration of nicotine in the brain that decreases the responsiveness of the nicotinic acetylcholine receptors, a phenomenon known as desensitization (Dani & Heinemann, 1996). Withdrawal effects are experienced between cigarettes, during sleep, and/or under conditions of abstinence; these effects occur because nicotine levels drop

and a portion of the once inactive receptors recover to a responsive state and become hyperexcitable. For this reason, smokers frequently report that the first cigarette smoked after an extended period of abstinence is particularly rewarding (Heatherton, Kozlowski, Frecker & Fagerstrom, 1991).

As with many addictive substances, the subjective effects of withdrawal are often the opposite of the acute nicotine administration effects experienced immediately after smoking. During normal patterns of cigarette smoking, these effects may wax and wane throughout the day with repeated periods of smoking and withdrawal (Hughes & Hatsukami, 1986). In order to examine the acute effects of nicotine withdrawal, the current study utilized the Wisconsin Smoking Withdrawal Scale (WSWS; Welsch, et al., 1999) at two separate time points throughout the study. The first time point served as the baseline assessment, and the second time point was used to measure the subjective effects of withdrawal after nicotine administration (see Table 1). Thus, the current study examined differences in withdrawal symptoms between groups immediately after smoking, while controlling for baseline differences (e.g., using Time 1 as a covariate in the analyses of the main and interactive effects of instructional set and nicotine dose on withdrawal reports at Time 2).

Nicotine's Effects on Attention

Despite the health risks, many smokers perceive that cigarettes provide certain psychological benefits. The role of nicotine in the enhancement of cognition has been studied extensively (Heishman, Taylor & Henningfield, 1994; Levin, McClernon, & Rezvani, 2006), and most research indicates that cognitive arousal is one of the reasons people engage in smoking behavior (Brandon & Baker, 1991; Provost & Woodward,

1991; Spielberger & Reheiser, 2006; West & Hajek, 2004). More specifically, nicotine has been shown to potentiate certain attentional processes, such as sustained attention and rapid information processing (Rose, 2006).

Attention is a complex cognitive function, making it difficult to characterize for research purposes. It can be divided into 4 different categories: focused, sustained, selective, and divided. Focused attention requires an individual to attend to a specific task for *less than* 10 minutes at a time; whereas sustained attention requires participants to focus on a specific task for a continual amount of time, usually *at least* 10 minutes (Heishman et al., 1994). Selective attention is the ability to pay attention to a target stimulus while simultaneously ignoring distractions. Finally, divided attention is the ability to respond simultaneously to multiple tasks.

Research examining the effects of nicotine on different types of attention have generally indicated that nicotine has a positive effect on sustained attention and either no effect or a negative effect on selective attention (Heishman et al., 1994). Nicotine exerts its cognitive effects by increasing activity in the brain regions that are associated with mechanisms of sustained attention, such as the frontal and parietal lobes, as well as the thalamus (Coull, 1998; Lawrence, Ross, & Stein, 2002). More specifically, sustained attention is thought to be primarily facilitated by the function of the frontal and parietal cortices (Coull, Frackowiak, & Frith, 1998; Lawrence et al., 2002), by increasing blood flow in these regions of the brain (Pardo, Fox, & Raichle, 1991; Sarter, Givens, & Bruno, 2001). For instance, the rapid visual information-processing (RVIP) task is a commonly used task for the assessment of sustained attentional processing, which asks participants to respond to three consecutive odd (or even) digits in a row for an extended period of

time (Wesnes & Warburton, 1983). This task has been shown to activate the frontal and parietal cortexes of the brain (Coull, Frackowiak, & Frith, 1998; Lawrence et al., 2002). Based on previous research evaluating the effects of nicotine on cognitive processing (Ceballos, Tivis, Lawton-Craddock, & Nixon, 2006; Coull et al., 1998; Heishman et al., 1994; Lawrence et al., 2002), the current study used the RVIP task to assess the effects of nicotine pharmacology and expectancies on sustained attention.

The RVIP task has been used extensively in the field of nicotine research; however, results on the effects of nicotine on the RVIP have been somewhat inconsistent. These discrepancies might be due in part to methodological differences in study designs. Overall, a majority of studies have found that nicotine improves both reaction time and the number of correct responses on the RVIP task when compared to a placebo (Edwards, Wesnes, Warburton, & Gale, 1985; Revell, 1988; Wesnes & Warburton, 1983). Nevertheless, the results of one study have indicated that nicotine does *not* have an effect on reaction time or number of correct responses on the RVIP task (Michel, Hasenfratz, Nil & Battig, 1988; Wesnes & Revell, 1984). However, it is important to note that the two studies that failed to find improved performance on the RVIP as a result of nicotine administration used nicotine *gum* rather than cigarettes. As compared to cigarettes, nicotine gum lacks many of the expectancies associated with smoking and also results in a slower absorption rate. Thus, this methodological difference may have contributed significantly to the differential findings in the aforementioned work.

Nicotine Replacement Therapy (NRT)

Studies examining the interplay between nicotine expectancies and pharmacology have obvious applications to the "real world". For instance, smoking cessation therapies present one practical application of such research. Traditional NRT products, such as gums, transdermal patches, inhalers, nasal sprays, and lozenges (Fiore, Jaén, & Baker, 2008; Jorenby et al., 1996; Rigotti, 2002) were developed with the intention of providing a controlled administration of nicotine in order to alleviate withdrawal symptoms during smoking cessation. Even though these products deliver just as much nicotine as a cigarette and may even increase abstinence rates compared to a placebo (Fiore et al., 2008), research has generally shown that they have low utilization (Hajek et al., 1999) and dismal long-term rates of success (Benowitz, 1986; Bohadana, Nilsson, Rasmussen, & Martinet, 2000; Stapleton et al., 1995). One pharmacological explanation for the lack of success of NRT products is that they typically fail to provide the initial "spike" in nicotine concentration levels in the bloodstream that a smoker receives when inhaling a cigarette. Because this factor is thought to contribute to the reinforcing nature of cigarette smoking, more successful NRT products tend to be administered in a way that creates the same (or similar) acute effects as cigarettes. However, in addition to the "spike", it is obvious that factors other than the administration method of nicotine contribute to the reinforcing properties of smoking cigarettes. These additional factors may be related to the various expectancies that smokers tend to have about the act of smoking itself.

Compared to traditional NRT, an opposite approach is utilized by newer therapeutics such as de-nicotinized cigarettes. In de-nicotinized cigarettes, the

pharmacological component of the cigarette is removed, but the behavioral factors surrounding cigarette use remain. De-nicotinized cigarettes have the same look, feel, taste, and draw characteristics as a "regular" cigarette, while providing comparable tar and CO levels (Pickworth, Fant, Nelson, Rohrer, & Henningfield, 1999). Research has shown that de-nicotinized cigarettes may be effective in producing the desired effects that experienced smokers *expect* from smoking tobacco. In one study, participants who smoked de-nicotinized cigarettes reported a reduction in subjective feelings of withdrawal symptoms and cravings similar to participants who smoked cigarettes with nicotine (Gross et al., 1997). Thus, de-nicotinized cigarettes represent an important innovation in tobacco research that may help researchers to pinpoint the elusive relationship between nicotine pharmacology and various behavioral aspects of addiction, and the impact of this relationship on the maintenance of smoking behavior.

Unfortunately, fully de-nicotinized cigarettes (e.g., Quest level 3 cigarettes, less than 0.05mg nicotine; Liggett Vector Brands, Inc.) have recently been discontinued by the manufacturer due to a lack of consumer and health advocacy support that would aid in making these types of products a viable candidate for smoking cessation. Thus, as an alternative, the current study utilized partially de-nicotinized cigarettes (e.g., Quest level 2 cigarettes, 0.30mg nicotine; Liggett Vector Brands, Inc.). One aim of the current study was to examine factors other than nicotine that are likely to be involved in the maintenance of smoking behavior, and to that end, the current study created an expectancy effect using a modified balanced placebo design. Conceivably, resulting data could contribute to the development of newer smoking cessation techniques that take advantage of the non-pharmacological effects involved in nicotine addiction. For

instance, rather than traditional methods of patches or gum, *cigarettes* with decreasing levels of nicotine may be utilized in order to wean individuals off nicotine, while still providing the behavioral reinforcement of the maintenance of smoking behavior. Once the individual has adjusted to smoking a de-nicotinized cigarette, cessation may be facilitated as the pharmacological phenomenon of nicotine withdrawal will no longer be a significant factor in the addiction.

CHAPTER 3

SMOKING EXPECTANCIES

The act of smoking a cigarette is a complex process comprised not only of pharmacological factors, but also cognitive and behavioral components. Research on the addictiveness of cigarettes has generally failed to acknowledge the importance of behavioral aspects, such as social reinforcement and the handling of a cigarette (Gross et al., 1997), as well as cognitive aspects such as expectancies and attention (Levin, McClernon & Rezvani, 2006). One aim of the current study was to examine the impact of stimulus expectancies on withdrawal and the facilitation of attentional functioning.

Definitions

As previously noted, balanced placebo designs are an effective means of isolating the pharmacological components of a drug from the cognitive issues surrounding addiction. One non-pharmacological aspect of smoking, which can be effectively manipulated through the balanced placebo design, is a participant's expectancies. This design allows for researchers to examine whether the outcome of smoking a cigarette (e.g., impact on withdrawal or attention) is significantly influenced by the nicotine content of a cigarette, by the perceived outcomes of smoking a cigarette, or by some interaction of these two components. Several types of expectancies have been noted in tobacco research. For instance, stimulus expectancy can be defined as one's belief about the drug content of a substance, in this case nicotine in a cigarette (Kelemen, 2008). Stimulus expectancies may be manipulated by instructional set.

On the other hand, outcome expectancy, defined as "the anticipation of automatic, subjective, and behavioral responses to particular situational cues" (Kirsch, 1985, p. 825), is another issue that plays a role in the addiction process. Historically, social learning theory (Bandura, 1977) attempted to explain human social behavior as an interaction between cognitive, behavioral, and environmental influences. More recently, response expectancy theory (Kirsch, 1985) expanded on social learning theory to distinguish response (or outcome) expectancy from self-efficacy. When applied to tobacco research, outcome expectancies are the outcomes that an individual predicts will occur following the consumption of a cigarette. These outcome expectancies can often be more powerful than the actual pharmacological actions of the substance being used. For instance, many smokers endorse the notion that cigarettes will help control negative affect, craving, and weight relative to other nicotine replacement therapies (Juliano & Brandon, 2004), even though these NRT products generally contain similar levels of nicotine as cigarettes. To measure outcome expectancies in the current study, the researchers utilized the Smoking Consequences Questionnaire (SCQ; Brandon & Baker, 1991), which assesses expectancies in terms of positive reinforcement/sensory satisfaction associated with smoking, negative reinforcement/negative affect reduction associated with smoking, and smoking's effects on appetite/weight control. The total score derived from this instrument is thought to reflect participants' overall level of expectancies about smoking.

Effects of Expectancies on Nicotine Withdrawal

Smoking is a learned behavior. Over time, smokers learn to self-administer nicotine in order to enhance their mood and alleviate symptoms of withdrawal. In addition, non-nicotinic, conditioned sensory effects associated with smoking have also

been shown to reduce subjective cravings and withdrawal (Pickworth et al., 1999; Robinson et al., 2000; Shiffman et al., 2004). Such effects are typically measured via a placebo. Placebos are substances containing *no* pharmacologically active ingredients. These substances are used as experimental controls in studies designed to determine the effectiveness of pharmacologically active substances. Therefore, placebo effects generally correspond with an individuals' knowledge or beliefs about the kind of active ingredient they expect that they are going to receive. These expectancies can be formed through classical conditioning (Kirsch, 1985). In terms of smoking behavior, smoking a nicotine cigarette serves as the conditioning trial and the subjective effects associated with smoking the nicotine cigarette can be thought of as the conditioned stimuli. When the active ingredient, nicotine, is removed, the smoker may still experience the subjective effects (i.e., alleviation of withdrawal symptoms) because past experiences with smoking have always been associated with these subjective effects. Thus, this conditioned association may lead the smoker to expect the subjective effects linked to the smoking of a cigarette.

Research has shown that the alleviation of withdrawal symptoms can be seen even in the absence of nicotine administration (Gross et al., 1997; Pickworth et al., 1999). In particular, one recent study compared the effects of nicotine and stimulus expectancies on the subjective effects of smoking in the presence of a stressor (Juilano & Brandon, 2002). Using a research design similar to the current study, four experimental conditions were established: told nicotine/given nicotine cigarette, told nicotine/received de-nicotinized cigarette, told no nicotine/given nicotine cigarette, and told no nicotine/given de-

nicotinized cigarette. In addition, the researchers induced anxiety by informing participants that they would be required to engage in public speaking. Results indicated that stimulus expectancies were sufficient to reduce smoking urges. Therefore, informing a participant that a cigarette contains high levels of nicotine may lead to a reduction in withdrawal symptoms and drug cravings, even if the cigarette contains only low levels of nicotine. Similar results were found by Gottlieb and colleagues (1987) in a study examining the effects of stimulus expectancies about nicotine on the relief of withdrawal symptoms. In this study, regardless of the actual nicotine levels they received, participants who believed they were receiving nicotine gum reported fewer physical withdrawal symptoms compared to those who thought they there receiving a placebo (Gottlieb, Killen, Marlatt, & Taylor, 1987). Taken together, these studies suggest that, compared to the actual pharmacology of nicotine, smoking expectancies may have an even stronger impact on the relief of withdrawal symptoms under some conditions. Alcohol and caffeine research studies have indicated similar patterns regarding the effects of stimulus expectancies on withdrawal, regardless of the pharmacological potency of the administered substance (Kirsch, 1985; Knight, Barbaree, & Boland, 1986).

Effects of Smoking Expectancies on Attention

Although the stimulant properties of nicotine have been established (Benowitz, 1986; Rigotti, 2002; Rose, 2006), less is known about the role non-pharmacological smoking components play in attentional tasks. To the researcher's knowledge, no studies to date have examined the influence of nicotine stimulus expectancies on the facilitation of sustained attentional functioning. In fact, only one study has attempted to determine

the role of nicotine expectancies on cognitive functioning (Kelemen & Kaighobadi, 2007). However, this study focused on memory rather than on attention and failed to reveal significant effects of instructional set/expectancies on the facilitation of short-term memory (via a Swahili-English vocabulary recall task). In addition, Kelemen & Kaighobadi's findings were limited, as baseline performance on the memory task was not assessed. Thus, the researchers were unable to examine the impact of instruction set/expectancies while controlling for baseline memory function.

Because the effects of nicotine's stimulus expectancies have not been evaluated in terms of sustained attention, hypotheses regarding the nature of the relationships between these variables in the current study were not declared. However, research has shown that the *pharmacological* effects of nicotine may enhance performance on sustained attention tasks (Wesnes & Warburton, 1983). Therefore, it was expected that individuals receiving a high-dose nicotine cigarette would exhibit better performance on the RVIP task compared to those participants who received a low-dose nicotine cigarette.

As noted, the effects of the pharmacology of nicotine on withdrawal symptoms and sustained attention have been documented, as have the effects of stimulus expectancies on withdrawal. However, no studies have using the balanced placebo design to examine the potential impact of pharmacology *and* expectancies on withdrawal *and* sustained attention. Thus, the current study represents both replication and extension of the tobacco research literature.

CHAPTER 4

BALANCED PLACEBO DESIGN

In order to examine the independent and potentially interactive effects of nicotine and expectancies on cigarette administration, the current study utilized a modified balanced placebo design (BPD). In this design, participants were divided into two groups: those who were told they would receive a cigarette containing a high dose of nicotine and those who were told they would receive a cigarette containing a low dose of nicotine. Within those two groups, half of the participants were given a high-dose nicotine cigarette and half were given a low-dose nicotine cigarette. Thus, this design resulted in four conditions: 1) told high-dose nicotine/received high-dose nicotine, 2) told high-dose nicotine/received low-dose nicotine, 3) told low-dose nicotine/received low-dose nicotine, and 4) told low-dose nicotine/received high-dose nicotine.

The group differences between the two conditions that are given a low-dose nicotine cigarette (e.g., told high-dose nicotine/received low-dose nicotine and told low-dose nicotine/received low-dose nicotine) are known as placebo effects. The placebo effect essentially captures the impact of expecting a drug in the absence of pharmacological actions (Perkins et al., 2003). Similarly, the group differences between the two conditions in which participants actually receive a high-dose of nicotine (e.g., told high-dose nicotine/received high-dose nicotine and told low-dose nicotine/received high-dose nicotine) are referred to as anti-placebo effects. All four of these conditions

are necessary in order to assess the cognitive and behavioral effects of smoking and the pharmacological effects of the nicotine (Perkins et al., 2003).

The balanced placebo design is preferable to a traditional double-blind design because the latter tends to overemphasize pharmacological effects, while simultaneously underestimating the role of behavioral and cognitive factors (Kelemen, 2008; Perkins et al., 2003; Sutton, 1991). Although this design has been used extensively in alcohol research (Martin & Sayette, 1993), to date, relatively few studies in tobacco research have utilized the balanced placebo design (Juliano & Brandon, 2002; Kelemen & Kaighobadi, 2007; Perkins et al., 2004; Perkins et al., 2008).

For instance, a recent study by Kelemen and Kaighobadi (2007) used a balanced placebo design to examine these issues with respect to the subjective impact of cigarettes on craving, satisfaction, and short-term memory. Results indicate that both nicotine pharmacology and expectancies play a significant role in the subjective effects of cigarettes. Pharmacological components reduced smoking urges, while expectancies reduced subjective tension. The combined effects of pharmacology and expectancy were associated with an increase in wakefulness, concentration, relaxation, cigarette satisfaction, and hunger reduction, although pharmacology had a stronger impact than expectancies on these measures, which were assessed using the Cigarette Evaluation Scale (Westman, Levin, & Rose, 1992). However, no significant effects of nicotine pharmacology or smoking expectancy were found in terms of short-term memory facilitation. The results of this study underscore the significance of non-nicotinic factors in the reinforcing effects of smoking cigarettes. Thus, one aim of the current study was to expand upon Kelemen and Kaghobadi's (2007) research by examining the individual

and interactive effects of nicotine pharmacology and stimulus expectancies on the subjective effects of withdrawal *and* sustained attention.

Methodological Issues Associated with the Balanced Placebo Design

Despite the potential advantages of the balanced placebo design, there are also several caveats that must be taken into account. The first methodological issue is the deceptive nature of the balanced placebo design. It is difficult to convince participants that they have consumed a de-nicotinized cigarette when, in fact, they have not. To address this issue, Sutton (1991) suggests using a smaller dose of the pharmacologically active substance (e.g., the use of a "light" cigarette compared to a "regular" cigarette). The instructional set for a smaller dose of the drug is more believable than an instructional set for a large dose of the drug. For this reason, the current study utilized a "high-dose nicotine cigarette", Quest 1 (0.60mg of nicotine; Liggett Vector Brands, Inc.), that was comparable in nicotine and tar content to a typical "light" cigarette (i.e., Marlboro Lights, 0.50mg of nicotine). The other deceptive condition (e.g., told nicotine/not given nicotine) is less problematic because people generally have little experience with de-nicotinized cigarettes; thus, social desirability or experimental factors may lead participants to believe they smoked a cigarette that contains nicotine, regardless of the true nicotine content (Hull & Bond, 1986; Perkins et al., 2003).

The second major issue is the extent of participants' prior experiences with inactive forms of a given drug. When examining expectancies, the role of learning in participants' perceptions of drug use outcomes should be acknowledged by the researcher. For instance, the conditioning of the subjective effects of alcohol and cigarettes may differ significantly from one another because of the fact that, in the course

of everyday life, participants are much more likely to encounter non-alcoholic beverages than non-nicotine cigarettes. Thus, heavy drinkers might be hyperaware of the pharmacological effects of alcohol because they have experience in drinking non-alcoholic beverages. Consequently, the placebo effect might not be robust in alcohol research. When applied to smokers, who may have little or no previous exposure to low-dose nicotine cigarettes, smoking behavior may be invariably linked to the pharmacological actions of nicotine, creating a falsely robust placebo effect (Perkins et al., 2003; Sutton, 1991).

Aim of the Study

In summary, the current study expanded upon the work of Kelemen & Kaighobadi (2007) as well as the literature regarding nicotine and attention by comparing the effects of high-dose nicotine vs. low-dose nicotine cigarettes on withdrawal and attentional functioning. A 2 (nicotine content: high-dose or low-dose) X 2 (expectancy: told high-dose nicotine or told low-dose nicotine) design was employed, resulting in the establishment of four experimental groups: 1) told high-dose nicotine/received high-dose nicotine, told high-dose nicotine/received low-dose nicotine, told low-dose nicotine/received high-dose nicotine and told low-dose nicotine/received low-dose nicotine. Based on previous research, it was hypothesized that participants within the high-dose nicotine expectancy group would report fewer withdrawal symptoms after smoking a cigarette compared to those within the low-dose nicotine expectancy group. Further, with regard to attentional functions, it was hypothesized that individuals who received a high-dose of nicotine would perform more efficiently on the attentional task

(e.g., quicker reaction time to targets) compared to those who received a low-dose of nicotine.

CHAPTER 5

METHODS

Participants

Participants were 23 healthy smokers who reported consuming at least 10 cigarettes a day over the past year (Ceballos, Tivis, Prather, & Nixon, 2008). Participants were recruited through flyers placed throughout the university, word of mouth, and an advertisement placed on a website featuring "classifieds". Participants were given a choice of compensation for participating: either $10 in cash or extra credit in a Psychology course.

A total of four participants were excluded from the study. According to previous research, the successful manipulation of expectancies about drugs and their effects is a vital component of studies utilizing a BPD (Martin & Sayette, 1993). In the current study, participants were asked the following question immediately after smoking: "What type of cigarette did you just smoke?" Answer choices were, "High-dose nicotine cigarette" or "Low-dose nicotine cigarette." Based on recommendations from past researchers (Martin & Sayette, 1993), two participants were excluded because their answers indicated that they did not believe the instructional manipulation. Furthermore, two additional participants were eliminated because of their responses on the computerized attention task. Both participants eliminated for this reason were extreme

outliers (±3 standard deviations from the overall mean) in terms of false positive responses, which indicated either that they were not attending to the tasks, or that they did not understand the task instructions. Thus, the final sample was composed of 19 participants (9 male).

Nicotine Administration (Cigarettes)

Two types of cigarettes, a high-dose nicotine cigarette and a low-dose nicotine cigarette, were used in this study. Quest 1 cigarettes (Liggett Vector Brands, Inc.) were chosen as the high-dose option and contain 0.60 mg of nicotine in each cigarette. Quest 2 cigarettes (Liggett Vector Brands, Inc.) were chosen as the low-dose option and contain less that 0.30 mg of nicotine per cigarette. Both cigarettes were non-mentholated and were identical in tar content (10 mg) and size (85mm). These cigarettes were tested by Liggett Vector Brands, Inc using tar and nicotine detection methods approved by the Federal Trade Commission (US Department of Health and Human Services 1997).

Self-Report Measures

Smoking Consequences Questionnaire. The participants' outcome expectancies of smoking a cigarette were assessed using the Smoking Consequences Questionnaire (SCQ; Brandon & Baker, 1991). This 50-item questionnaire was used as an index to assess nicotine outcome expectancies associated with negative consequences, positive and negative reinforcements, and appetite control associated with smoking a cigarette. In the SCQ, respondents are presented with a series of statements and asked to indicate their level of agreement using a 5-point Likert-type scale (Example item: "Smoking calms me down when I feel nervous."). This measure has a high degree of validity for use within adult populations, with alpha ranging from 0.83 to 0.95 (Wetter et al., 1994). For

statistical purposes, a total SCQ score was included in the analysis of participants' background characteristics to detect any group differences in baseline expectancies.

Wisconsin Smoking Withdrawal Scale. Tobacco withdrawal symptoms were assessed using the Wisconsin Smoking Withdrawal Scale (WSWS; Welsch, Smith, Wetter, Jorenby, Fiore, & Baker, 1999). The WSWS is a 28-item measure in which respondents are presented with a series of statements and asked to indicate their level of agreement using a 5-point Likert-type scale (Example item: "It is hard to pay attention to things."). The WSWS is comprised of statements assessing the major symptoms of nicotine withdrawal syndrome, including withdrawal-related effects on levels of anger, anxiety, concentration, craving, hunger, sadness and sleep. The WSWS has been validated in previous research, with alpha levels of 0.90 for the full scale (Hendricks, Ditre, Drobes, & Brandon, 2006; Welsch et al., 1999). A total WSWS score was examined as the dependent variable to address experimental Question #1.

Attentional Task

Rapid Visual Information Processing Task. The Rapid Visual Information Processing task (RVIP; Wesnes & Warburton, 1983) assesses cognitive efficiency with respect to sustained attention. In this task, random numerical digits (i.e., "1" "2" and "3") were presented one at a time on the center of a computer screen at a rate of 150 digits per minute and participants were asked to press a button when either three consecutive even or odd digits (counterbalanced conditions) appeared on the screen. Each digit remained on the screen for 200 ms, followed by a fixation screen with a centrally-located cross that remained on the screen for 200 ms. During each administration of the task, participants were presented with 3,000 trials, 120 of which belonged to the target sequences. Both the

digit and the cross were black in color and presented on a completely white screen in size 72 font. Superlab 4.0 (San Pedro, CA) was utilized to present the RVIP task. Data for both accuracy (e.g., number of correct responses), and latency (in milliseconds) of correct responses were collected. However, due to response characteristics of the participant sample, reaction time was used as the sole dependent variable in final analyses for experimental Question #2 (for additional details see results section).

Design and Procedure

The study utilized a 2 x 2 between-subjects modified balanced placebo design with repeated assessments (pre-smoking session and post-smoking session). The two between-subjects variables were instructional set received (told high-dose nicotine or told low-dose nicotine) and type of cigarette received (containing high-dose nicotine or containing low-dose nicotine). The repeated measures component involved the assessment of withdrawal symptoms and performance on a computerized attentional task at two time points (e.g., before and after a smoking session). Participants were randomly assigned to one of four conditions: 1) told high-dose nicotine/received high-dose nicotine, 2) told high-dose nicotine/received low-dose nicotine, 3) told low-dose nicotine/received high-dose nicotine, and 4) told low-dose nicotine/received low-dose nicotine. Procedures for human subjects and consent materials were approved by the Institutional Review Board at Texas State University–San Marcos.

Upon entering the lab, informed consent was obtained and a carbon monoxide (CO) breath analysis was performed using a Vitalograph Breath CO Monitor (Vitalograph, Lenexa, KS) to verify nicotine abstinence. Participants were asked to smoke normally on the day before participating, but to abstain from nicotine and caffeine

products for 8 hours prior to participating on the day of the study. To ensure compliance with these instructions, participants underwent breath analysis at two time points: 1) on the day prior to testing and 2) on the actual experiment day. On the day of the experiment, participants were rescheduled if their abstinent CO levels had not decreased by at least 50% or more from their non-abstinent CO levels of the previous day (Ceballos, Tivis, Lawton-Craddock, & Nixon, 2006). All participants met this criterion.

Participants then completed questionnaires assessing basic demographic information, as well as the Smoking Consequences Questionnaire (SCQ; Brandon & Baker, 1991) and the Wisconsin Smoking Withdrawal Scale (WSWS, Welsch et al., 1999; baseline administration). Following the completion of self-report measures, the participants were then presented with the computerized RVIP task (Wesnes & Warburton, 1983; baseline administration). Next, the participants were given an instructional set to inform them of the type of cigarette they would be receiving, either high-dose nicotine or low-dose nicotine.

The experimenter then escorted the participant to an appropriate outdoor smoking area and verified that the entire cigarette was consumed. All participants smoked the entire cigarette. Upon returning to the lab, the participant completed the instructional manipulation check (as described above) and the RVIP task for a second time. Finally, the participants completed a second administration of the WSWS before being debriefed and leaving the laboratory (See Table 1 below).

Table 1. Experimental timetable.					
9* to 9:20am	9:20am	9:35am	9:40am	9:45am	10:00am
CO Analysis, Demographics, SCQ, Baseline WSWS	Baseline RVIP	Smoking session	Manipulation Check	RVIP	WSWS, Debriefing, Exit Lab

*Table is organized according to a 9am testing schedule.

Data Analysis

Age, years of education, hours of nicotine deprivation prior to study participation (e.g., time since last cigarette), and smoking outcome expectancies (as assessed by the total score on the SCQ) were examined across the four conditions to detect any group differences in background characteristics (See Table 2).

For the main analyses of interest, separate analyses of covariance (ANCOVAs) were performed for post-smoking assessments of withdrawal symptoms (e.g., WSWS) and RVIP performance. Inspection of the accuracy data for the RVIP task indicated low variability in the number of correct responses (low accuracy overall); whereas, reaction time data appeared to be a more sensitive measure of expectancy and dose-related effects. For this reason, subsequent analyses focused exclusively on reaction time as the measure of RVIP task performance.

For each ANCOVA, the two between-subjects factors were instructional set received (told high-dose nicotine or low-dose nicotine) and type of cigarette received (containing high-dose nicotine or low-dose nicotine). The covariate was the baseline (e.g. "pre-smoking") assessment of either the WSWS or reaction time on the RVIP. In each ANCOVA, the dependent variable was the "post-smoking" assessment of the WSWS or the RVIP reaction time.

CHAPTER 6

RESULTS

Background Characteristics

The final sample of 19 participants (9 male) had a mean age of 23.1 years (S.D. = 8.3). Participants were predominantly Caucasian (84.2%) and had a mean education level of 14.3 years (S.D. = 1.5). Participants were well matched on all background variables and no significant group differences were noted on these factors. The means of the background characteristics are displayed by group assignment in Table 2. The told high-dose nicotine/given high-dose nicotine group had a mean age that was slightly higher than that of the other groups, as a result of one individual who was significantly older than the overall mean age of participants in the study. Due to a small sample size (N=19), this participant was retained for further analyses after comparing her data to the rest of the sample and validating that it did not appear to be significantly different.

Table 2. Background characteristics of participants by condition.

Condition	Instructional set received			
	Told high nicotine		Told low nicotine	
	Given high nic (n=5)	Given low nic (n=4)	Given high nic (n=6)	Given low nic (n=4)
Demographic Variable				
Age	19.2 (1.1)	28.0 (16.0)	23.8 (7.5)	21 8 (1 0)
Education (in years)	13.2 (0.8)	14.3 (1.0)	14.5 (2.3)	15.0 (1.4)
Hours since last cigarette	11.6 (2.2)	11.8 (2 4)	11.4 (4 5)	11.6 (3 1)
Outcome expectancies (SCQ)	175.8 (14.4)	173.7 (17.0)	198.6 (26.3)	174.3 (14.9)
SCQ–Negative Consequences	58 2 (8.0)	66.3 (4.7)	60 5 (11 8)	60.5 (9 5)
SCQ–Positive Reinforcements	56.4 (4 7)	53 0 (5 3)	61 4 (10.2)	56 8 (1.7)

Note values in parentheses are standard deviations

Nicotine Withdrawal

Withdrawal was assessed using the Wisconsin Smoking Withdrawal Scale. A series of 2 (cigarette dose) x 2 (instruction set) ANCOVAs were conducted on the WSWS. The covariate was the total score on the pre-smoking WSWS assessment, the fixed factors were cigarette dose and instruction set, and the dependent variables was total WSWS response after the smoking session.

There was a significant main effect of instruction set on withdrawal symptoms. When controlling for pre-smoking baseline assessment of withdrawal, the groups that were told that they received a low-dose nicotine cigarette (M = 3.059) reported fewer withdrawal symptoms compared to participants in the conditions that were expecting a

high-dose nicotine cigarette (M = 3.115; $F(1, 18) = 9.72$; $p = .01$) This finding is illustrated in Figure 1.

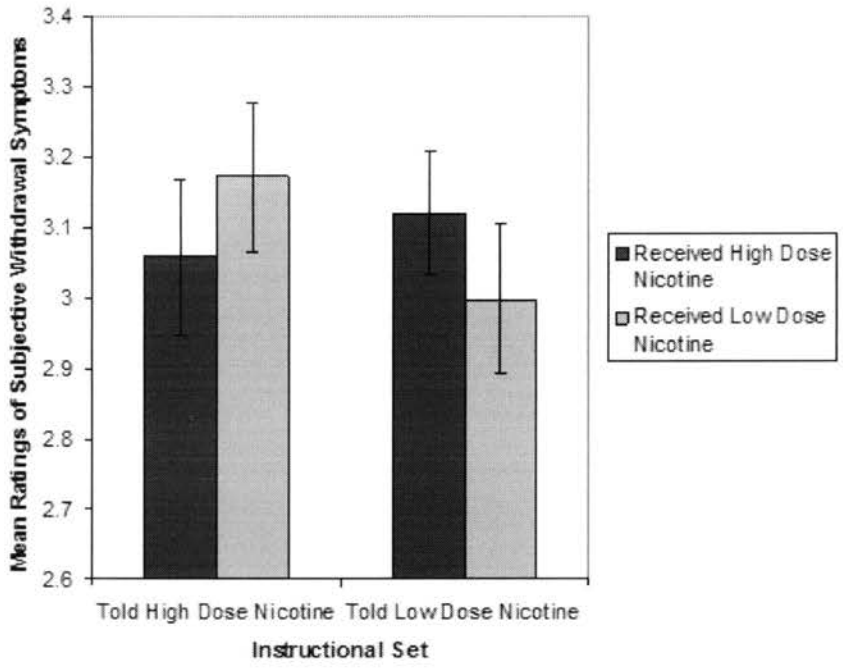

Figure 1. Subjective Rating of Nicotine Withdrawal by condition.

Sustained Attention

The computerized RVIP task was used to assess the effects of nicotine and expectancies on sustained attention. Data were analyzed via a 2 (cigarette dose) x 2 (instruction set) ANCOVAs, conducted on performance on the RVIP (e.g. reaction time; in milliseconds; correct responses only). The pre-smoking reaction time was entered as a co-variate, while the post-smoking reaction time served as the dependent measure.

Results indicated a significant main effect of actual nicotine dose on reaction time ($F(1, 18) = 9.41$; $p = .01$) for the RVIP task, when controlling for the baseline assessment. The conditions that actually received a high-dose nicotine cigarette (e.g.,

told high-dose nicotine/received high-dose nicotine and told low-dose nicotine/received high-dose nicotine) displayed faster response times on the post-smoking RVIP assessment compared to the conditions that received a low-dose nicotine cigarette (See Figure 2 below).

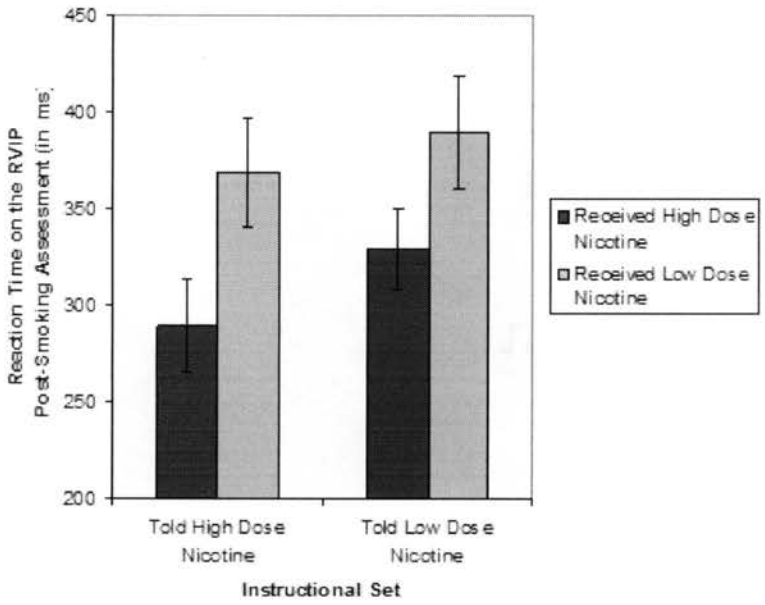

Figure 2. Reaction Time on the RVIP at Post-Smoking Assessment by condition.

CHAPTER 7

DISCUSSION

The current study used a modified balanced placebo design to assess the separate and interactive effects of expectancy and pharmacology on cigarette-related withdrawal symptoms and attentional functioning. Results indicated that withdrawal and sustained attention were differentially influenced by expectancies and pharmacology, and no interactions of expectancies and pharmacology were noted.

The first research question asked, "Will participants who are told that they have received a high amount of nicotine, and therefore are expecting a high amount of nicotine, report a lower level of withdrawal symptoms compared to those participants who are expecting a low amount of nicotine?" It was hypothesized that participants in the two groups that were expecting to receive a high dose of nicotine (told high-dose nicotine/received high-dose nicotine and told high-dose nicotine/received low-dose nicotine) would report a lower level of withdrawal symptoms after smoking a cigarette compared to the other two conditions. However, results indicated that expectancy (e.g., instructional set) alone influenced the subjective effects of withdrawal, with participants expecting the low-dose nicotine cigarette reporting lower levels of subjective withdrawal symptoms.

The finding of a main effect of instructional set on subjective withdrawal symptoms is partially supported by a study conducted by Pickworth and collegues (1999), which found that both de-nicotinized and nicotine cigarettes reduced subjective

ratings of tobacco craving and withdrawal. Although instructional set was not a variable in this design, participants reported similar withdrawal alleviation regardless of the nicotine level. Both this finding and the results of the current study indicate that some factor, other than nicotine, may mediate the effects of smoking behavior.

An early study by Herning and colleagues (1981) may provide one explanation for the lack of a pharmacological effect. In Herning's study, smokers were found to compensate for a lack of nicotine in their cigarettes by increasing the depth of inhalation when smoking. Thus, in the current study, smokers who were told that they would receive a low dose of nicotine may have increased their pulmonary effort by taking deeper breaths while smoking; whereas smokers who were told that they would receive a high dose of nicotine may have smoked "normally" because they did not perceive a need to compensate for the lack of nicotine. Thus, with adjustment of their pulmonary effort, it may be possible that participants who were expecting to receive a low-dose nicotine cigarette ingested the same amount of nicotine (or even more nicotine) than those who were expecting to receive a high-dose nicotine cigarette. Future research assessing pharmacology, instructions, and behavioral aspects (i.e., inhalation depth and frequency) associated with smoking would be necessary to investigate this claim.

The second question focused on cigarettes' role in the enhancement of attentional functioning by asking: "Will participants who are expecting a high-dose of nicotine exhibit enhanced sustained attention after a smoking session compared to those expecting a low-dose of nicotine?" It was hypothesized that individuals who received a high-dose of nicotine would perform more efficiently on the RVIP (e.g., exhibit a quicker reaction time to targets) compared to those who received a low-dose of nicotine. Results

supported this hypothesis by indicating that nicotine pharmacology, *not* expectancy, influenced participants' performance on the sustained attention task. Those who were given the high-dose nicotine cigarette displayed quicker reaction times on the RVIP task compared to those who were given a low-dose nicotine cigarette, when controlling for pre-smoking baseline assessments.

The results of the current study suggest that pharmacology may have had a stronger effect on sustained attention than did expectancy. The role of nicotine pharmacology on cognitive vigilance is historically well-documented (Edwards, Wesnes, Warburton, & Gale, 1986; Revell, 1988; Wesnes & Warburton, 1984).

Furthermore, nicotine enhanced attention regardless of the instructions given to the participants. Similarly, Kelemen and Kaighobadi (2007) failed to find an effect of instructional set on memory. Taken together, these findings may indicate that expectancies have the ability to influence subjective behavioral aspects (i.e., smoking to alleviate withdrawal symptoms), but not the cognitive aspects associated with nicotine addiction (i.e., cognitive arousal). Future research should examine the impact of expectancies on other types of attention and memory. In addition, it should be noted that the enhancement of sustained attention in the current study could be attributed to the reversal of a withdrawal-induced deficit, rather than absolute improvements in cognitive processing. Further examination of this issue (e.g., facilitation vs. withdrawal alleviation) was beyond the scope of the current study.

Limitations

The most concerning limitation of the current study was the small sample size (N=19), which negatively impacted the power of the statistical analyses. Although the researcher did adjust the significance values to reflect the number of ANCOVA's run (e.g., testing the analyses at a significance level of p=0.025 instead of the standard p=0.05) the results of this study should be replicated using a larger sample size. It should also be noted that the homogeneity of variance assumption was not met in either of the models, at a significance level of p=0.05).

In addition to increasing the sample size, future studies should consider the use of alternative strategies. For instance, ideally, the balanced placebo design should employ completely de-nicotinized cigarettes in order to more thoroughly separate the pharmacological and non-pharmacological effects of smoking. Unfortunately, the manufacturer of Quest 3 de-nicotinized cigarettes (Liggett Vector Brands, Inc.) discontinued the production of this item in the months before data collection ensued; thus, out of necessity, researchers were forced to use only partially de-nicotinized cigarettes in the current project.

In addition, the use of an airflow measuring system would have enabled the researcher to control for such variables as puff volume and duration, number of puffs, and interpuff interval. However, due to the cost-prohibitive nature of a thesis project, we were unable to employ an airflow measuring system in the current study. Future research examining the relationship between expectancy and pharmacology should take into account these potentially confounding variables.

Conclusions

The current study sought to expand upon the relatively limited amount of tobacco research that has addressed *both* the pharmacological and expectancy effects on withdrawal and attentional functioning. Results supported the notion that expectancies are an important aspect of the smoking experience and may influence smokers' subjective experience of nicotine withdrawal. These findings could have implications for smoking cessation. Modern cessation strategies, such as nicotine replacement therapies, have been largely unsuccessful (Benowitz, 1986; Bohadana et al., 2000; Fiore et al., 2008; Hajek et al., 1999; Stapleton et al., 1995), as they only address the nicotinic components of cigarette addiction while ignoring other aspects involved in the maintenance of smoking behavior. Ultimately, a better understanding of the relationship between smoking stimulus expectancies and the pharmacological aspects of nicotine consumption could lead to improvements in smoking cessation techniques, as well as strategies to prevent smoking initiation.

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