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Impulsivity As A Predictor Of Smoking Cessation Outcomes In Bupropion Treatment Of Community Corrections Smokers

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IMPULSIVITY AS A PREDICTOR OF SMOKING CESSATION OUTCOMES IN BUPROPION TREATMENT OF COMMUNITY CORRECTIONS SMOKERS

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MEDICAL CLINICAL PSYCHOLOGY

ABSTRACT

Cigarette smoking is the leading cause of death and disability in the United States. Prevalence of smoking among participants in community corrections far exceeds those in the general population. The purpose of the study was to examine predictors of smoking cessation outcome among community correction participants who were enrolled in a randomized control trial that used bupropion to treat tobacco dependence. This study found that inattention was a significant barrier to treatment. Specifically, performance on measures of attention including number of omissions errors on the Conner's Continuous Performance Task – Second Edition (CPT-II) and time to complete Trails A were the best indicators of negative treatment outcome. It is possible that inattentive smokers may benefit from higher doses of bupropion to quit smoking or alternative forms of treatment. Impulsivity, on the other hand, was found to not interfere with treatment. Those who engage in criminal activities may demonstrate higher levels of impulsivity than the general population. By enrolling only those under criminal justice supervision, our sample may have demonstrated a limited range of impulsivity necessary to detect problem levels of impulsivity that may interfere with treatment outcome. It is recommended that future studies enroll a matched control group of smokers from the general population for comparison.

Keywords: bupropion, inattention, impulsivity, smoking cessation, community corrections, criminal justice system

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This study was approved by the University of Alabama at Birmingham Institutional Review Board (Protocol # F101011001) on 10/27/2010. The data from the study was merged with data from a longitudinal Randomized Control Trial entitled "Integrated Smoking Cessation Treatment for Low Income Community Corrections Smokers" (UAB IRB protocol number: F090430005) headed by Karen Cropsey, Psy.D. The study was an ancillary research project to Dr. Cropsey's R01 (National Institutes of Health, National Cancer Institute, 5 years) supported by Dr. Cropsey's departmental start-up funds and conducted in the Substance Abuse Center at the University of Alabama at Birmingham. All materials for the study (i.e., computers and software) are the property of UAB. Data was collected by trained research staff under the supervision of Adam Perkins. Special thanks to UAB students and staff for collecting data including Brendan Clark, Kimberly Crouch, Michael Jensen, and my dissertation committee members: Drs. Karen Cropsey – chair, Adrienne Lahti, Kristine Lokken, Jesse Milby, and Xiao Zhang.

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INTRODUCTION

OVERVIEW

Smoking remains the leading cause of death and disability in the United States (Garrett, Dube, Trosclair, Caraballo, & Pechacek, 2011) and more research is needed to understand the impediments of successful cessation. Impulsivity is a characteristic that has been linked with both smoking behavior outcomes as well as criminal behavior. Criminal justice populations smoke at rates 3-4 higher than the general population (Cropsey, Jones-Whaley, Jackson, & Hale, 2010) and few studies have examined factors associated with successful cessation in this high risk population. This study assesses impulsivity in smokers under community corrections supervision who were actively participating in a Randomized Control Trial (RCT) that used bupropion (i.e., generic Zyban®) to treat tobacco use. The study merged treatment outcome data from the RCT with baseline impulsivity and attention measures to examine predictors of smoking cessation outcomes at the end of treatment. In particular, the study examined various aspects of impulsivity at baseline that might further impede treatment in this at risk population.

Impulsivity, in general, increases tobacco use, reduces the effectiveness of treatment, and increases risk for relapse (Covey, Manubay, Jiang, Nortick, & Palumbo, 2008; Doran, Spring, McChargue, Pergadia, & Richmond, 2004; Krishnan-Sarin, et al., 2007; Mitchell, 2004; VanderVeen, Cohen, Cukrowicz, & Trotter, 2008). Previous findings support the belief that bupropion used for smoking cessation reduces inattention

but does not improve problems of impulsivity (Acheson & de Wit, 2008). Therefore, it was expected that participants who were less impulsive would respond better to treatment than more impulsive individuals. In addition, higher levels of impulsiveness were expected to interfere with medication adherence, thereby reducing the positive effect the medication would have on problems of inattention. In short, individuals who were both impulsive and inattentive were likely to benefit the least from bupropion with or without counseling because of the cyclic interaction between the two deficits.

PREVALENCE OF TOBACCO USE IN CRIMINAL JUSTICE POPULATIONS

Smoking rates are extremely high among participants in the community justice system especially in comparison to the general population. Approximately 60% - 80% of incarcerated individuals use some form of tobacco (Kauffman, Ferketich, Murray, Bellair, & Wewers, 2011). Seventy-two percent of female prisoners in the Mississippi Department of Corrections were current smokers in 2004 (Cropsey, Eldridge, & Ladner, 2004). While only one study has examined smoking among the community correction population, smoking rates are virtually the same (72.3%) as for inmates (Cropsey, et al., 2010). However, smoking rates among the general population are considerably lower and have been steadily declining since 1964 from 40% - 20% (Garrett, et al., 2011).

Despite the increasing awareness among the general population about the harmful effects of smoking since the early 1970s (Center for Disease Control and Prevention, 2010; CDC) smoking is still responsible for 443,000 premature deaths each year (Garrett, et al., 2011) and remains the most preventable cause of death and disability in the United State (Garrett, et al., 2011). According to the 2004 Surgeon General's Report, it is

causally associated with numerous cancers and cardiovascular events as well as the exacerbation of other health problems (e.g., asthma, diabetes, upper respiratory infections, etc.; Stewart, et al., 2008).

With increased education, legislation, and effective treatments surrounding smoking cessation, smoking is now generally concentrated in vulnerable and other disenfranchised populations (Lee, Cutler, & Burns, 2004; Lee, Turner, Burns, & Lee, 2007). For example, Himelhoch and colleagues (2004) found that 60.5% of those with chronic mental illness were current smokers. Similarly, while smokers with mental illness only comprise only 7.1% of the U.S. population, they consume more than a third of all cigarettes sold in the U.S. (Grant, Hasin, Chou, Stinson, & Dawson, 2004). This suggests that the medical consequences of smoking are more severe among individuals with mental illness. Similarly, individuals with substance use disorders are also more likely to be daily smokers (Duhig, Cavallo, McKee, George, & Krishnan-Sarin, 2005; Morissette, et al., 2008). Psychiatric and substance use disorders are common among criminal justice involved individuals (Fazel & Danesh, 2002) with about 36.5% of the correctional population diagnosed with a psychiatric disorder and 74% with a substance use disorder over their lifetime (Sung, Mahoney, & Mellow, 2011). While on parole, 20.4% of individuals demonstrate having an active mental health disorder (Louden & Skeem, 2011). In short, a high prevalence of psychiatric and substance use disorders in criminal justice populations suggest higher smoking rates and greater barriers to quitting smoking. Therefore, the need to provide interventions that are modified to the individuals within this population is very important to improve cessation rates and overall to reduce long-term health care cost.

TREATMENT

Various interventions have been proven to be effective smoking cessation treatments (Fiore & Jaen, 2008); these include medications, counseling, and a combination of both. Counseling may be brief (i.e., approximately 5 minutes) or intensive (i.e., 30 minutes or more) and include techniques that may be exclusively behavioral or cognitive but typically are a mixture of both such as strategies utilized in Cognitive Behavioral Therapy. Behavioral tools commonly used in smoking cessation include such methods as self-monitoring (Peters & Hughes, 2009), substituting behavior (Kaplan, 1996) , and web-based intervention (Norman, McIntosh, Selby, & Eysenbach, 2008). Cognitive techniques include education training/awareness (Etter, 2007), thought stopping (Lamontagne, Gagnon, Trudel, & Boisvert, 1978), and motivation interviewing (Hettema & Hendricks, 2010).

Medication for smoking cessation treatment, approved by the FDA and outlined in the Clinical Practice Guidelines (Fiore & Jaen, 2008), has increased the availability and efficacy of smoking cessation treatment. Recommended treatment includes Nicotine Replacement Therapy (NRT; polacrilex gum, transdermal patches, lozenges, nasal spray, and inhalers) and Non-Nicotine Products such as bupropion (Zyban®) and varenicline (Chantix®). Type and dosing may vary among individuals to increase effectiveness. Medications, which are not approved by the FDA for smoking cessation treatment, include clonidine and nortriptyline but the smoking cessation benefits are undermined by the potential for side-effects. Other forms of treatment are available (e.g., hypnosis and

acupuncture) but have been shown to be no more effective than placebos (Fiore & Jaen, 2008).

Regarding medication, varenicline is the most effective first line treatment available; however, it is not available in generic form and is much less cost-effective than its non-nicotine predecessor, bupropion. With a prescription and without using insurance, Walmart Pharmacies offers a $9.00 smoking cessation starter kit which includes a 10 day supply of 17 bupropion ER tablets and also offers refills of bupropion ER in a 30 day, 60 tablet supply for $27.00 (Walmart, 2009). In a meta-analysis by Eisenberg and colleagues (2008), varenicline was found to be the most efficacious (OR 2.41) followed by bupropion SR (OR 2.07) when compared to placebo. The Institute on Safe Medication Practices (ISMP) released October 23, 2008 also noted more adverse side-effects associated with varenicline than bupropion.

Bupropion SR was used in the current RCT with a community corrections population for three reasons: 1) affordability; 2) few side effects; and 3) more smokers in community corrections had previously used NRT unsuccessfully in the past than any other pharmacotherapy (e.g., patches or gum; Cropsey, et al., 2010).

While research and implementation of smoking interventions are prevalent among the general population, smoking inventions have been examined less frequently in criminal justice populations. The first study of smoking cessation treatment in a correctional setting (Cropsey, et al., 2010) used nicotine patches and group counseling to treat female inmates and found similar smoking cessation rates to the general population at one year follow-up. While this one study demonstrated the efficacy of providing smoking cessation treatment to incarcerated populations, no studies have examined

smoking cessation treatment with individuals under community corrections supervision. The current RCT is the first study to provide smoking cessation treatment onsite where individuals under community corrections supervision come for monitoring.

COMMUNITY CORRECTIONS POPULATION

The Bureau of Justice Statistics (BJS, 2010) reported that over 7.2 million adults in the United States are under some form of local, state, or federal supervision (e.g., parole, probation, or imprisonment) and that the U.S. has more citizens incarcerated than any other country. The community corrections population, which is the largest sector of the correctional justice system, has quadrupled from 1980 (1.12 million persons) to 2009 (5 million; Glaze, Bonczar, & Zhang, 2010). For the first time in 2009, there was a decrease in participants in community corrections by 0.7% or approximately 48,800 people since the BJS started reporting on this population since 1980. By 2009, there were 4.2 individuals on probation and slightly over 819,000 on parole or under a mandated correctional condition after being released from prison (Glaze, 2010). Health care costs for participants in the correctional system have grown six-fold over twenty years, increasing the financial burden already imposed on each state (Legislative Analyst's Office, 2010). A substantial economic drain is attributed to smoking-related illnesses such as heart, respiratory, and circulatory problems (Beck & Maruschak, 2001). Despite limits or bans on smoking within prison, most inmates (approximately 97%) once released, relapse and resume smoking (Lincoln, et al., 2009).

Participants in the community corrections system typically are comprised of low income adults (19 years old and older) who are under criminal justice supervision, most

of whom are subject to random urine drug screens and need to contact their case managers regularly. According to a recent study, more than half of community corrections participants who smoke were interested in cessation assistance, including 63% of women and 56% of men (Cropsey, et al., 2010). Providing treatment to this population onsite has the opportunity to reach many low income smokers who would not typically access the medical system for this service. Further, providing cessation services at this point of care could be an accessible and efficient means to deliver treatment for both patient and provider.

Only one study (Cropsey, et al., 2010) has examined characteristics of smokers under community corrections supervision. Incarcerated individuals demonstrate smoking rates that are 3 to 4 times higher than the general population with 70 to 80% of men and 42 to 91% of women who smoke (Cropsey, et al., 2008; Durrah & Rosenberg, 2004; Foley, Proescholdbell, Herndon Malek, & Johnson, 2010; Hammond & Emmons, 2005; Kauffman, et al., 2011; Nijhawan, Salloway, Nunn, Poshkus, & Clarke, 2010) compared to about 21% of adults in the general population who are current smokers (Garrett, et al., 2011). Integrating smoking cessation and other health services at this point of contact can be an important way to reach low income individuals who need such services. Furthermore, providing intervention services at the point of contact may reduce the racial disparity since about 60% of this population is African-American and these individuals may not access health services in more traditional ways (Cropsey, et al., 2010).

In summary, few smoking cessation treatments have been implemented among correctional populations, all of which have been conducted with inmates. Results from these studies (Cropsey, et al., 2008) show promising results that suggest that successful

smoking interventions should be provided to incarcerated smokers. Further, these promising results may generalize to those under community correction supervision but additional studies are needed in this area.

IMPULSIVITY

Impulsivity is a range of behavioral responses that include acting without forethought or acting out in lieu of negative consequences or at the expense of losing positive gains (Zermatten, Van der Linden, d'Acremont, Jermann, & Bechara, 2005). Impulsivity is the key attribute associated with the use of both illicit (e.g., heroin) and legal drugs (e.g., tobacco and alcohol; Bornovalova, Daughters, Hernandez, Richards, & Lejuez, 2005; MacKillop & Kahler, 2009). This response style also serves as a hallmark characteristic of Attention Deficit Hyperactivity Disorder (ADHD), specifically the hyperactive/impulsive type or combined type (i.e., impulsive and inattention; Toplak, et al., 2009).

Multiple facets of impulsivity are distinct (Spillane, Smith, & Kahler, 2010) suggesting that impulsivity is a complex term that impacts many different behaviors and cognitions (e.g.., response inhibition and impulsive decision-making); however, all suggest a form of urgency to engage in behavior or thoughts without pre-planning regardless of the consequences. Therefore, it is important to examine various acts of impulsivity to cover the full gamut of the domain. Furthermore, it is important to discuss inattention when talking about impulsivity because the domains appear to reside upon a single continuum rather than exist as two completely separate entities: one refers to over responding and the other refers to the lack of response (Kenemans, et al., 2005).

Types of impulsiveness, as well as types of inattention, are defined by the immediacy of a response. In regards to impulsivity, short (or acute) responses may encompass a behavioral reflex to overreact to stimuli, hence the term hyperactivity. While acute inattention refers to an individual's inability to follow a particular task (or lacking the skill to attend to simple stimuli; Johnstone, Watt, & Dimoska, 2010).

Long term impulsivity indicates cognitive-behavioral dysfunction such as decision-making where there is preference for immediate gratification. Long-term attention would best encompass sustained attention or the ability to stay attentive to stimuli consistently overtime regardless of distractions (Dockree, et al., 2004).

Individuals who are more impulsive tend to discount delayed rewards more than non-impulsive individuals, and therefore tend to indulge more frequently in immediate gratifications, at the expense of forfeiting larger delayed gains (Mobini, Grant, Kass, & Yeomans, 2007). Delay discounting measures are sensitive to detecting impulsive decision-making. Discounting the values of alternative rewards is a common behavioral phenomenon among humans and other animals, including food consumption to financial decision making (Acheson & de Wit, 2008; Ainslie; McDonald, Schleifer, Richards, & de Wit, 2003). The amount of discounting increases as delay increase (Rachlin, Raineri, & Cross, 1991).

Individuals in the criminal justice system show greater neurocognitive deficits than controls including impulsivity and sustained attention (Kavanagh, Rowe, Hersch, Barnett, & Reznik, 2009). Emotional impulsiveness has been shown to be associated with criminal outcome (Barkley & Fischer, 2010). These and other factors likely contribute to criminal justice involved individuals smoking more cigarettes per day than the general

population. These traits of offenders may also contribute to problems of being receptive to provider recommendations, treatment adherence, and maintaining abstinence following smoking cessation intervention.

IMPULSIVITY, INATTENTION, AND SMOKING

Nicotine is a stimulant and the acute administration of nicotine immediately enhances attention. On tasks of attention such as the Conner's Continuous Performance Task Second Edition (CPT-II), nicotine helped to increase attention by reducing the number of omission errors (Hahn, et al., 2007). However, in a meta-analysis by Heisman and colleagues, acute nicotine administration significantly decreased reaction time in non-smokers but not in smokers. It is suspected that naïve smokers are more sensitive to the effects of nicotine and reaction time decreases with chronic exposure to the drug. This may possibly be the result of regular smokers either being desensitized to the effect of nicotine or they may experience an increase in reaction time only after a decrease during nicotine deprivation (Heishman, Kleykamp, & Singleton, 2010). Smokers also were found to be more accurate in responding to stimuli than non-smokers, and smokers who were given nicotine patches were more accurate than those who received placebos (Rose, Ross, Kurup, & Stein, 2010).

Drug users tend to be more impulsive than non-users – that is, they engage in risky behavior (e.g., drug use) because of impulsive decision-making, and the effects of the drugs at least in the acute stages can make a user more impulsive (de Wit & Mitchell, 2010). Smokers repeatedly have been shown to be more impulsive than non-smokers on batteries of neuropsychological tests including the Trail Making Test, Stroop test, Barratt Impulsivity Scale, Version 11 (BIS-11) and other impulsivity measures (Dinn, Aycicegi,

& Harris, 2004; Doran, Spring, McChargue, Pergadia, & Richmond, 2004; Kassel, Shiffman, Gnys, Paty, & Zettler-Segal, 1994; Mitchell, 1999; Reuter & Netter, 2001; Whiteside & Lynam, 2003). Current tobacco smokers are more likely to indulge in immediate gratifications (i.e., discount delayed rewards) more than ex-smokers and non-smokers (MacKillop & Kahler, 2009).

Similarly, Attention Deficit Hyperactivity Disorder (ADHD) symptoms (i.e., inattention and impulsivity) were found to be associated with ever having smoked among alcohol dependent persons (Halperin, et al., 1988; Heffner, Johnson, Blom, & Anthenelli, 2010; Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001). In general, those diagnosed with ADHD are nearly twice more likely to be smokers than non-ADHD controls (Lambert & Hartsough, 1998; Laucht, Hohm, Esser, Schmidt, & Becker, 2007). Furthermore, individuals with ADHD are more likely to smoke cigarettes daily and be nicotine dependent (Biederman, et al., 2006; Fuemmeler, Kollins, & McClernon, 2007).

Deprivation of nicotine has been found to have deleterious behavioral and cognitive effects on smokers including increases in errors, reaction time, variability in responding, and inhibitory control problems (Harrison, Coppola, & McKee, 2009a 2009). Interestingly, Harrison and colleagues (2010) reported that less impulsive smokers (assessed with the BIS-11) were more negatively impacted cognitively (as detected by CPT-II and Cued Go/No-Go Task) with increased nicotine deprivation than impulsive smokers; this may be an indication of a floor effect in performance after deprivation. ADHD smokers typically report more severe nicotine withdrawal symptoms such as decreased concentration (Pomerleau, et al., 2003). Deprivation also leads smokers to demonstrate greater preference for both cigarettes and monetary rewards (Field,

Santarcangelo, Sumnall, Goudie, & Cole, 2006). Ohmura and colleagues (2005) also reported that the number of cigarettes smoked is directly related to an increase in discounting of delayed monetary rewards. However, Mitchell (2004) found that smokers deprived of nicotine for 24 hours preferred cigarettes over monetary rewards unlike the non-deprived smokers, which may suggests a desire to reduce the negative effect of nicotine withdrawal.

Impulsivity is a risk factor for successful smoking cessation. In a study by MacKillop and Kahler (2009), current smokers who discounted delayed rewards more than others at baseline were likely to relapse during the second and eighth week follow-up assessments. VanderVeen and colleagues (2008) found that higher levels of impulsivity among smokers were associated with higher levels of anxiety and craving, which may likely interfere with smokers' ability to quit smoking. Novelty seeking has also been linked to smoking including heavy smoking (>20 CPD), even after controlling for caffeine intake (Gurpegui, et al., 2007). Current smokers, but not past smokers, demonstrated greater errors on the Continuous Performance Task (CPT) than controls (Yakir, et al., 2007). Flory and Manuck (2009) found that both reward seeking and disinhibition predicted smoking but only disinhibition predicted smoking dependence after controlling for reward seeking.

Demographic variables are associated with impulsive smokers' response to treatment, with sex differences in impulsivity found among tobacco users (Waldeck & Miller, 1997). Specifically, male smokers were significantly more impulsive than male non-smokers and their female counterparts (Reynolds, et al., 2007). Gender differences also moderate the interaction between impulsivity and substance use (Stoltenberg, Batien,

& Birgenheir, 2008). While there are no gender differences at high levels of impulsivity, men at low levels of impulsivity are significantly more likely to abuse alcohol than women.

In addition, IQ is associated with performance to appropriately inhibit responses such that smokers who abstained from tobacco overnight demonstrated increased response inhibition as measured by errors in a person's ability to look away from novel stimuli (i.e., antisaccade performance). These errors were positively correlated with higher cotinine levels and negatively correlated with IQ (Pettiford, et al., 2007). Significant racial differences were also evident, with African Americans less likely to be current smokers (Burke, Loeber, White, Stouthamer-Loeber, & Pardini, 2007).

Several models of the interaction between impulsivity and smoking have been proposed to account for these associations (Mitchell, 2004). First, impulsivity may predispose an individual to initiate smoking. Second, acute stages of abstinence of nicotine in addition to perceived positive gains, may trigger cravings and subsequently increase impulsive responses. Third, neuroadaption of the reward system involved in reward processing may cause smokers to become more impulsive. Harrison and colleagues (2009b) suggest that nicotine deprivation may not increase risk for relapse of smoking behaviors; however, more studies investigating the three possibilities are warranted to draw a solid conclusion.

Most studies published have examined the effects of having a diagnosis of ADHD on smoking and smoking cessation treatment outcome. Fewer studies have examined smoking and symptoms that only partially meet DSM-IV-TR criteria for ADHD but still demonstrate significant levels of inattention or impulsivity (Kessler, et al., 2006). While studies have looked at the effects of bupropion on inattention and impulsivity, no studies to date have investigated these sub-clinical ADHD symptoms and their interaction with bupropion treatment on smoking among specific populations, such as participants in community corrections.

While 18% of children and adolescents (Faraone, Sergeant, Gillberg, & Biederman, 2003) and 4.4% of adults (Kessler, et al., 2006) are diagnosed with ADHD, a much larger prevalence of sub-clinical cases are suspected to exist throughout society (Kessler, et al., 2006). Identifying these symptoms associated with ADHD may be an important strategy for treating smokers since smokers with ADHD-like symptoms show lower abstinence rates than smokers without such problems. In particular, symptoms associated with ADHD hyperactivity/impulsivity (HI), versus ADHD inattention alone, appear to be problematic for smokers seeking to quit smoking (Covey, et al., 2008). The reason for this is that since nicotine has been found to improve attention (Conners, et al., 1996; Poltavski & Petros, 2006; Potter & Newhouse, 2004); cigarettes may be used by smokers with such symptoms to self-medicate to improve focus and concentration.

While nicotine improves attention, it may have either no impact or even deleterious effects on HI (Bekker, Bocker, Van Hunsel, van den Berg, & Kenemans, 2005; Blondel, Simon, Sanger, & Moser, 1999; Burke, et al., 2007; Decamp & Schneider,

2006; Lerman, et al., 2001. Studies that have examined smoking cessation outcome demonstrated that impulsivity compared to inattention was associated with a higher likelihood of relapse (Colomer, et al., 1999; Elkins, McGue, & Iacono, 2007; Kollins, McClernon, & Fuemmeler, 2005). Several studies reported that ADHD smokers who quit smoking reported an increase in hyperactivity/impulsivity but no improvements with attention (McClernon & Kollins, 2008; Rukstalis, Jepson, Patterson, & Lerman, 2005), suggesting higher HI symptoms may promote relapse. Furthermore, other studies have shown that nicotine alone may exacerbate impulsiveness (Bekker, et al., 2005; Blondel, et al., 1999).

Considering that nicotine might increase impulsivity and attempts at quitting smoking may further worsen HI symptoms, individuals who are naturally more impulsive may be at significant risk for relapse. Users may seek to relieve the adverse physiological effects of nicotine depletion, or users may act on impulses to seek out the positive reinforcement of smoking cigarettes. While bupropion has been found to reduce inattention but not impulsivity (Acheson & de Wit, 2008; Wilens, et al., 2001), bupropion may only benefit those without HI issues. Covey and colleagues (2008) reported that at the end of smoking cessation treatment inattentive individuals did not differ in quit rates compared to non-ADHD persons. However, those with impulsive symptoms had significantly lower quit rates than both of the other groups. In addition, significance was only found when using cutoffs of one standard deviation above the mean that were used by investigators to categorize ADHD subgroups instead of continuous variables, suggesting only high levels of impulsivity interfere with treatment, but mild or moderate cases of impulsiveness were not impacted.

HYPOTHESES

The purpose of the study was to determine if *impulsivity* but not *inattention* would interfere with responsiveness to smoking cessation treatment. Inattention without any indication of impulsivity was expected to reduce when taking bupropion (Acheson & de Wit, 2008). However, if impulsivity were to co-exist with inattention then it was expected that impulsivity would interfere with attention by promoting poor treatment adherence and increasing the potential for relapse. Therefore, the interaction of both impulsivity and inattention was believed to further exacerbate the negative impact to smoking cessation treatment outcome.

Hypothesis 1: *Inattention* typically interferes with smoking cessation treatment by blocking the ability to attend to and encode information pertinent to treatment and interferes with the ability to maintain adequate medication adherence and appointment attendance. However, bupropion has been shown to improve attention and alleviate depressive symptoms that impair focus and concentration. Therefore, it was expected that the problems typically associated with inattention would dissipate after the medication was administered and would not negatively impact treatment gains.

Hypothesis 2: *Impulsivity* would interfere with smoking cessation treatment among individuals without attention problems. Bupropion has been shown to improve attention but not impulsive behaviors (Acheson & de Wit, 2008). Therefore, it was expected that individuals who were impulsive would not benefit from the medication and would remain impulsive throughout treatment. Impulsivity, therefore, would

significantly interfere with intervention (e.g., attrition rates and average cigarettes smoked per day.)

Hypothesis 3: The *interaction* of inattention and impulsivity would interfere with treatment more among individuals who suffer from impulsivity alone. It was expected that impulsivity would negatively impact an individual's treatment attendance and medication adherence, thereby, reducing the positive benefits of bupropion on attention. In short, individuals with problems of inattention and impulsivity would have compounding barriers that impair treatment outcomes more than individuals with problems of inattention or impulsivity alone.

METHODS

PARTICIPANT RECRUITMENT AND SELECTION

Participants were recruited from the Jefferson County community corrections program, Treatment Alternatives for Safer Communities (TASC) of Alabama. Flyers were posted throughout the building and information was spread by word of mouth via TASC case managers, counselors, and participants. Interested individuals were screened over the phone or in person. Inclusion and exclusion criteria are listed below:

Inclusion Criteria:

- Enrolled in the RCT (F090430005) entitled Integrated Smoking Cessation Treatment for Low Income Community Correction Smokers (PI, Karen Cropsey). Inclusion Criteria for the above RCT includes:
- Smoking at least 5 cigarettes per day (CPD) for at least one year
- At least 19 years old
- Current under criminal justice supervision (e.g., probation, parole, TASC, Drug Court, etc.)
- Living in an unrestricted environment

Exclusion Criteria:

- Cognitive impairment that interferes with the ability to provide informed consent.
- Meet exclusion criteria for the RCT above, which include:
- Pregnant or breastfeeding

- Non-English Speaking
- History of seizures
- Elevation in liver enzymes or liver failure
- Moderate to severe kidney impairment
- Current diagnosis of bipolar disorder
- History of an eating disorder

Two additional exclusion criteria below was included during the screening of participants for the impulsivity study.

- Currently prescribed medication for ADD/ADHD (e.g., Strattera®, Ritalin®, and Adderall®);
- Illiterate

Participants were approached at the time that they were consented for the RCT. Interested persons who met eligibility for both studies were enrolled. All participants were scheduled after the RCT baseline assessment and prior to being prescribed bupropion. In the RCT, there was approximately 5 days between baseline assessments and being prescribed medication. Prior to receiving medication, all participants received a physical exam by the RCT physician. If the physician deemed the participant medically eligible to participate in the study, participants were then prescribed bupropion for 12 weeks.

Of the 136 individuals enrolled in the RCT, all 105 (77%) persons who expressed interest in being screened for the auxiliary study were eligible to participate. People declined screening primarily because they were unable to commit to an additional

hour of testing. The specific reasons for declining to participate were not formally asked of the individuals nor were any responses recorded. An authorized research personnel thoroughly explained the details of the study and obtained written consent prior to testing. A person not related to the study was asked to witness the participant signing the consent form. Signatures from the witness and investigator were also obtained.

During testing, it was determined that 4 participants could not adequately read after a reading test, the Wechsler Test of Adult Reading (WTAR), was administered and their data was not used in subsequent analyses. These few cases were removed altogether from the database. The remaining participants, after being tested, returned the following week to meet with the RCT physician to determine if they were medically eligible to participate in treatment. The physician concluded final eligibility by conducting a physical exam, reviewing lab results, and obtaining medical histories. While the screening process aimed to eliminate ineligible cases prior to enrollment, the information gathered during the baseline assessment and the physician's clinical judgment ultimately determined if certain people had to be withdrawn before treatment began. Eight additional people were deemed unfit for treatment because of contraindications with the study medication, in particular, elevated liver enzymes (n=6), meeting criteria for mania (n=1), or having a history of seizures (n=1). Data from these 8 individuals were withdrawn and their data were removed from the database. No participants who participated in this project were withdrawn during the 12 weeks of treatment or stopped taking their medication. The remaining sample size included 93 participants.

PROCEDURES

Participants were required to attend one 1-hour assessment session conducted in a quiet, private room. A trained research assistant administered a series of tests, which assessed estimated IQ, attention, and impulsivity. Participants were compensated for their time with $20 cash and were paid immediately upon completion of the session.

Participants enrolled in this study authorized merging data from the RCT together with information collected in the current investigation. Thus, outcome variables and additional baseline information was merged with information of inattention and impulsivity. Information included demographics, number of sessions attended, substance use history, compliance with medication, and number of cigarettes smoked on average per day at each time point.

MEASURES

Wechsler Test of Adult Reading (WTAR; Pearson Education, Inc, 2001) – This is a brief, 5-minute assessment of overall intellectual functioning. It is a list of spelled words, which become increasing difficult to pronounce, that was read aloud by the examinee. The WTAR scores correlate highly with the Full Scale IQ (FSIQ) of the WAIS-III, an estimation of overall intelligence. However, it is an invalid estimation of IQ for illiterate testers.

Golden Stroop test (Golden, 1978) – This is a brief, 5-minute assessment of impulse control. It is composed of three forms of 100 items each. The examiner recorded the number of items verbalized in 45 seconds. The first form consists of reading words (red, blue, and green) in black text. The second form is a series of "XXXX"

printed in different colored inks (red, blue, and green). The third form is a list of words that are printed in incongruent colored inks. The examinee named the colors of the words but does not read the words. This form measures a person's ability to inhibit responses. To reduce the effect that processing speed might have on examinee's performance on the third form, Lansbergen and colleagues (2007) suggested using the equation:

> I=CW/C (I=Interference, CW = score on third "Color-Word" form, C = score on the second "Color" form).

The lower the ratio indicates greater interference.

Barratt Impulsivity Scale, Version 11 (BIS-11; Patton et al., 1995) – This is a 30-item self-report questionnaire employing a 4-point Likert scale ("Rarely/Never" to "Almost Always/Always"). It assesses multiple scales of impulsivity including "1st Order Factor Item Content" (e.g., Attention, Self-Control, and Cognitive Instability) and composite scores called "2nd Order Factor Item Content" (Attentional Impulsiveness, Motor Impulsiveness, and Nonplanning Impulsiveness). Examples of some of the listed statements include "I plan tasks carefully" and "I buy things on impulse."

Perceived Stress Scale – 10 Item (PSS-10; Cohen, S., & Williamson, G., 1988) – This is a self-report questionnaire that assesses a person's stress in the past month. It utilizes a Likert scale of 5 items ("Never" to "Very Often") with 4 reverse scores (items 4, 5, 6, & 8). A total score of 0 to 40 was utilized, where higher scores indicate greater stress. An example of one of the items includes "In the last month, how often have you been upset because of something that happened unexpectedly?"

Trail Making Test: Trail A (Reitan, 1955) – This is a paper and pencil task that was timed-to-completion. It measures attention to visual stimuli by connecting numbered dots in order. Participants were given a practice test (5 items) prior to completing the larger timed version (25 items). Trail B was not administered because it measures goal directed behavior (i.e., executive functioning) which does not support the study's purpose.

Wechsler Assessment of Intelligence Scale – Third Edition (WAIS-III): Digits Forward (The Psychological Corporation, 1997) – This is a test of auditory attention. A series of numbers was presented orally by the examiner and immediately recalled in the same order by the respondent. Digits Backwards was not used because it measures a cognitive domain (i.e., working memory) other than attention and impulsivity.

Conner's Continuous Performance Task – Second Edition (CPT-II; Multi-Health Systems Inc., 2004) – This is a 20-minute computerized administered task that measures sustained attention and impulsivity or response inhibition. The examinee was presented with a one-minute practice trial before beginning the real task. A letter was presented in the middle of the screen one at a time. Each time a letter appeared, the respondent pressed the spacebar on the keyboard except when the letter "X" appeared, at which time no buttons were pressed. The CPT-II provides a series of subscales that discriminate between deficits of inattention (e.g., omission errors and perseverations) or impulsivity (e.g., commission errors and response style).

Delay Discounting Task (Human Behavioral Pharmacology Lab, University of Vermont, 2007) – This is a temporal discounting task that was administered via computer. Participants were presented with on-screen instructions for each task, followed

by a series of choices between two hypothetical monetary rewards. The delay discounting task included seven sets of choices between a larger delayed amount (LLR) and a smaller money amount available immediately (SSR). Each choice set corresponds to a different delay of the $1000 (1, 7, 30, 183, 365, 1825, and 9125 days, respectively).

Every set of choices generated a single money amount through a titration process developed by Green, Fry, and Myerson (1996). The procedure derived an indifference point for each delay. The indifference point is the amount of immediately available money that is subjectively equivalent in value to an LLR of $1,000. Each set consisted of six forced choices between a SSR and LLR. Each choice adjusted the subsequent SSR amount up or down in order to approach the indifference point with increasing accuracy. The initial choice for each set consisted of an immediate reward of $500 (SSR) and a delayed amount of $1000 (LLR). If an LLR was chosen then the SSR was adjusted up, and if an SSR was chosen then the SSR was adjusted down.

A single estimated rate of discounting (est. k) was derived from a set of 7 indifference points for each participant. A hyperbolic discounting function (below) was developed by Mazur (1987) to describe the rate of discounting as an alternative to an exponential discounting function used in classical economics:

$$v = A / [1 + k*Delay]$$

The hyperbolic model has been repeatedly found to accurately predict individual and group preferences between smaller-sooner rewards versus larger-later rewards (e.g., Kirby, 1997; Loewenstein, Prelec, & Elster, 1992).

For practical purposes, the rewards (e.g., $1,000) presented to participants were hypothetical. Johnson and Bickel (2002) demonstrated that hypothetic rewards and real monetary payouts did not influence the participants' rate of discounting.

Mini-International Neuropsychiatric Interview English Version 5.0.0 (Sheehan, et al., 1998) – This is a structured diagnostic interview that assesses for DSM-IV psychiatric disorders. For the purpose of this study, only questions from the substance use disorder section were utilized. This section screened for alcohol and drug abuse and dependence over the past 12 months. Lifetime diagnoses were not measured.

Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) – This is a 20-item questionnaire that assesses depression in the past week. It utilizes a Likert Scale of 4 responses (0='Rarely or none of the time' to 3='Most or all of the time'). Examples of rated items include "My sleep was restless" and "I had crying spells." The sum of all the items was computed and ranged from 0 to 60. Higher scores indicate greater depression.

OUTCOME VARIABLE

The number of participants who complete 12 weeks of treatment and quit smoking was projected to be 5-10%. While self-quit rates have been reported to be between 3 to 4%, medication especially coupled with other supportive interventions (e.g., counseling) was expected to increase rates in the general population to 20 to 35%. However, the instability of the community corrections population, comorbid substance abuse and mental health characteristics of the population, and the anticipated desire for financial compensation provided by the study was believed to possibly overshadow

motivation to quit smoking. Therefore, the rate to quit smoking was anticipated to fall between self-quit rates and quit rates associated with treatment. If 100 participants enrolled in the purposed study, a conservative estimation was between 5 to 19 individuals would actually quit. To circumvent the problem of dramatically unequal group size between those who successfully quit and those who continue to smoke (i.e., a dichotomous variable), utilizing a continuous outcome variable helped to detect declines in smoking at each time point. The following variable was used:

Cigarettes Smoked Per Day (CPD) - These data were collected at each session as a self report of the number of cigarettes smoked per day (CPD) on average over the past week.

BASELINE VARIABLES

Predictor variables were partitioned into inattention and impulsivity domains. Normative data (e.g., age-adjusted norms) was not used because this information was not available for all variables. Raw data was used instead for all variables to maintain consistency.

All variables except number of cigarettes smoked per day were collected at baseline (see Table 1). Attentional measures include: 1) Trails A; 2) WAIS III: Digit Forward; BIS-11: (3) Attention, and (4) Cognitive Instability; and CPT-II: (5) Omission Errors, and (6) Hit Reaction Time Block Change. Impulsivity measures included: (1) Stroop Ratio; BIS-11: (2) Self-Control, and (3) Cognitive Complexity; (4) Delay Discounting; and CPT-II: (5) Commission Errors, and (6) Perseverations. Variables that were expected to affect the impact inattention and impulsivity have on treatment

response: 1) IQ, (2) CPD at baseline, (3) Perceived Stress Scale, (4) CES-D: depression rating, (5) having a substance use disorder, (6) race, (7) income, (8) age, (9) marital status, (10) education, and (11) gender.

Table 1

Variables of Composite Scores

Inattention	Impulsivity
Trails A	Stroop ratio - Reverse
WAIS-III Digit Span Forward - Reverse	Delay Discounting
BIS-11 Attention	BIS-11 Self-Control
BIS-11 Cognitive Instability	BIS-11 – Cognitive Complexity
CPT-II Omissions	CPT-II Commission
CPT-II Hit Rate Block Change	CPT-II Perseveration

DATA CLEANING

Using SPSS 15.0 for Windows, the dataset was inspected for missing data, data entry errors, and outliers. All errors were corrected. Among the 93 cases, complete data was obtained on most participants (96%). The missing baseline characteristic information was due to failure of the examiner to administer a questionnaire. Some test information, described below, was removed because of suspected random responses on the computerized tasks.

One delay discounting task was not administered due to technical problems. A non-linear regression using the hyperbolic discounting model failed to produce R^2 greater than zero on 7 cases, suggesting a series of choices were randomly selected by these participants. A Mann-Whitney U test was utilized to test if participants with valid discounting data (n=85) differed from the other 8 cases. The groups did not differ on any

demographic variables or baseline characteristics. Composite scores were still computed for cases with missing discounting values (i.e., estimated k).

Two participants failed to produce valid CPT-II results as noted by the computer program due to either failure to respond or randomly hitting buttons during testing. An additional validity criterion was established to eliminate participants who stopped responding to the test (excessive Omission errors) or those who responded repeatedly regardless of stimuli (excessive Perseveration). CPT-II results from two additional cases were removed based on these secondary validity criteria. One case included an Omission z-score greater than 6.0 (38 errors) and the other case noted a Perseveration z-score greater than 7.0 (26 Errors.) Again, cases without CPT-II were still able to obtain composite scores for each domain.

DISCOUNTING MODEL

Non-linear regression was used to compute individual parameters for temporal discounting (estimated k). The seven delay discounting indifference points, detailed in the Measures section, were utilized within one regression analysis to generate an estimated k for each participant. Estimated discounting parameters were always 0 or greater. Elevated estimated k values indicate greater impulsivity and greater SSR preference (Richards, Zhang, Mitchell, & de Wit, 1999).

Two delay discounting rates were produced using different models, a hyperbolic and exponential function. A paired sample t-test (81) = 4.673, $p < .001$ revealed that the hyperbolic function was a significantly better fit of the data. The hyperbolic function produced more cases with R^2 greater than 0 (85 vs. 82) and a better fit overall ($R^2 = 0.874$

vs. 0.837) than the exponential function. These results were expected; according to Ainslie (1974) the hyperbolic model best account for human behavior. Based on these preliminary results, the discounting rates (estimated k) produced using the hyperbolic model were used in subsequent steps in the analysis.

TRANSFORMATIONS

Continuous variables were inspected for normal distributions. Descriptive information that revealed skewness greater than |1.0| were transformed. A constant of 0.0001 was added to raw scores to allow natural logarithm (Ln) transformations of scores of zero, otherwise the zero value could not be transformed. The addition of a constant did not affect any further analyses. Delay Discounting scores were highly positively skewed (4.676) and were transformed using Ln, thereby, reducing the skewness to -0.38. Monthly income and CPT-II Omissions were moderately positively skewed (1.303, 1.608) and a square root transformation was used to reduce skewness to 0.036 and 0.235, respectively. In addition, Trails A and CPT-II Perseverations (1.736, 2.139) were transformed using Ln (0.713, 0.235). Histograms with normal curves were plotted for the number of cigarettes consumed at each time point. Upon visual inspection, data were noted to be abnormally distributed with skewness ranging from 0.589 to 2.905. A square root best adjusted skewness across all time points with a range from -0.612 to 0.264. No other variables revealed abnormal distributions. Transformed values were only utilized in analyses that required normal distributions.

COMPOSITE SCORES

A single score for each domain (i.e., attention and impulsivity) was calculated to better summarize each construct. The six measures within each category were theoretically chosen to represent different facets of each category. By obtaining a single score, the main analysis would be feasible, simplified, and subsequently increase statistical power. All the measures did not have normative data so adjusted T-scores were not readily available to be combined or averaged (see Table 1).

Pearson Correlation Coefficient (see Tables 2 and 3) revealed that the raw scores within each domain were not highly correlated ($r < .425$) suggesting the overlap between measures were minimal and each measure safely measured a different facet of each

Table 2

Inattention Variables – Correlations

	Trails A (Ln)	Digit Span - Forward	BIS-II: Attention	BIS-11: Cognitive Instability	CPT-II: Omissions (SQRT)	CPT-II: Hit Rate Block Change
Composite Score	.470***	-.413***	.656***	.474***	.225*	.275**
Trails A (Ln)	-	-.149	.147	.033	.024	-.216*
Digit Span - Forward	-	-	.037	.082	-.074	.054
BIS-II: Attention	-	-	-	.419***	.205	.063
BIS-11: Cognitive Instability	-	-	-	-	.141	-.029
CPT-II: Omissions (SQRT)	-	-	-	-	-	-.048

Note: $\leq .05^{*}$, $p \leq .01^{**}$, $p \leq .001^{***}$; Raw scores were used for all measures.

Table 3

Impulsivity Variables – Correlations

	Stroop Ratio	Discounting (Ln)	BIS-11: Self-Control	BIS-11: Cognitive Complexity	CPT-II: Commissions	CPT-II: Perseverations (Ln)
Composite Score	-.452***	.600***	.591***	.485***	.540***	.577***
Stroop Ratio	-	-.228*	-.014	-.104	-.059	-.068
Discounting (Ln)	-	-	.175	.076	.313**	.132
BIS-11: Self-Control	-	-	-	.338***	.107	.235*
BIS-11: Cognitive Complexity	-	-	-	-	-.070	.071
CPT-II: Commissions	-	-	-	-	-	.334***

Note: $\leq .05^{*}$, $p \leq .01^{**}$, $p \leq .001^{***}$

domain. Standardized scores or z-scores were obtained using raw scores or transformed scores when appropriate (i.e., highly skewed). Higher scores from two measures, WAIS-III Digit Span and Stroop ratio, indicated better performance, therefore, reverse z-scores were utilized to be consistent with the direction of the value of the other measures. The means of available z-scores for each domain were used as composite scores. Four percent of Attention scores and 15% of Impulsivity scores had missing measures but no more than two measures were missing among any one case. Therefore, composite scores were able to be obtained for all cases. While composite scores were utilized to test the hypotheses, individuals tests were also inspected in the event that composite scores underestimated the impact specific aspects of inattention or impulsivity have on treatment

response. Averaging normative data on each measure to obtain a single score for a domain is common clinical practice in interpreting results from neuropsychological assessments, however, the performance on individual measures were still carefully inspected (Filskov & Boll, 1981).

RESULTS

PARTICIPANT DESCRIPTIONS

Baseline descriptive characteristics are listed in Tables 4 and 5. The genders were approximately equal (48 Males and 45 Females). Race was exactly as expected: 60% African Americans and 40% Caucasians. Nearly half met criteria for a DSM-IV-TR Substance Use Disorder (SUD) within the past year, most of which (94%) involved drug abuse or dependence whereas only 17% had an alcohol addiction. Five participants (11%) possessed both a drug and alcohol use disorder. The majority of the sample (90%)

Table 4

Demographics

Variable	n	Mean(SD) or %	Min	Max
Age	93	38.65 (10.792)	20	64
Education	93	11.97 (2.134)	6	17
Income	93	586.30 (561.448)	$0	$2500
CES-D	93	14.31 (10.493)	0	47
PSS	91	18.56 (7.112)	0	36
CPD: Baseline	93	14.98 (8.443)	0	50
WTAR: Predicted FSIQ	93	91.06 (12.78)	67	117
African American	93	60.2		
Males	93	51.6		
Not married (n=93)	84	90.4		
Never married	56	60.2		
Divorced/Separated	26	28		
Widowed	2	2.2		
SUD (n=93)	48	51.6		
Drugs	45	48.4		
Alcohol	9	9.7		
Both	6	6.5		

was not married: 60% have never been married, 28% were divorced or separated, and 2% were widowed. Most had a high school education or equivalent (i.e., GED) with a predicted IQ within the lower end of the average range (M = 91, SD = 12.78). Participants earned less than $600 on average in the last month and smoked approximately 15 cigarettes per day during the baseline assessment. They reported elevated stress (PSS; M = 18 on a scale from 0 to 36) and mild depressive symptoms (CES-D; M = 14 on a scale from 0 to 47; clinical cutoff of 16).

Table 5

Means and Standard Deviations of Attention and Impulsivity

Measure	n	Mean (SD)	Min	Max
Attention (Raw Scores)				
Trails A	93	33.34 (12.937)	16	81
WAIS-III: Digit Span - Forward	93	9.99 (2.334)	5	16
BIS-11: Attention	92	11.14 (2.617)	5	18
BIS-11: Cognitive Instability	92	5.97 (1.918)	3	11
CPT-II: Omissions	89	2.9 (3.618)	0	16
CPT-II: RT Block Change	89	0.0004 (0.025)	-0.06	0.06
Impulsivity (Raw Scores)				
Stroop ratio	91	0.554 (0.116)	0.28	0.9
Delay Discounting	85	0.073 (0.185)	0	1.186
BIS-11: Self-Control	92	14.39 (3.292)	7	23
BIS-11: Cognitive Complexity	92	12.71 (2.332)	6	19
CPT-II: Commission	89	12.91 (6.755)	1	29
CPT-II: Perseverations	89	1.112 (1.812)	0	9

ATTRITION AND MISSING DATA

The attrition rate was higher than expected. Of the 93 eligible participants, 14 people (15%) dropped out immediately after treatment began, evident at Week 2 (See Table 6). Over the course of 3 months, only 54 people (58%) completed treatment. Most

(97%) who completed treatment did not miss any sessions. Peak drop outs were at Week 2 and Week 8.

Table 6

Drop Out Frequency by Visit

N=93	Baseline	Week 1	Week 2	Week 3	Week 4	Week 8	Week 12
Complete	93	93	79	71	65	56	54
Drop Out frequency(Δ)	0	0	14	22 (+8)	28 (+6)	37 (+9)	39 (+2)
Drop Out %(Δ)	0	0	15.1	23.7 (10.1)	30.1 (8.5)	39.8 (13.8)	41.9 (3.6)

Participants who dropped out of treatment significantly differed from those who completed treatment. One-way ANOVA revealed that they smoked more cigarettes at baseline, $F(1, 91) = 5.108$, $p = .026$ and at week one, $F(1, 90) = 5.207$, $p = .025$. Participants who dropped out of treatment smoked on average 17 cigarettes daily compared to 13 cigarettes smoked by those who stayed in treatment. Those who dropped out may have foreseen the challenge to quit as too daunting.

In addition, those who dropped out were significantly less depressed, indicated by CES-D mean scores of 11.23 vs. 16.54, $F(1, 91) = 6.113$, $p = .015$. It is speculated that depressed participants likely stayed in treatment because the medication helped their depressive symptoms.

African Americans were more likely to complete treatment, 67.9% of African Americans versus 43.2% of Caucasians, $\chi^2=5.54$, $p = .016$. Caucasians in the criminal justice system typically have more psychological dysfunctions (e.g., anxiety disorders and substance use disorders that may interfered with treatment adherence (Amaro, et al.,

2005; Hartwell, 2001; Youman, Drapalski, Stuewig, Bagley, & Tangney, 2010). No other variables were significantly different, including gender and income. In addition, inattention and impulsivity were not associated with adherence rate nor dropping out from treatment.

HYPOTHESES TESTING

A longitudinal model was utilized to test the hypotheses and accommodate the data with the following parameters. 1) Longitudinal data – this model determined the presence of significant changes with categorical, continuous, or mixed variables over time. In addition, the model was adjusted for specific variables such as age and IQ; 2) Non-normal distributions of outcome variables – this model eliminated the necessity of transforming the distribution prior to analysis; 3) Missing data – instead of having to impute missing data, this model was able to bypass this step and directly analyze the data. The model used only the data points available to calculate the likelihood that a variable (i.e., inattention or impulsivity) significantly impacted the change of the number of cigarettes consumed over the course of treatment. 4) Adjacent time points were correlated – each subsequent report of the number of cigarettes smoked was either associated with the previous report: a decrease (a successful decline), an increase (a relapse), or maintained amount (no progress). During the computation process, this method used the available data to produce a set of probable values rather than a single imputed value to test the hypotheses. This approach was chosen because it is a single step process and reduces the potential error of inference. This model was performed using PROC MIXED in SAS 9.2.

The outcome variable (i.e., cpd) was first inspected for changes over time. The null model was utilized and expressed as:

```
proc mixed data=work.cpd method=ml covtest;
        class id;
        model cpd = /solution;
        random intercept / subject=id;
        run;
```

Findings indicate that there was a significant decrease in the number of cigarettes participants smoked over 12 weeks. (See Table 7 and Figure 1). At baseline

Table 7

Cigarettes Smoked Daily by Visit

		Last appointment					
Week	Overall N=93	Week 1 N=12	Week 2 N=8	Week 3 N=7	Week 4 N=9	Week 8 N=3	Week 12 N=54
Baseline	14.98	16.25	13.38	20.43	21.11	12.67	13.33
1	15	18.33	12.63	18.71	17.78	18.33	13.45
2	10.68		11.29	14.29	11.89	11.67	9.87
3	9.2			14.83	12.11	4.67	8.31
4	7.55				10.89	8	6.96
8	5.8					2	6.02
12	5.86						5.86

Note: Treatment began at Week 1

participants smoked an average of 14.98 cpd; SD=8.476; by 12 week end of treatment, participants smoked an average of 5.86 cpd; SD=5.275. The number of cigarettes smoked at the end of treatment is an underestimation of the entire sample because many of the heavy smokers dropped out of treatment before completing all sessions.

Variables that were expected to influence the predictive value of inattention or impulsivity (e.g., age) were first analyzed. This step was conducted to determine and eliminate variables that decreased the power of the final model. All interactions for each

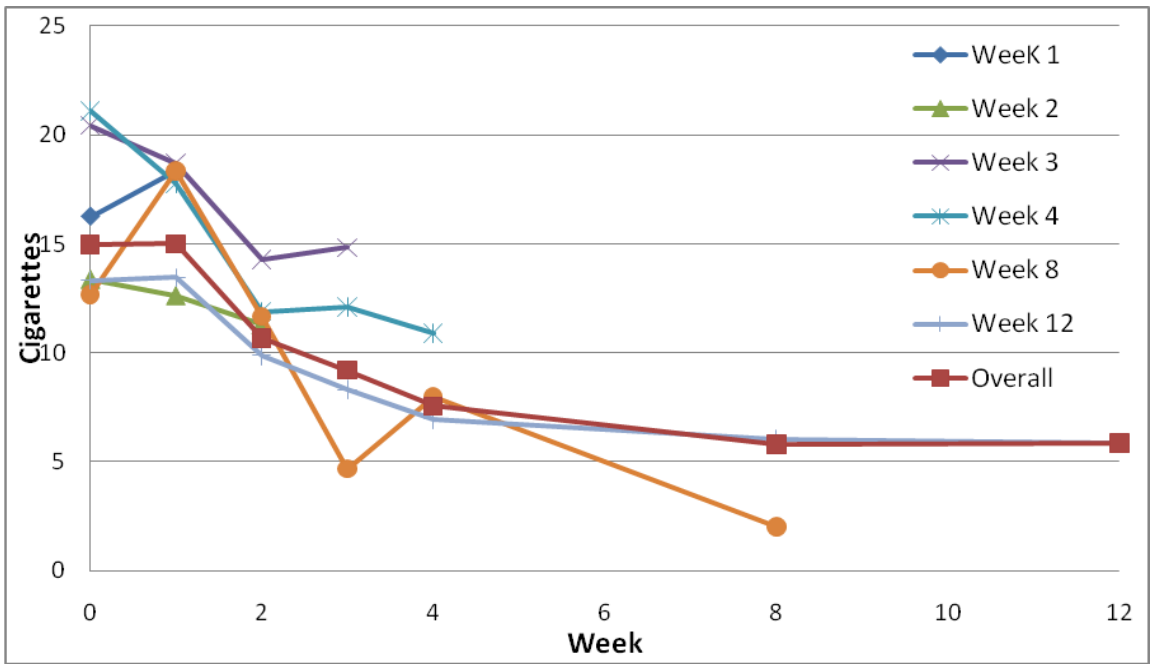

Figure 1. Mean cigarettes smoked per day by specific drop out groups. Participants who completed treatment smoked significantly less cigarettes at the beginning of treatment than those who dropped out before the 12th week. Note: Week 0 = Baseline.

domain were processed together as a single model (e.g. age x inattention interaction). The interactions were analyzed together to determine which variables best accounted for the variance. Non-significant interactions suggested that the certain variable did not add to the model and were better explained by other variables. Variables that did not contribute to the model were excluded in a secondary analysis. An example of the first model with all the interaction with inattention was expressed as:

```
proc mixed data=dissertation.cpd method=ml covtest;
        class id;
        model cpd = inattention*income inattention*age Inattention*baseline_cpd
        inattention*depression inattention*education inattention*married
        inattention*stress inattention*race inattention*sex inattention*SUD
        inattention*IQ/solution;
        random intercept;
        run;
```

Interestingly, none of the variables accounted for the effect of inattention on the number of cigarettes per day.

It was hypothesized that inattention would not affect the response to treatment because of the psychotropic effects of bupropion. This medication has been reported to alleviate problems of attention. If differences of attention existed at baseline, it was expected that they would dissipate with time and thereby not directly hinder process of quitting smoking. A second model (see below) examined attention alone because none of the interactions in the first model were significant. This model tests the first hypothesis.

```
proc mixed data=dissertation.cpd method=ml covtest;
        class id;
        model cpd = week inattention week*inattention /solution;
        random intercept/ subject=id;
        run;
```

The findings refute the hypothesis. The results indicated that the influence of inattention had a significant effect on treatment $F(1,318) = 8.26$, $p = .0043$. Those who had better attention demonstrated greater declines in the number of cigarettes they smoked over 12 weeks and appeared to maintain their gains. Inattention appears to significantly interfere with outcome at each time point. Specifically, individuals who were most inattentive struggled to show a decline in smoking after week 4 and declines in cigarette smoking did not steadily decline, rather declines were sporadic. Smokers who were less impaired showed improvements through week 8. The successes of individuals who showed some degree of inattentiveness tended to converge and were indistinguishable by week 12 (See Figure 2).

The measures of attention were inspected closely. The number of seconds to complete Trails A of the TMT, $F(1, 318) = 10.79$; $p = .0011$, and number of omissions

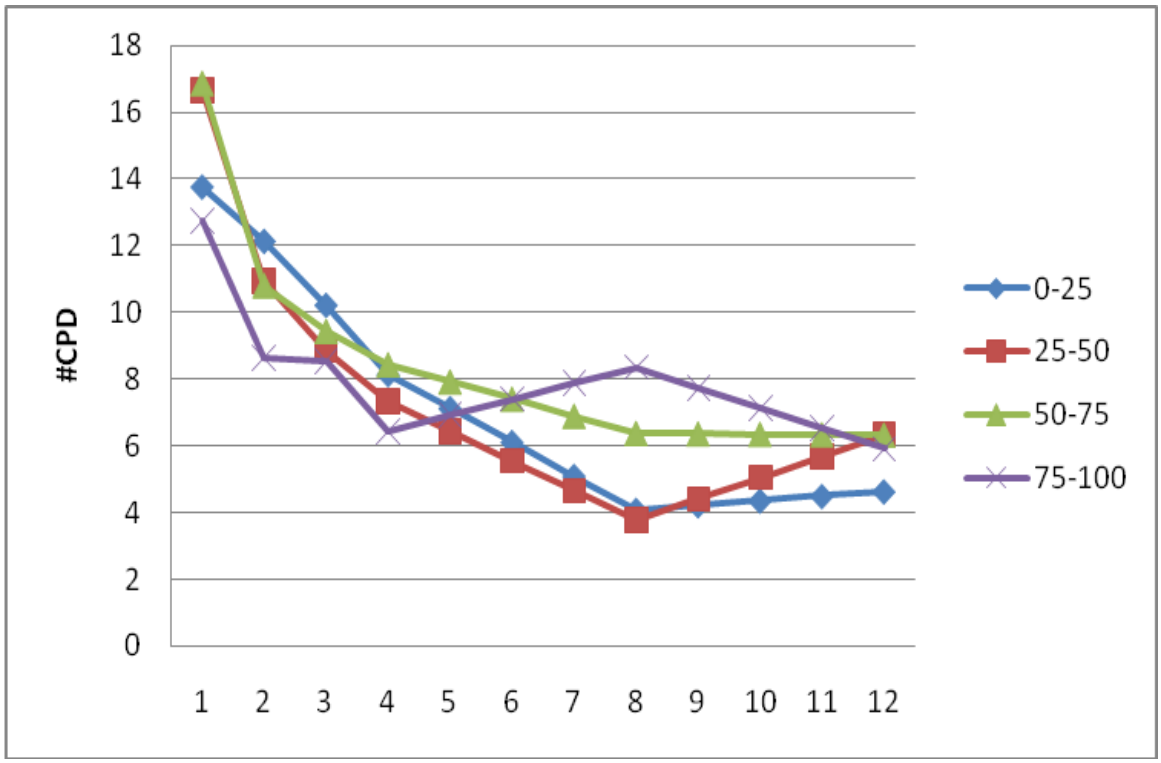

Figure 2. Cases grouped by percentile of inattention. While the main analysis did not use grouping variables of inattention, this figure illustrates the findings in the main analysis. This graph is a rudimentary means of demonstrates trends.

errors on CPT-II, $F(1, 301) = 8.7$; $p = .0034$, were the only significant predictors of smoking declining over time, with better performance on both tasks resulting in better outcomes. Self-reported problems of attention were non-significant.

Using the models for inattention as a proxy for impulsivity, potential interactions were inspected. Impulsivity as a predictor of smoking was significantly affected by two variables. This included gender, $F(1,78) = 7.99$, $p = .006$ and having a substance abuse diagnosis (SUD), $F(1,78) = 6.47$, $p = .0129$. Impulsiveness among females interfered with treatment more than males. In addition, those with a current SUD and were more inattentive, demonstrated less declines in smoking than those without a diagnosis of abuse or dependence. The correlations between these variables are presented in Table 8.

Table 8

Demographics – Correlations

	Baseline CPD	Depression	Educ.	Income (SQRT)	IQ	Married	Race
Age	-.03	.115	.112	.007	.100	.091	.340***
Baseline CPD	-	.091	.206*	-.014	.111	.012	-.513***
Depression	-	-	-.035	-.214*	.097	-.044	.021
Educ.	-	-	-	.047	.043	.274**	-.136
Income (SQRT)	-	-	-	-	-.207*	.127	.029
IQ	-	-	-	-	-	-.008	-.148
Married	-	-	-	-	-	-	-.036

	Gender	Stress	SUD
Age	-.020	-.034	-.179
Baseline CPD	-.083	.190	-.096
Depression	-.312**	.491***	.192
Education	.059	.140	.017
Gender	-	-	.085
Income	.092	-.106	.064
IQ	-.103	.028	.017
Married	.022	-.043	.022
Race	.124	-.165	.035
Stress	-.221*	-	.229*

Note: $\leq .05^{*}$, $p \leq .01^{**}$, $p \leq .001^{***}$; Race (White = 0 and Black = 1); GED = 12 years of education; Gender (Female = 0 and Male = 1); Substance Abuse Disorder (SUD; None=0 and Yes=1).

The second hypothesis was tested. In this hypothesis, it was expected that impulsivity would negatively impact response to treatment. Surprisingly, impulsivity was not a barrier to treatment as was initially hypothesized. Even after controlling for gender and having a SUD during last 12 months, impulsivity was not significantly associated with changes in number of cigarettes smoked per day over 12 weeks.

Inspections of the individual measures of impulsivity were conducted to determine if the specific deficits may be overshadowed by the composite score. Results revealed that three of six variables were significantly associated with a change in the number of cigarettes smoked over time. The CPT-II facet Perseverations was highly significant, $F(1,301) = 15.62$, $p < .0001$, with greater perseveration associated with an increase in smoking at weeks 8 and 12.

In addition, delay discounting was also significant, $F(1,293) = 4.88$, $p = .0279$. Smokers who discounted delayed rewards more than other smokers demonstrated erratic declines in their smoking. While they declined during the first several weeks, they struggled to maintain those gains and tended to rebound during the 4th week. Surprisingly, they tended to decline again more towards the end of treatment. Again, the gains were more sporadic and did not reflect steady declines over the course of treatment.

Finally, the Self-Control factor of the BIS-11 was associated with a decrease in smoking over time, $F(1,312) = 4.48$, $p = .0351$. Those who perceived having greater problems with self-control smoked more cigarettes at each time point than those who reported better self-control.

The analyses of the individual measures of impulsivity were recomputed after controlling for Gender and being diagnosed with a current SUD. All impulsivity variables including Perseverations on the CPT-II, delay discounting, and BIS-II Self Control were non-significant. This was consistent with the results found when using the composite score.

While impulsivity was not a significant predictor of treatment outcome, the interaction of inattention and impulsivity were still analyzed. Inattention and impulsivity

were significantly correlated (r = .359, p = .012): as impulsivity increased, the levels of inattention also rose. The third hypothesis stated that participants with deficits in both domains would have greater difficulty reducing the number of cigarettes they smoked over the course of 12 weeks. The results suggested that impulsivity does not contribute anything to the model that was not already explained by problems of inattention, even when the model accounted for gender and having a SUD.

DISCUSSION

Bupropion has been found to help with problems of inattention and in addition to treating depression, is also indicated as a non-stimulant alternative for the treatment of ADHD. Bupropion has not been shown to impact impulsivity (Acheson & de Wit, 2008). It was hypothesized that participants who were inattentive would reap the benefit of the medication but the medication would not improve treatment response for individuals who did not have any problems with attention or impulsivity. It was expected that the medication would improve attention which would allow these individuals to better adhere to treatment (e.g., complete treatment and take their medication as prescribed) and better absorb information about quitting smoking.

On the other hand, it was expected that those who were impulsive would not follow the treatment plan and would have a harder time resisting the urge to smoke. They were hypothesized to not decrease the number of cigarettes they smoked over 12 weeks compared to non-impulsive individuals. In addition, participants with problems of impulsivity and inattention would benefit the least from treatment. It was anticipated that impulsivity would prevent the same individuals from gaining the inattention-alleviating properties of bupropion and suffer from compounding barriers to treatment.

The findings were much different than were expected. The primary finding was that inattention and not impulsivity interfered with treatment. Those who were inattentive showed less declines in their smoking habits than all other groups. In

addition, those with both inattention and impulsivity did not demonstrate any additional problems with quitting smoking than what was already accounted for by inattention.

Neither inattention nor impulsivity appeared to interfere with completing sessions. Unfortunately, information was unavailable about medication adherence on the initial half of participants, which may have helped to explain the findings. Factors that were associated with dropping out of treatment were not associated with either impulsivity or attention. The variables associated with impulsivity were being female and having a substance use disorder; neither of which were related to attrition. It still may be likely that those who were inattentive may have forgotten to take their medication. It is also possible that the dose of the medication was not at the threshold to successfully treat inattention, considering the dose for smoking cessation (150 mg, twice per day) was lower than might be prescribed for ADHD (mean dose of 362mg per day; Wilens, et al., 2001). It would have been important to assess participants' attention and impulsivity levels at the end of treatment. This could be an important procedure for future research to evaluate. Intervention for patients who are inattentive may benefit from higher doses of medication to treat both attention and nicotine dependence. Alternative interventions may also be possible, such as providing behavioral interventions that specifically target inattention, or adding another medication to bupropion to treat inattention, and depending on the severity of the problem, adding atomoxetine or a stimulant medication for ADHD. Further assessment of the longitudinal effects of inattention is warranted before being able to draw firm conclusions about effective smoking cessation treatment to treat inattentive smokers.

Furthermore, those with problems of inattention often rely on nicotine to improve their attention and concentration. It is possible that reduction in smoking may have caused these smokers to experience greater withdrawal problems, specifically with loss of attention, and resorted to smoking more than planned. The dependence on cigarettes may be more severe for those who are inattentive than those without attention problems. Again, interventions that reduce the need to self-medicate with cigarettes may be an effective and perhaps more healthy alternatives.

It is surprising that individuals who scored high on impulsivity measures at baseline did not show markedly different responses to treatment. It is certainly possible that this may be evidence of a confound in the design of the study. By recruiting only individuals in the criminal justice system may have resulted in examining only individuals who are highly impulsive. Criminal activity is highly associated with impulsive behaviors, specifically response inhibition (Swann, et al., 2011). While no previous studies have compared the range of impulsivity levels of individuals in the criminal justice systems to those in the general population, it is speculated that the range of impulsivity demonstrated by this study sample, may have created a ceiling effect in the analysis. It would have been better to enroll individual controls who did not have a criminal history. In short, by examining only a sample of highly impulsive criminal justice participants may have limited the ability to determine the role impulsivity has on smoking cessation treatment.

This study had several additional limitations not already mentioned above. It would have been important to collect information about medication adherence and we began to do so after the first forty participants were enrolled. Specifically, it would have

been useful to know if inattentive individuals were taking their medication or, if due to inattentiveness, forgot to take doses. In addition, it would have been valuable to note the time from last cigarette the participants smoked until the start of testing. Heavy smokers who had a greater lapse of time since their last cigarette may have performed worse on the various tests (McClernon, Kozink, Lutz, & Rose, 2009).

In conclusion, the results from the study reveal some important information. While impulsivity did not appear to be associated with changes in smoking behavior during this trial, inattentive smokers appeared to have worse outcomes. This is the first study to look at inattentive smokers in this population. The community correction population is particularly susceptible to being dependent on smoking tobacco, information that may helpful to treating these individuals even if it is a subset of this population would be extremely important.

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APPENDIX

UAB IRB APPROVAL FORM

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on September 29, 2013. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator:	PERKINS, ADAM
Co-Investigator(s):	CROPSEY, KAREN L.
Protocol Number:	**F101011001**
Protocol Title:	*Attention and Decision-making as Outcome Predictors in Bupropion Treatment of Smoking Cessation*

The IRB reviewed and approved the above named project on 10/27/2010. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received FULL COMMITTEE review.

IRB Approval Date: 10/27/2010

Date IRB Approval Issued: 11/16/10

Identification Number: IRB00000196

Ferdinand Urthaler, MD

Ferdinand Urthaler, M.D.
Chairman of the Institutional Review
Board for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

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