Targeting Impulsivity to Facilitate the Cessation of Cigarette Smoking

by

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Introduction and Overview

Despite the well-established health risks, tobacco smoking remains the leading preventable cause of illness and death worldwide. In 2015, over six million people died as a result of smoking and, if current trends persist, this number will exceed eight million by the year 2030 (World Health Organisation, 2015). Within Australia, tobacco smoking is also a significant problem. Each year, smoking kills an estimated 15,000 Australians and costs the government over $31.5 billion annually (Australian Institute of Health and Welfare, 2013).

Reflective of this global health problem, considerable effort has been dedicated towards the research and development of effective smoking cessation interventions. To date, over 60 Cochrane reviews have been published, demonstrating that pharmacological and behavioural interventions significantly improve one’s chances of achieving abstinence compared to no treatment (e.g., Cahill, Stevens, Perera, & Lancaster, 2013; Lancaster & Stead, 2008; Stead, Koilpillai, & Lancaster, 2015). Nonetheless, relapse rates remain high (Hughes, Stead, Hartmann-Boyce, Cahill, & Lancaster, 2014) and novel, innovative interventions are needed in order to reduce the global prevalence of smoking. Analysis of the risk factors involved in smoking initiation, dependence and relapse have implicated the broad construct of impulsivity in each of these stages and consequently, targeting this potentially modifiable risk factor may lead to improvements in smoking cessation and reduction outcomes.

Indeed, in recent years, impulse control training, commonly referred to as inhibitory control training (ICT), has emerged as a potentially efficacious intervention to reduce unwanted/unhealthy behaviours such as alcohol consumption (e.g., Houben, Havermans, Nederkoorn, & Jansen, 2012) and the consumption of unhealthy foods (e.g., Lawrence et al., 2015). ICT is predominantly conducted using modified Go/No-Go (GNG) and Stop Signal Tasks (SST); however, the theoretical underpinnings of each task subtly differ (Veling,
Holland, & van Knippenberg, 2008; Verbruggen & Logan, 2008a) and two separate meta-analyses have indicated that GNG tasks are superior to SST’s for training inhibitory control (Allom, Mullan, & Hagger, 2015; Jones et al., 2016). At present, no research has been conducted into the real-world application of internet-delivered ICT for smoking cessation and reduction. If shown to be effective, internet-delivered ICT could be an accessible, convenient and cost-efficient treatment for smokers with the potential of reducing smoking-related morbidity and mortality rates.

Chapter One of this thesis begins by examining the health consequences, risk factors and current treatments for smoking cessation. In Chapter Two, the association between impulsivity and cigarette use is discussed and a published meta-analytic review on the association between self-report impulsivity and adolescent cigarette smoking is presented. Chapter Three introduces the SST and GNG tasks and examines the underlying mechanisms via which both tasks influence behaviour. Chapter Four reviews the increasing number of studies that have examined the efficacy of laboratory-based and real-world ICT for additive/unhealthy behaviours. Subsequently, Chapter Five presents the findings from a pre-registered randomised controlled trial which investigated the effect of ICT for smoking cessation and reduction (please note, a published protocol paper; Staiger et al. (2018), which includes a detailed methodology relevant to this RCT is presented in Appendix A). Finally, key findings, implications and limitations pertinent to the above two studies are integrated in a general discussion in Chapter Six.
Chapter 1: Smoking: Health Consequences, Risk Factors and Current Treatments

Health Consequences of Smoking

Tobacco smoking is one of the world’s leading causes of preventative illness and premature death (World Health Organisation [WHO], 2015). It is known to cause a variety of chronic, life-threatening diseases, including cancer, cardiovascular disease, stroke, pneumonia and chronic obstructive pulmonary disease (Boyle, 1997; U.S. Department of Health and Human Services, 2014; Yanbaeva, Dentener, Creutzberg, Wesseling, & Wouters, 2007). While there has been a steady decline in global prevalence rates over the past three decades (Ng et al., 2014), an estimated 1.2 billion people continue to use tobacco (WHO, 2015) and, on average, half will die a smoking-related death (Doll, Peto, Boreham, & Sutherland, 2004). In 2015, over six million people died globally as a result of tobacco use and, if current trends persist, this number will exceed eight million by the year 2030 (WHO, 2015).

Within Australia, tobacco use is also a significant problem. Each year, smoking kills an estimated 15,000 Australians and costs the government $31.5 billion in social, health and economic costs (Begg et al., 2007; Collins & Lapsley, 2008). Data from the Australian Institute of Health and Welfare (AIHW, 2013) revealed that in 2013, 12.8% of the general population smoked cigarettes on a daily basis. Daily smokers were most likely to be people aged in their late-20s or 40s and, on average, smoked an estimated 96 cigarettes per week. The AIHW (2013) data also highlights the grip of nicotine addiction. In 2013, over 31% of smokers were unsuccessful in their quit attempts, reporting that they primarily wanted to cease smoking due to financial and health related reasons. Moreover, heavy smokers (i.e., more than 20 cigarettes per day) were more likely to make quit attempts compared to light smokers (i.e., less than 10 cigarettes), but were less likely to be successful with such attempts. As such, a large portion of the Australian smoking population are sufficiently
motivated to quit smoking; however, they find it difficult to remain abstinent for prolonged periods of time. It has been estimated that if the incidence of smoking in Australia reduced by only eight percent, it would lead to 2.2 million fewer lost working days, 158,000 fewer cases of disease, 5000 fewer deaths and 3000 fewer early retirements (Magnus et al., 2011). As such, considerable health and economic benefits can be yielded by continued efforts to reduce the prevalence of smoking.

**Risk Factors Associated with Smoking**

A broad range of dynamic, biopsychosocial risk factors are thought to be involved in smoking initiation, nicotine dependence and relapse. With regards to smoking initiation, personality traits, such as impulsivity (Wellman et al., 2016) and neuroticism (Munafo, Zetteler, & Clark, 2007), adverse childhood experiences (Sugaya et al., 2012), most psychiatric disorders (Breslau, Novak, & Kessler, 2004), parents and friends who smoke (Bidstrup et al., 2009) and, second-hand exposure to smoke (Okoli & Kodet, 2015) have been reliably associated with tobacco use. Additionally, expectations about the rewarding properties of smoking have been shown to facilitate the uptake of smoking (Audrain-McGovern et al., 2012), with a longitudinal study demonstrating that among 2034 U.S. non-smoking males, the belief that smoking can calm them when nervous was a significant predictor of initiation (Bernat, Klein, & Forster, 2012).

In contrast, less research has examined the correlates of nicotine dependence. The available evidence highlights that the risk of nicotine dependence is increased by the presence of a psychiatric disorder (Kandel, Hu, Griesler, & Schaffran, 2007), particularly depression and anxiety (Dierker et al., 2015; Griesler, Hu, Schaffran, & Kandel, 2011). Other factors include early age of smoking onset (Breslau, Fenn, & Peterson, 1993; Kendler, Myers, Damaj, & Chen, 2013), parental smoking (Kim, Fleming, & Catalano, 2009), expectations about the stress-relieving properties of smoking (Baker, Brandon, & Chassin, 2004; Heinz,
Kassel, Berbaum, & Mermelstein, 2010) and elevated levels of impulsivity (Billieux, Van der Linden, & Ceschi, 2007; Chase & Hogarth, 2011; Spinella, 2002; van de Venne, Bradford, Martin, Cox, & Omar, 2006).

With regards to relapse, the greatest risk factor is the severity of nicotine dependence (Chatkin, Mariante de Abreu, Haggström, Wagner, & Fritscher, 2004; Ferguson et al., 2003; Ong, Cheong, Prabhakaran, & Earnest, 2005) and the severity of withdrawals and cravings (Allen, Bade, Hatsukami, & Center, 2008). Other factors include the number of years smoking, previous quit attempts and the length of abstinence (Matheny & Weatherman, 1998; Norregaard, Tonnesen, & Petersen, 1993; Stapleton et al., 1995), as well as a history of any psychiatric disorder and other co-morbid substance-use disorders (Ferguson et al., 2003). The ability to cope with the difficulties associated with abstinence may also involve a variety of individual factors such as self-efficacy (Amodei & Lamb, 2009), motivation (Baker et al., 2004), readiness to change (Prochaska & Velicer, 1997) and personality factors. Specifically, personality factors, such as neuroticism (Gilbert, Crauthers, Mooney, McClernon, & Jensen, 1999) and, once again, elevated impulsivity (Doran, Spring, & McChargue, 2007; Powell, Dawkins, West, Powell, & Pickering, 2010), have been shown to predict higher rates of relapse following a cessation attempt.

**Smoking Cessation Treatments**

Without treatment, over 50% of smokers who try to quit will be unable to stop for more than seven days, and less than five percent will remain abstinent after 12 months (Hughes, Keely, & Naud, 2004). As such, considerable effort has been dedicated towards the research and development of effective smoking cessation interventions. Indeed, in 1996, the Cochrane Tobacco Addiction Group was established, tasked with the responsibility of providing up-to-date and accurate information regarding the efficacy of a broad range of smoking cessation interventions. Since its inception, over 60 Cochrane meta-analyses have
been published and they have demonstrated that pharmacological treatments, followed by behaviour interventions, are the most effective treatment options for the cessation of smoking.

Pharmacological treatments assist in the cessation of smoking by mitigating the psychological and physiological symptoms associated with nicotine craving and withdrawal (Polosa & Benowitz, 2011). Analysis of 14 Cochrane reviews (Cahill, Stead, Lancaster, & Polonio, 2012; Cahill et al., 2013; Cahill & Ussher, 2011; David, Lancaster, Stead, Evins, & Cahill, 2006; Gourlay, Stead, & Benowitz, 2004; Hartmann-Boyce, Cahill, Hatsukami, & Cornuz, 2012; Hollands et al., 2015; Hughes et al., 2014; Hughes, Stead, & Lancaster, 2000; Lancaster & Stead, 1997, 1998; Stead & Hughes, 1997; Stead & Lancaster, 2006; Stead et al., 2012) indicated that compared to no treatment, nicotine replacement therapy (NRT; Risk Ratio \( RR = 1.60 \)), antidepressants (bupropion and nortriptyline; \( RR = 1.62 – 2.2 \)), and nicotine partial receptor agonists (varenicline; \( RR = 2.24 \)) significantly increased the likelihood of abstinence, and are the most efficacious pharmacological interventions available. Additional studies regarding the efficacy of pharmacological treatments are not expected to alter these findings (Cahill et al., 2013).

Behavioural treatments include self-help materials, brief therapist delivered interventions, individual and group counselling, or combinations of these approaches (Lancaster & Stead, 2008). An analysis of eight Cochrane reviews (Cahill, Lancaster, & Green, 2010; Civljak, Sheikh, Stead, & Car, 2010; Hartmann-Boyce, Lancaster, & Stead, 2014; Lai, Cahill, Qin, & Tang, 2010; Lancaster & Stead, 2008; Stead, Bergson, & Lancaster, 2008; Stead & Lancaster, 2005; Stead, Perera, & Lancaster, 2006; Whittaker et al., 2012) revealed that individual counselling \( (RR = 1.39) \) and group counselling \( (RR = 1.98) \) are both efficacious interventions compared to no treatment (Lancaster & Stead, 2008; Stead & Lancaster, 2005). Additionally, individual counselling can be effectively administered via
telephone (RR = 1.37; Stead et al., 2006). With regards to the treatment modality, motivational interviewing has been shown to be superior to usual care, yielding a modest, yet significant increase in the likelihood of quitting (RR = 1.26; Lai et al., 2010). Similarly, one study found that acceptance and commitment therapy was superior to NRT at 1-year follow-up (Gifford et al., 2004). At present, there appears to be insufficient evidence to determine the efficacy of mindfulness-based interventions (de Souza et al., 2015), acupuncture (A. R. White, Rampes, Liu, Stead, & Campbell, 2014) and hypnotherapy (Barnes et al., 2010) for the treatment of smoking cessation.

Finally, combining pharmacological and behavioural interventions has been shown to increase the likelihood of abstinence compared to when each is administered alone (Stead et al., 2015; Stead & Lancaster, 2012b). For instance, a Cochrane review of 47 studies found that when behavioural support is used as an adjunct to pharmacotherapy, the probability of a successful quit attempt increased by 10 to 25% (Stead et al., 2015). Similarly, a Cochrane review of 53 studies demonstrated that interventions that combined pharmacotherapy and behavioural support increased smoking cessation success compared to minimal intervention or usual care (RR = 1.97; Stead & Lancaster, 2012b).

**Shortcomings of current treatments.**

Even with the most effective cessation treatments, relapse rates remain at unacceptably high levels (Hughes et al., 2014). The vast majority of treatment assisted quitters will relapse within five to ten days of treatment (Piasecki, 2006; Spanier, Shiffman, Maurer, Reynolds, & Quick, 1996) and, long-term cessation is even more challenging to achieve. Only 35% of individuals are able to remain abstinent after 6-months (Fiore et al., 2008) and, of these, relapses will continue to occur year after year from the initial quit date (Zhou et al., 2009).
While relapse is associated with a multitude of aforementioned risk factors, research suggests that it may also be influenced by treatment factors. For instance, pharmacological treatments are associated with a variety of health-related risks and adverse side-effects which have been shown to negatively correlate with treatment uptake and long-term adherence (Vogt, Hall, & Marteau, 2008). A recent meta-analysis of 14 double blind randomised controlled trials (RCT) demonstrated that varenicline (i.e., a nicotine partial receptor agonist) was associated with a significantly elevated risk of cardiovascular problems compared with placebo among tobacco users (Singh, Loke, Spangler, & Furberg, 2011). Similarly, a meta-analysis of 92 RCTs found that NRT use during smoking cessation significantly increased the risk of chest pains, nausea and vomiting, gastrointestinal complaints, insomnia, skin irritations, throat soreness and mouth ulcers in participants (Mills, Wu, Lockhart, Wilson, & Ebbert, 2010). A second drawback of current smoking interventions regards their long-term cost, as NRTs and psychological therapy can often be equally, if not more, expensive than cigarettes. This is particularly relevant given that: 1) the Australian population reported that the financial costs of tobacco were the primary reason underpinning their quit attempts (AIHW, 2013) and; 2) the incidence of smoking is increasing most rapidly in developing nations who have the lowest levels of disposable income (WHO, 2015). As such, interventions need not only be effective, but also cost-effective if they are to encourage long-term abstinence.

Finally, while pharmacological interventions alleviate the common psychological and physiological symptoms associated with withdrawal (Polosa & Benowitz, 2011), they do not provide smokers with the necessary skills to adequately manage their symptoms once they cease pharmacotherapy. This may account for the improvement in abstinence rates when behavioural treatments are used as an adjunct to pharmacotherapy, as opposed to when pharmacological interventions are administered alone (Stead et al., 2015).
Chapter Summary

Although the prevalence of smoking has reduced considerably over the past three decades, substantial health and economic gains can be yielded by continued efforts to reduce prevalence rates. Considering the high relapse rates associated with current smoking cessation treatments, one possible avenue to reduce prevalence is via the introduction of novel, innovate treatments that are both cost-effective and free from adverse side-effects. Impulsivity has consistently been implicated as a risk factor in all stages of smoking and consequently, targeting this potentially modifiable risk factor may lead to improvements in smoking cessation outcomes.
Chapter 2: Smoking and Impulsivity

Defining and Measuring Impulsivity

Impulsivity can broadly be defined as the predisposition to rapidly engage in behaviours with little forethought to the consequences of such behaviours (Evenden, 1999; Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001). Although impulsivity can serve a variety of adaptive roles (e.g., Dickman, 1990; Gullo & Dawe, 2008), it is most commonly associated with maladaptive behaviours; reflected in its role as a key criterion for many clinical disorders in the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association (APA), 2013).

As a broad and multidimensional construct, various measures have been developed to assess impulsive behaviour. Self-report questionnaires rely on an individual’s perception of their own behaviour and tend to capture the more enduring, trait-like facets of impulsivity. The most commonly used self-report measures include the Barratt Impulsiveness Scale (BIS-11; Patton, Stanford, & Barratt, 1995), the Eysenck Impulsiveness Questionnaire (I7; Eysenck, Pearson, Easting, & Allsopp, 1985), Cloninger’s Novelty Seeking Scale (NS; Cloninger, Svrakic, & Przybeck, 1993), Zuckerman’s Sensation Seeking Scale (SSS; Zuckerman, Eysenck, & Eysenck, 1978) and, more recently, the UPPS-P measure of impulsivity (Whiteside & Lynam, 2001). In contrast, behavioural measures are considered to be more objective and capture the transient, state-based forms of impulsivity, such as an individual’s ability to inhibit a prepotent response in a specific situation. The most prominent behavioural measures include the Go/No-Go task (GNG; Miller, Schäffer, & Hackley, 1991), the Stop Signal Task (SST; Logan, 1994) and the Delay Discounting Task (DDT; Rachlin, Raineri, & Cross, 1991); however, other measures include the Stroop test, the antisaccade task and the Continuous Performance Task (CPT; Dougherty et al., 1999). Finally, neurobiological measures of impulsivity utilise technologies such as functional magnetic
resonance imaging to examine brain structure and function; however, please see Luijten et al. (2014) for a detailed review as these measures are beyond the scope of this thesis.

Interestingly, although both self-report questionnaires and behavioural tasks fall under the auspices of impulsivity, research has demonstrated that they are only modestly correlated (Cyders & Coskunpinar, 2011; Mitchell, 1999; Reynolds, Dallery, Shroff, Patak, & Leraas, 2008) or, not correlated at all (e.g., Reynolds, Ortengren, Richards, & de Wit, 2006). This suggests that behavioural and self-report measures are assessing related, yet distinct, facets of impulsivity. Indeed, as Evenden (1999) initially posited, there does not appear to be one type of impulsive behaviour, but rather, several related phenomena which can be termed “varieties of impulsivity” (p. 348). Therefore, in order to adequately capture and understand the relationship between smoking and impulsivity, both measures need to be considered.

**Behavioural Measures of Impulsivity and Smoking**

A growing body of evidence has indicated that behavioural measures of impulsivity are, for the most part, associated with a variety of smoking-related variables in both adolescents and adults. Perhaps most pertinent are the findings from a recent meta-analysis which compared the performance of substance users and controls on SST and GNG tasks (Smith, Mattick, Jamadar, & Iredale, 2014). A review of 12 smoking studies found that overall, smokers exhibited small yet significant elevations in impulsivity in comparison to non-smokers (Hedges g = 0.25). However, these elevations were only evident when impulsivity was measured using GNG tasks, but not when using SSTs.

Other studies have found positive associations between behavioural measures of impulsivity and nicotine dependence, cigarette consumption (i.e., the quantity and/or frequency of smoking) and relapse (Billieux et al., 2010; Flaudias et al., 2016; Glass et al., 2009; Krishnan-Sarin et al., 2007; Luijten, Kleinjan, & Franken, 2016; Powell et al., 2010; Spinella, 2002). For example, Billieux et al. (2010) used a GNG task to examine the
impulsivity of 50 adult smokers and found that elevated impulsivity predicted higher levels of nicotine dependence and, was associated with increased cigarette consumption. Similarly, Krishnan-Sarin et al. (2007) examined whether performance on a GNG task could predict abstinence among adolescent smokers and found that non-abstinent participants, compared to abstinent participants, displayed significantly more GNG errors (i.e., elevated impulsivity).

**Self-report Measures of Impulsivity and Smoking**

An extensive body of literature has demonstrated that self-report impulsivity shares robust associations with a variety of smoking-related outcomes, including, initiation, smoking status, cigarette consumption, nicotine dependence and relapse (e.g., Chase & Hogarth, 2011; Doran, Spring, McChargue, Pergadia, & Richmond, 2004; Kale, Stautz, & Cooper, 2018; D. C. Lee, Peters, Adams, Milich, & Lynam, 2015; Mitchell, 1999; Spinella, 2002; J. W. VanderVeen, Cohen, Cukrowicz, & Trotter, 2008; Wellman et al., 2016). For example, Mitchell (1999) administered the BIS-11 and I7 to 40 adult smokers and non-smokers and found that across both measures, smokers reported significantly elevated levels of impulsivity compared to non-smokers. Chase and Hogarth (2011) found that scores on the BIS-11 were positively associated with the severity of nicotine dependence amongst 404 adult smokers, whereas Spinella (2002) demonstrated that elevated self-reported impulsivity, as measured by the BIS-11, positively correlated with the quantity of cigarette packets smoked per day. Doran et al. (2004) assessed whether scores on the BIS-11 could predict a more rapid relapse to smoking following a one day skills training workshop. They found that participants with elevated BIS-11 scores relapsed to smoking significantly quicker than smokers with lower BIS-11 scores. Furthermore, J. W. VanderVeen et al. (2008) demonstrated that both cravings and anxiety (key predictors for relapse) were heightened in participants with elevated impulsivity compared to participants with low impulsivity scores.
Notably, a recent meta-analysis was conducted which synthesised extant literature and examined whether self-report impulsivity could predict smoking status (i.e., smoker versus non-smoker) and, whether self-report impulsivity was significantly associated with nicotine dependence. Analogous to previous meta-analyses that have examined the relationship between impulsivity and addictive/risky behaviours (Dir, Coskunpinar, & Cyders, 2014; Stautz & Cooper, 2013; VanderVeen, Hershberger, & Cyders, 2016), the UPPS-P measure of impulsivity (Whiteside & Lynam, 2001) was utilised. A meta-analysis of 97 studies demonstrated that both adult smoking status and nicotine dependence shared small yet significant associations with each of the five UPPS-P impulsive traits.

Interestingly, no study has meta-analysed the association between self-report impulsivity and cigarette smoking using adolescent samples; however, such a study is worthy of investigation given that smoking initiation predominantly begins during adolescence (O’Loughlin, Dugas, O’Loughlin, Karp, & Sylvestre, 2014; U.S. Department of Health and Human Services, 2012) and, longitudinal research has demonstrated that cigarette consumption during adolescence predicts consumption and dependence in adulthood (Buchmann et al., 2013; Chassin, Presson, Pitts, & Sherman, 2000; Jefferis, Power, Graham, & Manor, 2003). As such, considerable reductions in the global prevalence of smoking can be achieved via identifying, and subsequently, intervening on, the modifiable risk-factors associated with adolescent cigarette smoking.

The following section presents the first study in this thesis; a meta-analysis of the association between self-report impulsivity (using the UPPS-P framework) and adolescent cigarette consumption and nicotine dependence. The meta-analysis presented below is published in the journal Drug and Alcohol Dependence under the title “UPPS-P Impulsive Personality Traits and Adolescent Cigarette Smoking: A Meta-Analysis”. Appendix B provides information regarding the contribution of each authors to the paper; Appendix C
presents the supplementary material referred to in this study and; Appendix E presents a pdf copy of the published article.
UPPS-P Impulsive Personality Traits and Adolescent Cigarette Smoking: A Meta-Analysis

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Conflicts of interest

No conflict declared.
Abstract

**Background:** Adolescence is a critical developmental period in the trajectory of nicotine dependence, highlighting the need for a greater understanding of the modifiable risk factors. An extensive body of research has found that trait impulsivity is associated with higher levels of adolescent smoking; however, findings have been mixed. The present study aimed to synthesise existing literature to determine the strength and nature of the relationship between the UPPS-P impulsive traits and both adolescent cigarette consumption and nicotine dependence.

**Methods:** Fifty-one studies were meta-analysed using a random effects model to determine the association between each UPPS-P impulsive trait and both adolescent cigarette consumption and nicotine dependence. Age, gender, ethnicity and sample type were examined as potential moderators.

**Results:** Cigarette consumption was positively associated with each UPPS-P impulsive trait ($r$’s ranging from 0.17-0.20). There were an insufficient number of studies to meta-analyse the association between nicotine dependence and the UPPS-P impulsive traits. There were no significant moderation effects of age, gender, ethnicity or sample type.

**Conclusions:** Findings suggest that each UPPS-P impulsive trait shares similar associations with adolescent cigarette consumption. Additional studies are needed to determine the relationship between adolescent nicotine dependence and impulsivity. As most adult smokers initiate during adolescence, targeting these impulsive traits via novel prevention and intervention strategies may assist in reducing the prevalence of smoking.

**Keywords:** adolescence; smoking; impulsivity; UPPS-P model; meta-analysis.
Introduction

Despite the well-established health risks, cigarette smoking remains one of the leading preventable causes of premature death worldwide (World Health Organisation [WHO], 2015). In 2015, over six million people died globally as a result of smoking and, if current trends persist, this number will exceed eight million by the year 2030 (WHO, 2015). Adolescence is a critical developmental period where increases in risk-taking behaviours and experimentation with a variety of substances, such as cigarette smoking, emerge (Backinger, Fagan, Matthews, & Grana, 2003; Ernst, Romeo, & Andersen, 2009; Lantz, 2003). Research has demonstrated that smoking initiation predominantly begins during adolescence (U.S. Department of Health and Human Services, 2012), and, longitudinal research has indicated that cigarette consumption (i.e., the quantity and frequency of cigarette use) during adolescence is associated with levels of consumption and dependence in adulthood (Buchmann et al., 2013; Chassin et al., 2000; Jefferis et al., 2003). For instance, a one-year increase in age at initiation among 213 ever-smokers, was associated with smoking 33.5 fewer cigarettes per month at age 22 and a decrease of 0.42 in the Fagerström Test for Nicotine Dependence score (Buchmann et al., 2013). Furthermore, adolescent cigarette smokers are more likely to engage in other addictive behaviours (Kandel & Kandel, 2014; Merline, O’Malley, Schulenberg, Bachman, & Johnston, 2004; Moss, Chen, & Yi, 2014) and, are at an increased risk of experiencing a range of negative outcomes, such as anxious and depressed mood and poor academic achievement (Leventhal & Zvolensky, 2015; Morin, Rodriguez, Fallu, Maïano, & Janosz, 2012). As such, research into the modifiable risk factors associated with adolescent cigarette smoking is critically important to effectively reduce the global prevalence of smoking. Doing so will enable the identification of adolescents who are at the greatest risk of smoking, and, importantly, allow for the development of tailored
prevention and intervention strategies to be directed towards those who would yield the greatest benefits.

**Trait Impulsivity and Adolescent Cigarette Smoking**

An increasing amount of attention has been placed on trait impulsivity and its role in the development and maintenance of cigarette smoking (Bloom, Matsko, & Cimino, 2013). Research has generally demonstrated that adolescent smokers are more impulsive than their non-smoking counterparts and, that trait impulsivity is associated with smoking initiation, cigarette consumption, poor cessation outcomes and nicotine dependence (Burris, Riley, Puleo, & Smith, 2017; Fields, Collins, Leraas, & Reynolds, 2009; D. C. Lee et al., 2015; Pang, Farrahi, Glazier, Sussman, & Leventhal, 2014; Reynolds et al., 2007; Spillane et al., 2010; Weckler et al., 2017). Yet, despite this well-examined relationship, no attempt has been made to systematically meta-analyse these studies. One potential reason is that quantifying the overall association between adolescent cigarette smoking and trait impulsivity poses challenges, largely because impulsivity is a multidimensional construct with varying definitions. For example, commonly used trait impulsivity variables such as novelty seeking, fun seeking, disinhibition and boredom susceptibility have all been subsumed under the construct of impulsivity; however, research has shown that these variables are both unique, and related, components of impulsivity (Lynam, Smith, Whiteside, & Cyders, 2006; Whiteside & Lynam, 2001).

Specifically, Whiteside and Lynam (2001) used factor analysis on a number of frequently used trait impulsivity measures and demonstrated that impulsivity comprises five distinct, yet interrelated, impulsive traits, including: 1) *sensation seeking*, defined as the tendency to seek sensory pleasure, excitement and novel experiences; 2) *lack of premeditation*, defined as the tendency to act without forethought; 3) *lack of perseverance*, defined as the tendency to not finish tasks, or heightened susceptibility to boredom; 4)
negative urgency, defined as the tendency to act rashly in negative emotional states, and; 5) positive urgency, defined as the tendency to act rashly in positive emotional states (UPPS-P; Lynam et al., 2006; Whiteside & Lynam, 2001). Studies have shown that the UPPS-P impulsive traits share between 6% and 27% of their variance, with negative and positive urgency sharing the largest proportion of variance (Cyders & Smith, 2007).

In recent years, several meta-analyses have utilised the UPPS-P model when quantifying the association between trait impulsivity and adolescent risky behaviours, including alcohol use (Stautz & Cooper, 2013), marijuana use (VanderVeen et al., 2016) and risky sexual behaviours (Dir et al., 2014). For example, Stautz and Cooper (2013) meta-analysed 87 studies to examine the relationship between impulsivity and adolescent alcohol consumption and found that sensation seeking and positive urgency were most strongly associated with alcohol consumption, whereas positive and negative urgency showed the largest associations with alcohol dependence. Similar meta-analyses have been conducted using adult samples, with results demonstrating that the UPPS-P impulsive traits share distinct associations with nicotine dependence (Kale et al., 2018) and alcohol consumption (Coskunpinar, Dir, & Cyders, 2013). As such, utilising the UPPS-P model of impulsivity allows for clarification of discrete relationships that might otherwise be hidden when impulsivity constructs are combined (G. T. Smith, Fischer, & Fister, 2003).

Indeed, research has demonstrated that the UPPS-P traits share unique associations with adolescent smoking outcomes. Sensation seeking has been the most widely studied impulsivity-related trait and it has been shown to positively associate with cigarette consumption (Kraft & Rise, 1994; P. Pokhrel, Sussman, Sun, Kniazer, & Masagutov, 2010; Urbán & Urbán, 2010), status as a smoker (Tercyak & Audrain-McGovern, 2003; Thrasher, Niederdeppe, Jackson, & Farrelly, 2006) and the initiation of smoking (Spillane et al., 2012; Wellman et al., 2016). There is initial evidence that positive and negative urgency are
associated with cigarette consumption (Balevich, Wein, & Flory, 2013; D. C. Lee et al., 2015) and nicotine dependence (Ryan et al., 2013; Spillane et al., 2010), whereas lack of perseverance has been found to relate to cigarette consumption (Frankenberger, 2004; Pedersen, Clausen, & Lavik, 1989), though with varying degrees of association, as well as smoking status (Balevich et al., 2013; Spillane et al., 2010). Lack of premeditation has been found to be strongly related to cigarette consumption in some studies (Cavalca et al., 2013; Reynolds et al., 2007), but weakly related in others (Leeman, Hoff, Krishnan-Sarin, Patock-Peckham, & Potenza, 2014; M. J. White, Young, Morris, & Lawford, 2011), and there is mixed evidence regarding its association with the severity of nicotine dependence (Ryan et al., 2013; Spillane et al., 2010). Such variations and inconsistencies in the relationships between impulsivity and adolescent cigarette smoking warrants a more comprehensive systematic review of current literature.

Present Study

The aim of the present study is to summarise and synthesise existent literature to determine the direction and magnitude of the relationship between each UPPS-P impulsive trait and both adolescent cigarette consumption and nicotine dependence. In addition, this review will investigate whether age, gender, ethnicity, and sample type moderate any relationships. To the best of our knowledge, this is the first meta-analysis to examine the association between the UPPS-P impulsive traits and adolescent cigarette smoking. It is our hope that improved understanding of the modifiable risk factors associated with adolescent cigarette consumption and nicotine dependence may enable the development of tailored prevention and intervention strategies, and ultimately, reduce the prevalence of smoking.

Methods

Study Design
We followed methods used by previous meta-analyses examining the association between adolescent risky behaviours and UPPS-P impulsive traits (Dir et al., 2014; Stautz & Cooper, 2013; VanderVeen et al., 2016). Relevant articles were identified following searches in PsycINFO, MEDLINE, CINAHL and Embase electronic databases to October 2018. Searches were conducted based on all keyword combinations of terms for adolescence (adolesc* OR youth OR teen*), impulsivity (impuls* OR disinhibit* OR premedit* OR “sensation seek*” OR “novelty seek*” OR “behavi* approach” OR “behavi* activation” OR BAS OR “reward sensitivity” OR “reward drive” OR “negative urgency” OR “positive urgency” OR perseverance OR (boredom N3 (prone* OR susce$$*))) and smoking-related behaviours (cigarette* OR tobacco OR smok* OR nicotine). The reference sections of all included articles were also examined to identify further studies that could be included.

**Inclusion and Exclusion Criteria**

Studies included in the final meta-analysis met the following criteria: 1) published in a peer-review journal reporting on an original piece of research; 2) measured self-report impulsivity and cigarette consumption (and not any other forms of tobacco such as cigars, hookah, e-cigarettes etc..) and/or severity of nicotine dependence; 3) included a sample of adolescents with a mean age between 10.0 and 19.9 years, a range of adolescence provided by the World Health Organisation (WHO, 2011) and; 4) published in English. Studies were excluded if they: 1) used a composite measure of substance use that combined cigarette and other drug use; 2) used a measure of impulsivity that was unable to be coded onto the UPPS-P model and; 3) were review studies, case studies, commentaries, systematic reviews or meta-analyses. Figure 1 summarises the studies removed following application of each criterion according to PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2009).
**Study Selection**

Following the removal of duplicate entries, one reviewer (JB) assessed all records. Twenty percent of title and abstracts were assessed by PS and 10% of full-text articles were assessed by MH. For 19 out of the 20 full-text articles (Cohen’s-kappa = 0.90), the reviewers independently agreed upon the appropriateness of each article for inclusion. Fifty-five studies did not include sufficient data to calculate effect sizes. For studies in the previous ten years, first authors were contacted with a request for data. A total of 35 authors were contacted and

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**Figure 1.** PRISMA flowchart of articles included in the meta-analytic review.
six provided the requested data. A total of 51 published studies were included and their data was extracted for the five separate meta-analyses.

**Data Extraction and Effect Size Calculation**

All studies were coded by the first author. Five randomly selected studies were coded by a second author (MH) to assess reliability. There was a 97% agreement between coders. The following information was extracted from each of the included studies: Author(s) and year of publication, study design (longitudinal or cross-sectional), sample size, sample type (normative, which included high school, university or community samples and non-normative, which included clinical or incarcerated samples), mean age of the sample (when the age range was reported and not the mean, the median value of the range was extracted), gender (percentage male), ethnicity (percentage Caucasian, as most studies reported samples of Caucasian ethnicity), trait impulsivity scale used and effect sizes reported.

Two variables were extracted from each study. The first was a measure of trait impulsivity and the second was a measure of cigarette use. The data extracted to measure trait impulsivity was categorised into one of the five relevant UPPS-P traits based on previous categorisation developed by Stautz and Cooper (2013) (see supplementary Table 1). The data extracted to measure cigarette use was the quantity, frequency or lifetime use of cigarettes consumed (i.e., consumption) and/or nicotine dependence.

The relationship between the UPPS-P impulsive traits and both cigarette consumption and nicotine dependence was Pearson’s $r$ correlation coefficient. Using this effect size permits our results to be compared with previous meta-analyses on this topic (Coskunpinar et al., 2013; Dir et al., 2014; Kale et al., 2018; Stautz & Cooper, 2013; VanderVeen et al., 2016). For studies that did not report a correlation, $r$ was converted from Cohen’s $d$, $F$, odds ratios using Comprehensive Meta-Analysis (CMA; Borenstein, Rothstein, & Cohen, 2005). Several studies provided more than one effect size for the association between the UPPS-P
impulsive traits and cigarette consumption. In these cases, CMA was used to generate one effect size across all measures, ensuring each study contributed only one effect size to any one meta-analysis. Multiple effect sizes from longitudinal studies were averaged using CMA. Effect sizes were coded such that higher positive values indicated higher levels of trait impulsivity.

**Meta-analytic Procedure**

Study level Pearson’s $r$ values were pooled, and an average value was computed using a random effects model. This model assumes that variability in effect sizes reflects both random error and true heterogeneity/non-random error (Borenstein, Hedges, Higgins, & Rothstein, 2009). An alpha level of 0.05 was used for all statistical tests. The values of the $r$ coefficients were interpreted according to (Cohen, 1988) guidelines: Small ($r = 0.10$), Medium ($r = .30$) and Large ($r = .50$). Forrest plots were calculated to illustrate the heterogeneity of included studies in each meta-analysis (see Supplementary Figures 1-5).

For all meta-analyses, the $I^2$ statistic was computed. The $I^2$ statistic measures, as a percent, the variability between effect studies that is due to true heterogeneity. $I^2$ values of 25%, 50% and 75% correspond to low, moderate and high levels of heterogeneity between effect sizes respectively (Higgins, Thompson, Deeks, & Altman, 2003). When $I^2$ values exceeded 50%, meta-regression (Greenland, 1987) was conducted. Meta-regression examined whether participants’ age, gender and ethnicity were significant predictors of the effect sizes. Sub-group analysis using CMA examined whether sample type (i.e., normative versus non-normative) moderated effect sizes. Publication bias was assessed by computing fail-safe N (FSN) analyses (presented in Table 2) and funnel plots (see Supplementary Figures 6-10).
Results

Study Characteristics

A total of 51 studies, published between 1973 and 2017, were eligible for inclusion (see Table 1). The mean sample size was 645 ($SD = 866.03$; range 23-3783), and the mean age was 16.05 ($SD = 2.00$; range 10.30-19.44). On average, samples were 48.59% male ($SD = 11.04$, range 28.20-100), and 55.70% Caucasian ($SD = 29.75$; range 0-100). The majority of samples were from high school ($n = 25$, 49%), followed by community ($n = 14$, 28%), university ($n = 8$, 16%), clinical ($n = 2$, 4%) and incarcerated ($n = 2$, 4%), and most studies used a cross-sectional design ($n = 48$, 94%).
## Table 1

*Studies Included in the Meta-Analyses*

<table>
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<th>Mean Age</th>
<th>Gender (%Male)</th>
<th>Ethnicity (%Caucasian)</th>
<th>Sample Type</th>
<th>Study Design</th>
<th>Smoking Measure</th>
<th>Impulsivity Measure</th>
<th>UPPS-P Trait</th>
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### Impulsivity and Cigarette Smoking

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<td>Scale (B)</td>
<td>Impulsivity Measure (C)</td>
<td>Scale (D)</td>
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### IMPULSIVITY AND CIGARETTE SMOKING

<table>
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<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Cigarette Use (Per Year)</th>
<th>Nicotine Dependence</th>
<th>Type</th>
<th>Impulsivity Scale</th>
<th>Lack of Premeditation</th>
<th>p-value</th>
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<td>CS</td>
<td>C⁺</td>
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</table>

**Notes.** N=sample size; C=consumption; ND=nicotine dependence; Q=; F=frequency of cigarette use; LU=lifetime use; CS=cross sectional; r=r value prior to transformation; L=longitudinal; SS=sensation seeking; LPREM=lack of premeditation; LPERS=lack of perseverance; NU=negative urgency; PU=positive urgency; BIS-NPMI=Barratt Impulsivity Scale – Nonplanning and Motor Impulsivity; BIS-A=Barratt Impulsivity Scale – Attentional; BIS-T=Barratt Impulsivity Scale – Total score; I7-IMP=I-7 Impulsiveness; I7-VEN=I-7 Venturesomeness; UPPS-P-SS=UPPS-P – Sensation Seeking Scale; JPRF=Jackson Personality Research Form; ZKPQ-Imp=Zuckerman-Kuhlman Personality Questionnaire; ZKPQ-SS=Zuckerman-Kuhlman Personality Questionnaire; CPI=California Psychological Inventory; TPQ-NS=TPQ – Novelty Seeking; BSSS=brief sensation seeking scale; SSS-T=Sensation Seeking Scale – Total score; SSS-BS=Sensation Seeking Scale – Boredom Susceptibility; SSS-DIS=Sensation Seeking Scale – Disinhibition; SSS-TAS=Sensation Seeking Scale – Thrill and Adventure Seeking; SSS-S=Sensation Seeking Scale – Children; BIS/BAS FS=BIS/BAS Scales – Fun Seeking; SURPS-SS=Substance Use Risk Profile Scale– Sensation seeking; SURPS-IMP=Substance Use Risk Profile Scale– Impulsivity; ZKPQ-IMP=Zuckerman–Kuhlman Personality Questionnaire – Impulsivity; ZKPQ-SS=Zuckerman–Kuhlman Personality Questionnaire – Sensation Seeking; JCTI-NS=JCTI–Novelty Seeking; KPI-SS=Karolinska Scales of Personality – Sensation Seeking; KPI-IMP=Karolinska Scales of Personality – Impulsivity; ^=quantity of cigarette use; *=frequency of cigarette use; " quantity and frequency combined.
Meta-analysis

The relationship between UPPS-P impulsive traits and adolescent cigarette consumption. Five meta-analyses examined the association between the UPPS-P impulsive traits and adolescent cigarette consumption (see Table 2). Results from all meta-analyses showed impulsive traits to be significantly correlated with adolescent cigarette consumption. In each, the magnitude of the correlation can be considered small according to (Cohen, 1988) guidelines. All five meta-analyses showed similar weighted correlations, ranging between $r = 0.17$ and $r = 0.20$. FSN analyses revealed that the significant results observed in each meta-analysis is unlikely to be due to missed publications. The smallest number of missed studies was 23 and this was more than seven times the number studies found (i.e., for positive urgency). Funnel plots indicated that publication bias is unlikely to have influenced the results (see Supplementary Figures 6-10). Calculation of the $I^2$ statistic indicated that the percentage of true heterogeneity between effect sizes was high for sensation seeking and lack of premeditation. For lack of perseverance and positive urgency the $I^2$ value was moderate (see Table 2).

Table 2

| Meta-analyses for Each UPPS-P Impulsive Trait and Adolescent Cigarette Consumption |
|---------------------------------|-----|-----|-----|-----|-------|-----|-----|
|                                  | k   | N   | r   | CI  | Z    | $I^2$ (%) | Q   | FSN  |
| Lack of premeditation            | 25  | 16,364 | 0.18 | 0.14-0.23 | 8.37** | 92.39 | 314.52** | 2570 |
| Lack of perseverance             | 7   | 2619  | 0.19 | 0.12-0.25 | 5.57** | 63.87 | 16.61* | 150  |
| Sensation seeking                | 37  | 30,746 | 0.20 | 0.16-0.24 | 9.63** | 96.30 | 973.58** | 1345 |
| Negative urgency                 | 6   | 1330  | 0.19* | 0.14-0.24 | 7.87** | 0.00  | 3.12  | 59   |
| Positive urgency                 | 3   | 923   | 0.17 | 0.08-0.25 | 3.73** | 49.17 | 3.94  | 23   |

Notes. $k=$number of studies; $N=$aggregate sample size; $r=$weighted correlation; CI=95% confidence interval; $I^2=$percentage of true heterogeneity; $Q=$heterogeneity statistic; FSN=fail-safe-N; *Since $I^2$ was 0% for this meta-analysis, a fixed effects model will yield the same weighted average as a random effects model.

* = $p < .05$.

** = $p < .001$. 
The relationship between UPPS-P impulsive traits and adolescent nicotine dependence. Only two studies provided effect sizes for the association between the UPPS-P impulsive traits and adolescent nicotine dependence and therefore, meta-analyses could not be conducted. Bivariate correlations are presented in Table 1.

Moderator analysis. Moderator analyses examined systematic influences for the association between cigarette consumption, and sensation seeking, lack of premeditation and lack of perseverance. Meta-regression was used to assess the potential moderating effects of the continuous variables of age, gender and ethnicity (%Caucasian). No significant moderating effects were found for any of the continuous variables on the relationship between each UPPS-P impulsive trait and adolescent cigarette consumption. Following, sample type (i.e., normative vs non-normative) was considered as a potential categorical moderating variable. Similarly, no significant moderating effects were found for sample type on the relationship between each UPPS-P impulsive trait and adolescent cigarette consumption.

Discussion

A systematic review of relevant research literature was conducted to determine the strength and nature of the relationship between the UPPS-P impulsive traits and both adolescent cigarette consumption and nicotine dependence. Results from a review of 51 studies, comprising over 50,000 participants, found that adolescent cigarette consumption was positively related to impulsivity. Specifically, five separate meta-analyses demonstrated that each UPPS-P impulsive trait shared a small, positive association with cigarette consumption. Meta-analyses for the association between adolescent nicotine dependence and the UPPS-P impulsive traits could not be conducted as there were an insufficient number of studies.
The vast majority of included studies analysed the association between sensation seeking and lack of premeditation with cigarette consumption, whereas far less studies examined the lack of perseverance and urgency traits. Although sensation seeking yielded the largest association with cigarette consumption, and positive urgency the smallest, all associations were in the small range, with little variation between them (r’s ranging from .17-.20), indicating that each UPPS-P impulsive trait plays an important role in adolescent cigarette consumption. Unfortunately, only two studies fulfilled criteria in relation to the association between adolescent nicotine dependence and the UPPS-P impulsive traits and hence, meta-analyses could not be conducted. This is surprising given the large number of adult smoking studies which measure nicotine dependence. For instance, a recent meta-analysis of over 50 studies using adult samples found that positive and negative urgency yielded stronger associations with nicotine dependence compared to other UPPS-P impulsive traits (Kale et al., 2018). Findings from the present review highlight the need for future research to incorporate measures of nicotine dependence when examining the relationship between impulsivity and adolescent smoking. This will clarify the nature of the relationship between impulsivity and adolescent nicotine dependence, and also, highlight whether distinct impulsive traits contribute to the transition from casual cigarette consumption towards more problematic tobacco-use disorders. Lastly, moderator analyses were conducted to determine if any methodological characteristics moderated study level effect sizes. Consistent with previous meta-analyses that have examined the relationship between the UPPS-P impulsive traits and risky health behaviours (Kale et al., 2018; VanderVeen et al., 2016), age, gender, ethnicity or sample type were not found to moderate the association between impulsive traits and cigarette consumption.

Implications
Historically, impulsivity has been perceived as a stable trait characteristic not amenable to change; however, over the past decade, it has become increasingly clear that impulsive characteristics can be modified in treatment (Hershberger, Um, & Cyders, 2017; Staiger, Kambouropoulos, & Dawe, 2007). As such, findings from the present meta-analysis highlight the need to focus research efforts on the development of novel prevention and intervention strategies that target the UPPS-P impulsive traits in adolescents. Indeed, several studies have demonstrated that interventions which specifically target sensation seeking have resulted in significant reductions in adolescent alcohol consumption and binge drinking (Conrod, Castellanos-Ryan, & Mackie, 2011; Conrod, Stewart, Comeau, & Maclean, 2006) and have even delayed the onset of alcohol consumption by up to six-months (Conrod, Castellanos, & Mackie, 2008). Such interventions are sorely needed for adolescent smokers given that nicotine dependence can develop rapidly and at low levels of cigarette consumption (DiFranza et al., 2000; Rose, Dierker, & Donny, 2010) and we suggest that school-based intervention programs provide an ideal window of opportunity to implement and examine such strategies. Additionally, public media campaigns that have been tailored towards high sensation seeking individuals have been shown to be effective at reducing cannabis use (Palmgreen et al., 2001) and similar personality targeted communications that focus on adolescent cigarette use may be an effective public health strategy.

Importantly, this review proposes that prevention and intervention strategies should strive to incorporate all of the UPPS-P impulsive traits as they appear to share similar, positive associations with adolescent cigarette consumption. This multidimensional approach may result in enhanced treatment outcomes and reduce the economic and health burden related to adolescent cigarette consumption. For instance, the urgency traits, which are more affect driven, may benefit from interventions such as mindfulness (Robinson, Ladd & Anderson, 2016) or emotion regulation skills (Sloane et al., 2018), whereas lack of
premeditation, which is more automatic, may benefit from computerised cognitive training tasks such as cognitive bias modification (see Wiers et al., 2013) and impulse control training. Indeed, in recent years, impulse control training has emerged as a potentially efficacious intervention to reduce unhealthy behaviours such as risky alcohol consumption (Houben, Nederkoorn, Wiers, & Jansen, 2011; Jones & Field, 2013) and the consumption of unhealthy foods (Houben & Jansen, 2015; Lawrence et al., 2015). This computer-based training program involves repeatedly pairing target stimuli (i.e., alcohol or unhealthy food) with the requirement to exercise impulse control. At present, the efficacy of smoking-related impulse control training is being evaluated (Staiger et al. 2018), and, if found to be effective, could be offered as a standalone treatment, or as an adjunct to existing treatments for impulsive adolescents. Such interventions could feasibility be incorporated into school substance misuse prevention programs and/or delivered to at-risk adolescents.

**Limitations and Future Research**

Although this is the first study to examine the association between the UPPS-P impulsive traits and adolescent cigarette consumption and nicotine dependence, it has several limitations that are typically experienced with meta-analyses. First, it is recognised that data that could not be obtained from authors could have produced different results than that reported; however, we also see this as a limitation of the literature in general. There is a trend towards the online publication of data (Costello, 2009; B. Lawrence, Jones, Matthews, Pepler, & Callaghan, 2011) and, future research should aim to provide correlation matrices of all variables analysed. Second, there was substantial heterogeneity across studies, and, although a random effects model was used, and demographic and methodological variables were examined as potential moderators, it is likely that there are other sources of unexplained variance. Third, most of the included studies were from non-clinical populations which limits the generalisability of these findings to clinical populations. Additionally, all data pertaining
to cigarette consumption was self-reported, and while generally considered reliable, a lack of biochemical verification may have limited the accuracy of data (Gorber, Schofield-Hurwitz, Hardt, Levasseur, & Tremblay, 2009). Lastly, only three studies were included in the meta-analysis for positive urgency which limits our ability to draw conclusions regarding this impulsive trait. Future research may consider utilising the UPPS-P model when assessing impulsivity and adolescent cigarette use.

**Conclusion**

This study was the first to synthesise existing research to examine the relationship between the UPPS-P impulsive traits and both adolescent cigarette consumption and nicotine dependence. Results from a review of 51 studies demonstrated that each of the five UPPS-P impulsive traits are positively associated with adolescent cigarette consumption; however, additional research is needed to determine the association between the UPPS-P impulsive traits and adolescent nicotine dependence. Findings may help to inform novel prevention and intervention strategies that target these impulsive traits.
Chapter Summary

Overall, a breadth of research has demonstrated that self-report and behavioural measures of impulsivity are associated with a variety of cigarette-use outcomes. In conjunction with the meta-analytic review presented above, these findings provide the necessary impetus to focus research efforts on impulsivity-targeted interventions for smoking cessation; either as a standalone cessation treatment, or as an adjunct to existing treatments. As such, the following sections of this thesis focus on computerised impulse control training interventions, commonly referred to as inhibitory control training or response inhibition training. In recent years, inhibitory control training has emerged as a potentially efficacious intervention to reduce addictive/unhealthy behaviours such as alcohol consumption and the consumption of unhealthy foods (e.g., Houben et al., 2012; Lawrence et al., 2015). As such, the following chapters will: 1) describe inhibitory control training; 2) examine its theoretical underpinnings and; 3) evaluate the current evidence base regarding its efficacy.
Chapter 3: Inhibitory Control Training

Inhibitory control training (ICT) requires participants to establish prepotent motor responses towards neutral stimuli (e.g., clothes), while, on a minority of trials, pairs cue-specific stimuli (e.g., unhealthy food/alcohol/cigarettes) with stop or No-Go signals (Jones et al., 2016). While ICT is a relatively new training paradigm, an accumulating body of research has demonstrated its potential efficacy in reducing unwanted/unhealthy behaviours such as alcohol consumption (e.g., Houben et al., 2012; Houben et al., 2011; Jones & Field, 2013) and the consumption of unhealthy foods (e.g., Houben, 2011; Houben & Jansen, 2011; Lawrence et al., 2015; Veling, Aarts, & Stroebe, 2013b; Veling, van Koningsbruggen, Aarts, & Stroebe, 2014).

Predominantly, ICT tasks are modified versions of the Go/No-Go and Stop-Signal paradigms, which require participants to firstly learn a dominant motor response and then subsequently inhibit it. Unlike other training tasks (e.g., the Stroop or antisaccade task), SST and GNG tasks are preferred methods for ICT as they require response inhibition, yet draw minimally upon other cognitive components such as attention or working memory (Allom et al., 2015). While they are often equated across the inhibitory control literature, SST and GNG tasks tend to capture subtly different components of inhibitory control (Jones & Field, 2013) and differ slightly with regards to their underlying assumptions and mechanisms of action (Smith et al., 2014). As such, prior to critically reviewing the efficacy of ICT in reducing unwanted behaviours, it is necessary to firstly provide an overview of the SST and GNG tasks that are used in ICT and secondly, examine the underlying mechanisms proposed to account for behavioural change following ICT.

The Go/No-Go Task

Historically, GNG tasks have been used to measure inhibitory control (Miller et al., 1991). In a typical GNG task, participants are required to respond as quickly and as
accurately as possible to a series of stimuli (Go stimuli), thereby creating a strong prepotent tendency to respond (Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014). However, on a small number of trials, participants are required to withhold this response when faced with stimuli of a different type (No-Go stimuli). For example, a participant might be required to rapidly respond to all letters in the alphabet except the letter B, or all numbers except the number 2. As such, GNG tasks directly challenge the ability of an individual to inhibit, or withhold, a prepotent motor response (Smith et al., 2014). The rate of commission errors (i.e., the proportion of responses that are not successfully inhibited) is the primary variable of interest, and, a high proportion of commission errors indicates poor inhibitory control/elevated impulsivity (Wright et al., 2014).

When used in ICT, GNG tasks require participants to respond as rapidly as possible to a neutral set of stimuli (e.g., clothes), while consistently withholding responses to a set of stimuli that represent the target behaviour (e.g., cigarettes, alcohol or unhealthy food). While these cues can be presented in a variety of ways, Figure 1 illustrates one version of the task that was utilised by Lawrence et al. (2015). In this instance, unhealthy foods were consistently paired with No-Go signals, whereas healthy foods were consistently paired with Go signals. Filler images, which were non-food items (e.g., socks), were equally paired with Go and No-Go signals. In Go trials, participants were required to use designated letters on a keyboard to indicate as quickly and as accurately as possible whether stimuli were oriented to the left or to the right of the centre of the border. For No-Go trials (i.e., when stimuli are presented in a bold border), participants are required to withhold their response.
**The Stop-Signal Task**

Similar to the GNG task, SSTs were originally conceived as a prototype for measuring inhibitory control (Logan & Cowan, 1984). In a typical SST, participants perform a Go task that requires a speeded response, such as reporting the identity of a certain stimulus. On some trials however, the Go stimulus is rapidly followed by a stop signal which instructs participants to withhold their response on that specific trial (Verbruggen & Logan, 2008b). While the stop signal is usually an auditory tone, other studies have used visual (Verbruggen, Aron, Stevens, & Chambers, 2010) or tactile stop signals (Åkerfelt, Colonius, & Diederich, 2006). Importantly, the stop signal is presented randomly and at variable delays so that participants are unable to predict when it will occur. As such, stopping requires the activation of a rapid control mechanism which blocks the execution of an already initiated motor response (Logan, 1994).

*Figure 1.* Modified Go/No-Go task used to train inhibitory control towards unhealthy food consumption in a study by Lawrence et al. (2015).
When applied to ICT, SSTs require participants to categorise the content of stimuli (i.e., either target or neutral) as quickly as possible by pressing a left or a right response key on the keyboard. However, on a certain percentage of trials, a stop signal will appear after a picture has been presented, indicating that participants are required to inhibit their response. Importantly, unlike the GNG task, which pairs stop signals with 100% of target stimuli, SSTs pair both target and neutral stimuli with stop cues. While the modifications and instructions vary across studies, Figure 2 illustrates one such example utilised by Jones and Field (2013). Participants were required to quickly and accurately indicate which pictures were alcohol-related and which were neutral by pressing designated letters on the keyboard. On 50% of all trials, an auditory signal occurred at one of four latencies (50, 150, 250 and 350 milliseconds [ms]) after the picture had appeared, signifying that participants should withhold their response. If participants responded within the 2000-ms timeout period, this was deemed an inhibition error.

*Figure 2.* Modified Stop Signal Task used to train inhibitory control towards alcohol consumption in a study by Jones and Field (2013).
Comparison of Tasks

As described above, the mechanisms by which SST and GNG tasks influence health behaviour differ; namely, the cancellation of a response that is already underway (SST) versus the withholding of a response that has not yet been initiated (GNG; Smith et al., 2014). This difference is highlighted when comparing two separate studies which examined whether ICT can reduce alcohol consumption. Jones and Field (2013) trained participants using a SST, whereas Houben et al. (2011) trained participants using a GNG training task. Participants that were trained via GNG tasks consumed significantly less alcohol at follow up (seven days) but drank equivalent amounts of ad-libitum alcohol immediately after training compared to controls (Houben et al., 2011). Jones and Field (2013) found the inverse; participants that were trained via SSTs drank significantly less ad libitum alcohol immediately after training, yet had equivalent levels of alcohol consumption at follow-up (seven days) compared to controls. Nigg (2000) explains that the cancellation of an already initiated response requires more effortful inhibitory control and therefore, tends to yield more immediate training effects compared to the GNG task.

Another salient difference concerns the frequency of pairings between cue-specific stimuli and stopping. On the GNG task, cue-specific stimuli are paired with No-Go cues on 100% of trials. Conversely, on SSTs, cue-specific stimuli are only paired with stop signals on a proportion of trials (e.g., 50%). While this difference may appear negligible, it has been shown to substantially impact the formation of automatised response inhibition (Verbruggen & Logan, 2008a). Discussed in detail below, Verbruggen and Logan (2008a) demonstrated that consistent stimulus-stop associations (as per the GNG task) led to the formation of automatised response inhibition; however, varied stop-stimulus mapping (as per the SST) did not. As such, GNG training tasks have been conceptualised as activating the automatic, bottom-up processes of inhibitory control (Bowditch, Verbruggen, & McLaren, 2016),
whereas SSTs are understood to target deliberate, top-down processes of inhibitory control (Verbruggen & Logan, 2008b). This has led to the suggestion that GNG tasks may be particularly beneficial for highly automatised behaviours such as snacking and substance misuse (Allom et al., 2015). Indeed, two separate meta-analyses have compared the efficacy of SST and GNG training tasks in reducing alcohol and unhealthy food-related consumption (Allom et al., 2015; Jones et al., 2016), with both demonstrating that GNG tasks (but not SSTs) were effective in eliciting behavioural change.

**Theoretical Underpinnings of Inhibitory Control Interventions**

Two theories have been proffered in an attempt to explain the underlying mechanisms of ICT when delivered via an SST and GNG paradigm. The first is the Automatic Inhibition Hypothesis (AIH; Verbruggen & Logan, 2008a), which proposes that consistently learning to stop when presented with specific stimuli can lead to the automatisation of inhibitory control towards these stimuli (Verbruggen, Best, Bowditch, Stevens, & McLaren, 2014). The second is the Behavioural Stimulus Interaction hypothesis (BSI; Veling et al., 2008), which posits that repeatedly stopping a response towards specific stimuli can lead to the devaluation of these stimuli. Both mechanisms are discussed below.

**Automatic inhibition hypothesis.**

The AIH stems from research examining the differences between consistent and varied mappings of stimuli onto responses (Schneider & Shiffrin, 1977). Specifically, when a stimulus is consistently mapped onto a response, it enables the development of automatic associations. Conversely, when a stimulus is variably mapped onto a response, it prevents the formation of automatic associations (Logan, 1988). As such, Verbruggen and Logan (2008b) examined whether automatic response inhibition can develop over practice if stimuli are consistently associated with stopping. In a series of experiments, certain stimuli were repeatedly paired with the requirement to either respond or withhold the response which
allowed for the development of stimulus specific associations. During a testing phase, they reversed the stimulus mappings and found that participants were substantially slower at responding to stimuli that had been previously paired with stopping than going. Secondly, they found that response inhibition only improved when stimulus-stop associations were consistently mapped with stopping rather than when they were mapped in varied fashion. In essence, following the establishment of consistent stimulus-stop associations, stimuli may automatically elicit inhibition, thereby bypassing slow, top-down (i.e., effortful) inhibitory control (Houben & Jansen, 2015).

While findings from previous studies are consistent with this theory, for example, the slowing of reaction times as ICT progresses (Jones & Field, 2013; Lawrence et al., 2015), Houben and Jansen (2015) directly examined whether consistently pairing food-related stimuli with stop cues would induce automatic associations between the stimuli and stopping. Fifty-two female participants were administered a GNG training task where chocolate-related stimuli were either consistently paired with Go cues or No-Go cues. Following training, participant’s automatic associations between chocolate and going versus stopping were measured via a single category implicit association test. Their findings were consistent with the AIH; participants in the No-Go condition associated chocolate significantly less strongly with going compared to participants in the Go condition.

**Behavioural stimulus interaction.**

Veling et al. (2008) theorised that when individuals encounter stimuli that elicit positive affect, they get ready to respond. Prior to responding however, the situational demands are processed which may be consistent or inconsistent with approach. The latter of these two cases gives rise to a response conflict, which is solved by spontaneously allocating negative affect to the approach-eliciting stimuli. By doing so, the stimuli become less desirable and hence, decreases the approach tendency. In essence, Veling et al. (2008) posited
that negative affect can function as an inhibitory mechanism which prevents a positively associated stimulus from eliciting approach behaviour. However, the question arises as to whether behavioural inhibition can generate the negative affect required to subsequently inhibit an approach. To test their theory, Veling et al. (2008) conducted a series of experiments where they consistently paired positive, neutral or negative stimuli with a Go or a No-Go cue. Subsequently, participants were asked to evaluate these stimuli. Overall, they found that consistently not responding to stimuli led to a devaluation of these stimuli. However, the perceived positive or negative affect of the stimuli moderated the extent of this devaluation. Specifically, withholding responses only led to devaluation when the stimuli were positive, but not when the stimuli were neutral or negative. This interaction suggests that for devaluation to occur, and consequently, for the approach tendency to decrease, stimuli must be positive.

Support for the BSI has been provided by a number of studies. For instance, Veling, Aarts, and Stroebe (2013a) conducted a mediation analysis to investigate whether food choice following a GNG training task was mediated by reduced evaluations of food. They found that the relationship between food choice and GNG training was fully mediated by reduced evaluations; however, this was only among participants with elevated appetites (i.e., those who were hungry). Furthermore, they demonstrated that the number of pairings (i.e., 4, 8 or 12) did not influence the relationship between stop signals and food evaluations, suggesting that decreased evaluations may be independent of extensive training (Ferrey, Frischen, & Fenske, 2012). Similarly, Houben et al. (2011) examined whether strengthening response inhibition for alcohol-related stimuli could result in decreased alcohol in-take. Participants were allocated to one of two conditions where alcohol-related stimuli were either consistently paired with Go or No-Go cues. Participants in the No-Go condition demonstrated reduced
alcohol intake and significantly increased negative implicit attitudes towards alcohol-related stimuli compared to pre-testing.

Houben et al. (2012) extended the above findings and examined whether reduced alcohol consumption following inhibitory control training was attributable to implicit attitudes or to increased inhibitory control over alcohol related responses. Mediation analysis indicated that negative implicit attitudes, but not increased inhibitory control, explained the relationship between ICT and alcohol intake. However, they found that the decrease in positive implicit attitudes was not associated with a reduced approach tendency, and therefore, their findings only partially supported the BSI theory. Rather, they hypothesised that the devaluation of alcohol related stimuli was associated with newly learned connections between alcohol and not-responding; a hypothesis more closely aligned with the AIH proposed by Verbruggen and Logan (2008a). Similarly, Bowley et al. (2013) found that implicit attitudes towards beer did not significantly change as a result of being paired with either go or no-go cues; however, they did note that the relationship between reduced implicit attitudes and alcohol consumption was approaching significance.

**Meta-analysis of the theoretical underpinnings of inhibitory control training.**

Jones et al. (2016) conducted a meta-analytic investigation which, amongst other things, tested the theoretical claims that the AIH and BSI can account for behaviour change following ICT. With regards to the AIH, Jones et al. (2016) found no significant relationship between the absolute number of trials and the magnitude of the effect of ICT on behaviour ($b = .0001, p = .82$). However, they did find that the effectiveness of ICT was contingent upon the number of successful inhibitions ($b = .013, p < .01$). In other words, the more errors participants made on critical inhibition trials, the more diminished the ICT effect size. This suggests that for ICT to be effective, participants need to associate stimuli with the actual
inhibition of behaviour, rather than with signals that inhibition is required (Verbruggen, McLaren, & Chambers, 2014).

With regards to the theoretical prediction that ICT leads to the devaluation of stimuli that are associated with stopping (i.e., BSI), the analysis of six studies failed to detect an overall effect of ICT on stimulus devaluation ($SMD = 0.06, p = .60$). However, one caveat highlighted by Jones et al. (2016) is that the devaluation of stimuli may depend upon the measurement of stimulus evaluation. Within the present meta-analysis, the majority of studies used implicit association tasks to measure stimulus devaluation following ICT. However, some studies have demonstrated that other measures of stimulus devaluation, such as Likert scales, yield significantly greater stimulus devaluation effects following ICT (Lawrence et al., 2015; Veling et al., 2008). These contrasting findings may be somewhat accounted for by the weak correlation between implicit and explicit measures (Friese, Hofmann, & Wänke, 2008) and therefore, they remain tentative.

Chapter Summary

ICT is a novel intervention which utilises modified versions of the SST and GNG tasks in order to influence health-related behaviours such as unhealthy food and alcohol consumption. However, the mechanisms by which SST and GNG training tasks influence behaviour subtly differ. Firstly, the consistent stimulus-stop associations as per the GNG leads to more rapid learning of associations and, are also necessary for the establishment of automatised response inhibition. Secondly, although SSTs are understood to demand greater inhibitory control, GNG tasks may be more effective when targeting highly automatised behaviours such as snacking or substance misuse. This has been supported by two separate meta-analyses (Allom et al., 2015; Jones et al., 2016) and, when taken together, indicates that GNG tasks are likely to be the more effective option for the treatment of cigarette smoking. Despite a lack of clarity regarding the precise mechanisms that underpin behavioural change
following ICT, a growing body of research has nonetheless investigated the efficacy of ICT in eliciting behavioural changes. These studies will be critically reviewed below.
Chapter 4: Efficacy of Inhibitory Control Training

To date, only one published study has examined the efficacy of ICT in reducing cigarette smoking (Adams, Mokrysz, Attwood, & Munafò, 2017). Consequently, the efficacy of ICT will be primarily reviewed in relation to the consumption of alcohol and unhealthy food. For the most part, studies have examined the efficacy of a single session of ICT within the laboratory; however, more recently, the online administration of ICT over multiple sessions have been investigated. Both methods will be reviewed below.

Inhibitory Control Training for Alcohol Consumption

Laboratory-based inhibitory control training for alcohol consumption.

Several studies have investigated the efficacy of ICT in reducing alcohol consumption within the laboratory (Bowley et al., 2013; Di Lemma & Field, 2017; Houben et al., 2012; Houben et al., 2011; Jones & Field, 2013; Kilwein, Bernhardt, Stryker, & Looby, 2018; Liu, Hu, Smith, & Mewton, 2019). Houben et al. (2011) were the first to provide experimental evidence that training inhibitory control in the laboratory via a GNG task could prompt a reduction in alcohol consumption. They randomly assigned 52 student alcohol-drinkers to one of two conditions: A No-Go condition, which paired alcohol-related stimuli with a stopping response, and a go condition, which paired alcohol-related stimuli with the requirement to respond. Following a single ICT session, participants in the No-Go condition consumed significantly less self-reported alcohol in the week following the intervention compared with pre-intervention alcohol consumption ($\eta_p^2 = .18$). These findings were replicated by Houben et al. (2012) using 57 drinkers; however, their findings only yielded a medium effect size ($\eta_p^2 = .08$). One criticism of the Houben et al. (2011; 2012) studies is that participants were trained to either inhibit their responses when faced with alcohol-related stimuli or vice-versa (Liu et al., 2019). As such, it is difficult to tease apart whether the group differences were attributable to the training of inhibitory control (Alcohol/No-Go condition)
or to the disinhibited responding towards alcohol cues (Alcohol/Go condition; Jones & Field, 2013).

Jones and Field (2013) subsequently examined whether a Stop-Signal training task in the laboratory could reduce the immediate and weekly consumption of alcohol in 90 university students and staff who were classified as social drinkers. They addressed the aforementioned shortcomings in Houben et al. (2011; 2012) and used three experimental groups: 1) an alcohol restraint group, in which participants were required to inhibit their responses to alcohol-related stimuli; 2) a neutral restraint group, in which participants were required to inhibit their responses to neutral stimuli and; 3) a disinhibition group, where participants were never required to inhibit their responses to alcohol-related stimuli. They found that after a single ICT session, participants in the alcohol-restraint group consumed significantly less alcohol compared to participants in the other groups immediately following training ($d = 0.54$). However, in contrast to Houben et al. (2011; 2012) they found no effect of training on self-reported drinking at one-week follow-up. As previously mentioned, this discrepancy may be attributable to the fact that SSTs require more effortful inhibitory control (i.e., the cancellation of an already initiated response) and therefore, tends to yield more immediate training effects compared to the GNG task (Nigg, 2000).

Bowley et al. (2013) attempted to replicate and extend the findings of Houben et al. (2012) by comparing ICT with a brief alcohol intervention (BAI). They randomly assigned 59 university students to one of three conditions: A Go condition, a No-Go condition and a BAI condition and subsequently measured the immediate and weekly consumption of alcohol. Results indicated that participants in the BAI and No-Go condition consumed significantly less alcohol than participants in the Go-condition immediately following training ($\eta_p^2 = .11$), with further analysis revealing that there were no significant differences between the GNG and BAI conditions on alcohol consumption. However, in contrast to these
findings, Liu et al. (2019) recently demonstrated that Alcohol-No-Go training did not lead to greater reductions in alcohol consumption at both one-and-four-weeks post training in comparison to Alcohol-Go training, BAI and an Oddball control condition (i.e., responding to letters). They argued that the promising findings in previous studies may be the result of suboptimal control groups (i.e., cue-specific Go tasks) and suggested that additional research is needed to determine the optimal comparison group.

**Internet-delivered inhibitory control training for alcohol consumption.**

Recently, Jones et al. (2018) examined the effectiveness of an internet-delivered ICT program in reducing alcohol consumption in a community sample of 246 problem drinkers. In their study, participants were randomly allocated to one of three training conditions (cue-specific GNG, cue-specific SST, general SST) or a control condition (self-monitoring only) and were required to complete a maximum of 14 ICT sessions over a four-week period. While all conditions reported reductions in alcohol consumption, they found no significant differences between conditions on any measures of alcohol consumption. Importantly however, the authors noted that prior to commencing ICT, participants were required to complete an online alcohol intervention in order to increase their motivation to reduce alcohol consumption, which may have masked the reduction effects of ICT.

**Inhibitory Control Training for Unhealthy Food Consumption**

**Laboratory-based inhibitory control training for food consumption.**

Houben and Jansen (2011) were the first to examine whether the repeated inhibition of responses towards chocolate-related stimuli could significantly decrease chocolate intake using a GNG task in the laboratory. Sixty-nine female university students were divided into three conditions: 1) consistently inhibit responses towards chocolate related stimuli (Chocolate/No-Go); 2) consistently respond to chocolate (Chocolate/Go); 3) respond to chocolate on half the trials (control). While chocolate consumption did not significantly differ
between the Chocolate/Go and the control conditions, after a single ICT session, participants in the Chocolate/No-Go condition consumed significantly less during a taste-test compared to the other groups ($d = 0.59$). Houben and Jansen (2015) replicated these findings with 52 female university students, yielding equivalent effect sizes ($d = 0.64$). Similarly, Veling, Aarts, and Papies (2011) conducted a study to determine whether a laboratory based GNG training task could modify the consumption of calorie dense foods in 38 female university students who were chronic dieters. Following a single session of ICT, they found that participants who were in the no-go condition consumed significantly less food at one-day follow-up compared with those in the control condition ($\eta_p^2 = .11$).

**Online inhibitory control training for food consumption.**

A total of three studies have examined the efficacy of multiple training sessions in the form of an online intervention (Lawrence et al., 2015; Oomen, Grol, Spronk, Booth, & Fox, 2018b; Veling et al., 2014). For example, Veling et al. (2014) implemented a four-week online ICT program in which overweight adult participants ($N = 113$) were randomly assigned to a GNG task condition (food versus control) and were required to complete a 30-minute training session on one specified day per week. Participants were also given training reminders in order to encourage training compliance. Results indicated that ICT significantly reduced weight loss, but only for participants with a high body mass index (BMI; $\eta_p^2 = .04$). Lawrence et al. (2015) examined the efficacy of a shorter online ICT program that spanned one week. Specifically, overweight and obese adult participants ($N = 83$) were randomly allocated to receive four, 10-minute training sessions in which either high calorie food (intervention) or non-food stimuli (control) were paired with No-Go signals. However, unlike the Veling et al. (2014) study, Lawrence et al. (2015) did not send participants training reminders as they wanted to examine feasibility and imitate real-world conditions. At one-week follow-up, participants in the No-Go condition consumed less food, showed significant
weight loss and had decreased positive evaluations towards high calorie foods compared to controls. Furthermore, at six months, participants in the No-Go condition displayed significantly higher average weight loss (2.21kg) compared to the control group (0.36kg; \(d = 0.47\)). However, it should be noted that at the follow-up time points, participants were no longer blind to their group allocation and their self-reports of weight may be influenced by training expectancies.

**Laboratory-based Inhibitory Control Training for Cigarette Consumption**

Adams et al. (2017) were the first study to examine the effect of a single session smoking-specific GNG training task on cigarette consumption in comparison to a control GNG training task. Using a sample of 55 nicotine dependent smokers, they found no significant differences between groups on post-training cigarette consumption seven days later. However, participants in their study were not required to have an intention to quit smoking and, their control task paired smoking-related stimuli with No-Go signals on 50% of trials, which may have had a reduction effect on cigarette consumption. Therefore, further research is warranted to examine whether these factors contributed to their null findings.

**Comparison of Inhibitory Control Training and Other Interventions**

Two studies have compared ICT to other well-known diet interventions (van Koningsbruggen, Veling, Stroebe, & Aarts, 2014; Veling et al., 2014). van Koningsbruggen et al. (2014) compared the effectiveness of ICT and dieting implementation intentions in reducing the portion size of high calorie foods that 89 university students served themselves. They found that both interventions were effective in reducing the amount of high calorie foods participants selected for themselves, with GNG training yielding a large effect size \((d = 0.84)\). However, they found no additive effects when the therapies were used in combination. While this finding was unexpected given that the interventions share few methodological similarities, they reasoned that the use of one intervention appeared to make the other
redundant given that they both diminish the impulse-evoking properties of high calorie foods. However, Veling et al. (2014) found evidence suggesting the contrary and demonstrated that a combination of GNG training and implementation intentions produced greater weight loss compared to when the two techniques were administered independently. More interestingly, Veling et al. (2014) found that the implementation intervention was sensitive to individual differences in the strength of dieting goal; however, no interaction between dieting goal strength and GNG training was found. This may suggest that ICT can be effective regardless of one’s motivation to change.

**Impulsivity as a Potential Moderator of Inhibitory Control Training Effectiveness**

As an emerging intervention, it is particularly important to examine whether any individual differences influence the effectiveness of ICT. To date, this has received minimal attention; however, one study (Houben, 2011) has suggested that ICT may be particularly effective for individuals with elevated levels of impulsivity. Specifically, Houben (2011) measured participants’ (N = 29) baseline impulsiveness using an SST and then manipulated their inhibition in one of three ways: 1) palatable foods were consistently paired with stop-signals (inhibition manipulation); 2) palatable foods were never presented with a stop-signal (impulsivity manipulation) and; 3) palatable food were paired with stop-signals on half the trials. Following the manipulation, participants were immediately presented with a variety of palatable and healthy foods and the quantity of calories consumed was the dependent variable. Houben (2011) found that ICT was particularly effective in reducing palatable food consumption for participants with elevated impulsivity compared to participants with low impulsivity.

While this finding is in need of replication, other studies have used indicators of impulsivity such as body mass index, appetite, or dietary restraint and found that ICT was more effective for individuals who possessed stronger impulses towards foods (Lawrence,
Verbruggen, Morrison, Adams, & Chambers, 2015; Veling et al., 2011; Veling et al., 2013b; Veling et al., 2014). For example, Veling et al. (2013b) examined whether high appetite (i.e., more hungry) or low appetite (i.e., less hungry) influenced the effectiveness of ICT on reducing the consumption of unhealthy foods. High and low appetite participants (N = 79) were allocated to one of two conditions: 1) No-Go signals were consistently paired with high calorie food and; 2) No-Go signals were not paired with high calorie food. Following training, healthy and high calorie foods were offered to participants. They found that participants who were in the high appetitive group consumed significantly less high calorie food following ICT compared with participants who were in the low appetitive group ($\eta_p^2 = .14$). This study was replicated by the same authors and produced similar results (Veling et al., 2013a). Similarly, Veling et al. (2014) demonstrated that ICT was particularly effective for participants with high BMI; however, Lawrence et al. (2015) was not able to replicate these results and reported that BMI did not influence weight loss during training.

While the exact mechanisms underlying this potential effect are unknown, Houben (2011) theorised that as per the BSI, participants with poor inhibitory control may have stronger impulses when they are exposed to high calorie foods. Therefore, ICT elicits a greater response conflict which subsequently reduces the rewarding value of food to a greater extent. As of yet, no studies have examined whether self-report impulsivity moderates the effectiveness of ICT; however, given the extensive literature demonstrating that it shares robust positive associations with cigarette consumption and relapse (Bloom et al., 2013; Kale et al., 2018; Stautz & Cooper, 2013), we also expect ICT to be more effective for participants with high self-report impulsivity.

**Meta-Analyses of Inhibitory Control Training Interventions**

Two meta-analyses have been conducted in order to quantify the effect of ICT on alcohol and food-related behaviours (Allom et al., 2015; Jones et al., 2016).
Allom et al. (2015) included 14 studies in their meta-analytic review and found a small overall training effect size ($d = 0.38$). However, moderator analyses yielded a number of important findings. First, they demonstrated that the efficacy of training depended upon the type of training paradigm employed. Studies that utilised GNG tasks produced substantially larger effect sizes ($d = 0.50$) compared to studies that used SST ($d = 0.19$). Second, they demonstrated that in order for ICT to be effective, training must be specific to the behaviour being targeted. Studies that tailored training to the specific behaviour were significantly more efficacious ($d = 0.42$), whereas general response inhibition was not significant ($d = 0.02$). Third, they found that when behaviours were measured immediately after training, as opposed to at a later time point, they produced significantly larger effect sizes. This suggests that while ICT appears influential, its effects may be more pronounced in the short-term. Finally, they demonstrated that both training duration (i.e., the number of trials) and the type of health behaviour (alcohol vs. eating) did not moderate training effectiveness.

Jones et al. (2016) included a total of 14 published and unpublished studies in their review. Similar to the Allom et al. (2015) study, they found a small overall training effect size ($SMD = 0.36$), with equivalent training effects for both alcohol and food-related behaviours. They also demonstrated a significant difference between ICT and control groups in studies that utilised GNG tasks ($SMD = 0.47$) but not for studies that used SSTs ($SMD = 0.23$, $p = .05$) and anticascade tasks ($SMD = 0.12$, $p = .36$). Lastly, a comparison of ICT with different psychological interventions produced no significant difference ($SMD = 0.06$, $p = .39$), suggesting that ICT is equally as effective as other interventions for changing alcohol and food-related behaviour.

**Chapter Summary**

ICT is an emerging intervention that shows considerable promise as an efficacious treatment for the reduction of unhealthy food and alcohol consumption. To date, only one
study has examined the role of laboratory-based ICT on smoking and, no studies have examined the real-world application of ICT on a community sample of adult smokers. Furthermore, no study has investigated whether self-report and behavioural impulsivity moderates the effectiveness of ICT. The following chapter presents the second study in this thesis; a pre-registered randomised controlled trial investigating the effect of ICT on adult cigarette consumption. The RCT presented below is under its second resubmission in the *Journal of Consulting and Clinical Psychology* under the title “A Randomised Controlled Trial of Inhibitory Control Training for Smoking Cessation and Reduction”. Please see Appendix A for an accompanying protocol paper that was published in open access (Staiger et al., 2018). Appendix B provides information regarding the contribution of each authors to the manuscript and Appendix D presents the supplementary material referred to in this study.
Chapter Five: A Randomised Controlled Trial of Inhibitory Control Training for Smoking Cessation and Reduction

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Abstract

**Objective:** The high rates of illness and mortality associated with cigarette smoking necessitate the development of novel reduction and cessation treatments. Inhibitory control training (ICT) has recently emerged as a potentially efficacious intervention to reduce the consumption of alcohol and unhealthy food. This randomised controlled trial was the first to investigate the effect of internet-delivered ICT on cigarette consumption in a community sample of heavy smokers.

**Method:** One-hundred and seven adult smokers (mean age = 46.15, 57 female), who smoked a minimum of 10 cigarettes per day, and met criteria for a moderate or severe Tobacco Use Disorder, were recruited for the present study. Participants were randomly allocated to receive Go/No-Go training in which either smoking stimuli (intervention) or non-smoking stimuli (control) were paired with No-Go signals and were instructed to complete one training session per day over a two-week period. This trial was pre-registered with the Australian and New Zealand Clinical Trials Registry (Trial ID: ACTRN12617000252314).

**Results:** We found no significant differences between conditions on percent days abstinent or daily cigarette consumption, although there was a significant decrease in daily cigarette consumption across both conditions. Further, we found no significant moderating effects of impulsivity, gender or training dose on the relationship between cigarette consumption and the two tasks. However, the magnitude of the difference between the two tasks in daily cigarette consumption was significantly moderated by age.

**Conclusions:** Although participants in both conditions reduced their daily cigarette consumption, the intervention task was no more successful than the control task in achieving cigarette abstinence or reduction.

**Keywords:** smoking; inhibitory control; impulsivity; cognitive training; e-health.
Introduction

Cigarette smoking is one of the leading preventable causes of illness and premature death worldwide (World Health Organisation [WHO], 2015). In 2015, over 6 million people died globally as a result of smoking and, if current mortality trends persist, this number will exceed eight million by the year 2030 (Forouzanfar et al., 2016 WHO, 2011). Despite a variety of effective behavioural and pharmacological treatments (Cahill et al., 2013; Lancaster & Stead, 2017; Stead & Lancaster, 2012b), relapse to smoking remains the most likely outcome (Hughes, Peters, & Naud, 2008; Piasecki, 2006) highlighting the need for novel and innovative smoking reduction and cessation treatments.

In recent years, inhibitory control training (ICT) has emerged as a potentially efficacious intervention to reduce addictive and unhealthy behaviours, such as the consumption of alcohol or unhealthy food (Allom, Mullan, & Hagger, 2015; Jones et al., 2016). Using modified Go/No-Go (GNG) or Stop-Signal tasks (SST), ICT requires participants to establish prepotent motor responses towards neutral stimuli (e.g., clothes), while, on a minority of trials, pairs cue-specific stimuli (e.g., unhealthy food/alcohol) with stop or No-Go signals (Jones et al., 2016). It has been proposed that the pairing of cue-specific stimuli with stop/No-Go cues leads to the automatisation of inhibition towards these stimuli (Logan, 1988; Verbruggen, Best, Bowditch, Stevens, & McLaren, 2014; Verbruggen & Logan, 2008a) or, alternatively, results in a reduced approach tendency towards these stimuli via devaluation (Veling, Holland, & van Knippenberg, 2008).

ICT interventions were developed from extensive research demonstrating that impaired inhibitory control, defined as the ability to stop, or withhold an unwanted or inappropriate response (Logan, Cowan, & Davis, 1984), is an important component in the development and maintenance of addictive and other health-related behaviours (Goldstein & Volkow, 2002; Hall, 2012; Luijten et al., 2014; Perry & Carroll, 2008; Smith et al., 2014).
Indeed, for smokers, research has shown that deficits in inhibitory control are positively associated with cigarette consumption (Billieux et al., 2010; Spinella, 2002), relapse following a cessation attempt (Krishnan-Sarin et al., 2007; Powell, Dawkins, West, Powell, & Pickering, 2010) and nicotine dependence (Billieux et al., 2010; Glass et al., 2009).

Further, a recent meta-analysis compared the inhibitory control capacities of substance users with controls and found that cigarette users exhibited significant inhibitory control deficits (via GNG tasks; Smith et al., 2014). Therefore, ‘training’ this potentially modifiable risk-factor may lead to improved reduction and cessation outcomes.

The effectiveness of ICT in reducing the consumption of alcohol (Bowley et al., 2013; Houben, Havermans, Nederkoorn, & Jansen, 2012; Houben, Nederkoorn, Wiers, & Jansen, 2011; Jones & Field, 2013) and unhealthy food (Houben, 2011; Houben & Jansen, 2011, 2015; Veling, Aarts, & Papes, 2011; Veling, Aarts, & Stroebe, 2013) and, more recently, smoking (Adams, Mokrysz, Attwood, & Munafò, 2017), has primarily been examined within a laboratory setting. For instance, Houben et al. (2011) embedded cue-specific (i.e., alcohol-related) and neutral pictures (i.e., water) into a GNG task and randomly allocated participants to one of two conditions: a No-Go condition, which consistently paired cue-specific stimuli with a stopping response, and a Go condition, which consistently paired cue-specific stimuli with the requirement to respond. Following a single ICT session within the laboratory, participants in the No-Go condition consumed significantly less self-reported alcohol in the week following the session compared with pre-intervention alcohol consumption. Similar findings were reported by Jones and Field (2013). In their study, following a single ICT session which utilised an alcohol-paired SST, social drinkers were found to consume significantly less alcohol in a subsequent taste test. Recently, Adams et al. (2017) conducted a laboratory-based ICT program with smokers and examined the effect of a single session smoking-specific GNG training task on cigarette consumption in comparison to a control
GNG training task. They found no significant differences between groups on post-training cigarette consumption seven days later; however, participants in their study were not required to have an intention to quit smoking and, their control task paired smoking-related stimuli with No-Go signals on 50% of trials, which may have had a reduction effect on cigarette consumption. Therefore, further research is warranted to examine whether these factors contributed to their null findings.

Importantly, ICT has been found to be effective when delivered outside of the laboratory and in real-world settings (Allom & Mullan, 2015; Lawrence et al., 2015; Veling, van Koningsbruggen, Aarts, & Stroebe, 2014). For example, Lawrence et al. (2015) implemented an internet-delivered ICT program for 83 mostly overweight and obese adults. Participants were randomly allocated to receive four, 10-minute training sessions in which either high calorie food (i.e., intervention) or non-food stimuli (i.e., control) were paired with No-Go signals. At one-week follow-up, participants in the intervention condition consumed less food and showed significant weight loss and had decreased positive evaluations of high calorie foods compared to the control condition. Furthermore, at six months, participants in the intervention condition displayed significantly higher average self-reported weight loss compared to the control condition ($d = .47$), suggesting that cue-specific ICT can yield sustained effects. In contrast, Jones et al. (2018) recently examined the effectiveness of an internet-delivered ICT program in reducing alcohol consumption in a community sample of 246 problem drinkers. In their study, participants were randomly allocated to one of three training conditions (cue-specific GNG, cue-specific SST, general SST) or a control condition (self-monitoring only) and were required to complete a maximum of 14 ICT sessions over a four-week period. While all conditions reported reductions in alcohol consumption, they found no significant differences between conditions on any measures of alcohol consumption. The authors noted that prior to commencing ICT, participants were required to
complete an online alcohol intervention (Linke, Brown, & Wallace, 2004) in order to increase their motivation to reduce alcohol consumption, which may have masked the reduction effects of ICT. In conclusion, there is mixed evidence regarding the effectiveness of ICT in real-world settings and interestingly no online study has examined whether it might be effective in assisting individuals to reduce or quit smoking. Given the accessibility and affordability potential of an effective internet-based ICT smoking intervention, such a study is worthy of investigation.

Since ICT is a relatively new intervention, it is also important to investigate whether any individual differences influence the effectiveness of training. That is, whom does it work best for? To date, this has received minimal attention. However, given that ICT purports to target impulses evoked by the exposure to cue-specific stimuli (Veling et al., 2008; Verbruggen & Logan, 2008a), it follows that individuals with low inhibitory control, and indeed more broadly, high trait impulsivity, would likely benefit the most. To date, only one study (Houben, 2011) has examined the moderating role of inhibitory control on the effectiveness of ICT. Specifically, Houben (2011) assessed 29 participants’ baseline inhibitory control using the SST and then subsequently measured their unhealthy food consumption following a single ICT session. It was found that ICT was more effective at reducing unhealthy food consumption for participants with low baseline inhibitory control abilities compared to high levels of baseline inhibitory control. Other studies have used indicators of impulsivity such as body mass index or dietary restraint and found that ICT was more effective for individuals who possessed stronger impulses towards foods (Lawrence, Verbruggen, Morrison, Adams, & Chambers, 2015; Veling et al., 2011; Veling et al., 2013; Veling et al., 2014). As of yet, no studies have examined whether trait impulsivity moderates the effectiveness of ICT; however, given the extensive literature demonstrating that it shares robust positive associations with cigarette consumption and relapse (Bloom et al., 2013; Bos,
Hayden, Lum, & Staiger, 2019; Kale et al., 2018), we also expect ICT to be more effective for participants with high trait impulsivity.

Overall, the primary aim of the present study was to investigate the effectiveness of ICT on smoking in a community sample of heavy smokers. We used a GNG paradigm as two recent meta-analyses (Allom et al., 2015; Jones et al., 2016) demonstrated that the magnitude of the effect of ICT on alcohol and unhealthy food consumption were in the medium range for GNG tasks, whereas for SSTs, they were in the small range (Cohen, 1992). Thus, based on the work of Lawrence et al. (2015), we examined the effect of an online smoking-specific GNG training task on cigarette consumption in comparison to a non-smoking GNG training task. We chose a non-smoking GNG task as our control as it was not expected to affect smoking behaviour (Guerrieri, Nederkoorn, & Jansen, 2012; Lawrence, Verbruggen, et al., 2015; Oomen, Grol, Spronk, Booth, & Fox, 2018a; Oomen et al., 2018b) and, it ensured that we controlled for the difficulty and demands of the intervention task so as to maximise participant blinding. As such, our control can be considered ‘active’. This is the first study to investigate ICT on smoking outside of the laboratory and in doing so, adds to the important body of literature testing the effectiveness of ICT in reducing unhealthy behaviours. If shown to be effective, internet-delivered ICT could be an accessible, convenient and cost-efficient treatment for smokers with the potential of reducing smoking-related mortality rates.

Our pre-registered hypotheses were:

1) Participants who received smoking-specific ICT would report higher abstinent rates compared to participants in the active control condition at post-intervention and one-month and three-months follow-up.

2) Participants who received smoking-specific ICT would report lower daily cigarette consumption compared to participants in the active control condition at post-intervention and one-month and three-months follow-up.
3) Impulsivity would moderate the relationship between smoking-specific ICT and cigarette consumption. Specifically, participants with low inhibitory control and/or high trait impulsivity would report greater reductions in cigarette consumption following smoking-specific ICT compared to participants with high inhibitory control and/or low trait impulsivity at post-intervention and one-month and three-months follow-up.

We also conducted three exploratory analyses that were not pre-registered which examined whether the standard demographic variables of gender and age, or training dose (i.e., the number of sessions completed) moderated the relationship between condition and cigarette consumption. This double blind randomised controlled trial (RCT) was pre-registered with the Australian and New Zealand Clinical Trials Registry and was implemented in accordance with JARS guidelines (Appelbaum et al., 2018).

Method

Design

We conducted a double-blind RCT comparing the effect of an intervention task to a control task in a group of heavy smokers who wished to quit/reduce. The intervention task was a smoking version of the food GNG task used in Lawrence et al. (2015) and the control task is similar to the non-food GNG task in Lawrence et al. (2015), with No-Go training to household items. A permuted block randomisation procedure was utilised (Altman & Schulz, 2001) whereby participants were automatically allocated to the intervention or control condition via the computer through the use of a randomly generated number. The permuted blocks were organised in groups of ten, the details of which were not known by researchers involved with the administration of the trial. The trial was registered prior to data collection (Trial ID: ACTRN12617000252314) and remained as per initial registration. An accompanying protocol paper is available in open access (Staiger et al., 2018). This study
was approved by the Deakin University Human Research Ethics Committee (Project ID: 2015-298).

**Participants**

A total of 107 (57 female) adult smokers with a mean age of 46.15 years ($SD = 9.38$, range = 20 – 60) took part in the present study (see Table 1). The sample size was smaller than intended (150; (Staiger et al., 2018)); however, we terminated recruitment early as attrition rates were substantially lower than expected and we had reached the necessary sample size for adequate statistical power. On average, participants smoked 18.79 cigarettes per day ($SD = 6.93$, range = 10 – 44) and all met criteria for a moderate ($n = 41, 38\%$) or severe ($n = 66, 72\%$) Tobacco Use Disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5; American Psychiatric Association [APA], 2013).

Participants were recruited via traditional media (radio, newspaper and television), social media (Facebook) and leaflets within Deakin University. Participants were included if they met the following criteria: 1) aged between 18-60 years; 2) smoked, on average, a minimum of 10 cigarettes per day regularly over the past 12-months; 3) met criteria for moderate or above Tobacco Use Disorder as defined by the DSM-5 (APA, 2013); 5) self-reported being motivated to make a quit attempt during the training stage of the intervention; 6) had computer and internet access and; 7) completed at least Year 9 (or equivalent) schooling; a proxy to rule out any intellectual disabilities which can interfere with cognitive task performance (Bexkens, Ruzzano, Collot d'Escury-Koenigs, Van der Molen, & Huizenga, 2014).
Table 1

Demographic and Questionnaire Variables at Baseline

<table>
<thead>
<tr>
<th></th>
<th>Control (SD)</th>
<th>Intervention (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n = 53 )</td>
<td>( n = 54 )</td>
</tr>
<tr>
<td>Age</td>
<td>46.09 (9.10)</td>
<td>46.20 (9.73)</td>
</tr>
<tr>
<td>Gender (%F)</td>
<td>50.94</td>
<td>55.55</td>
</tr>
<tr>
<td>Tertiary educated (%Y)</td>
<td>62.26</td>
<td>70.37</td>
</tr>
<tr>
<td>Employed (%Y)</td>
<td>79.25</td>
<td>81.48</td>
</tr>
<tr>
<td>Cigarette consumption per day</td>
<td>19.48 (6.74)</td>
<td>18.12 (7.12)</td>
</tr>
<tr>
<td>Age commenced smoking</td>
<td>15.75 (2.43)</td>
<td>16.69 (2.41)</td>
</tr>
<tr>
<td>FTND</td>
<td>5.72 (2.02)</td>
<td>5.41 (1.80)</td>
</tr>
<tr>
<td>DSM-5 Tobacco Use Disorder symptoms</td>
<td>6.57 (1.86)</td>
<td>6.59 (2.11)</td>
</tr>
<tr>
<td>SSRT (ms)</td>
<td>260 (48)</td>
<td>264 (63)</td>
</tr>
<tr>
<td>BIS attention</td>
<td>16.51 (3.01)</td>
<td>15.85 (2.90)</td>
</tr>
<tr>
<td>BIS motor</td>
<td>22.51 (3.72)</td>
<td>22.09 (3.67)</td>
</tr>
<tr>
<td>BIS non-planning</td>
<td>24.40 (4.37)</td>
<td>24.39 (4.70)</td>
</tr>
</tbody>
</table>

Note. SD = standard deviation; F = female; Y = yes; FTND = Fagerström Test of Nicotine Dependence; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; SSRT = stop signal reaction time; ms = milliseconds; BIS = Barratt Impulsiveness Scale.

Participants were excluded if they: 1) primarily used electronic cigarettes; 2) reported a non-smoking period of two-weeks or more in the past three-months; 3) were using anti-craving medication; 4) used nicotine replacement therapy (NRT) during the intervention period; 5) reported problematic alcohol or drug use other than tobacco; 6) reported a traumatic or acquired brain injury or loss of consciousness for more than 30 minutes and; 7) reported current use of psychotropic medication such as anti-depressant, anti-psychotic and/or anxiolytic medication as these have been shown to interfere with cognitive task performance (Dias et al., 2012; Stewart, 2005).
Go/No-Go Training Tasks

**Smoking-specific GNG task.** The smoking-specific GNG task was originally developed by Lawrence et al. (2015) and was modified to incorporate images of smoking using an online JavaScript library (de Leeuw, 2015). The task consisted of nine salient smoking-related images, nine relaxing images (e.g., depicting relaxing/enjoyable activities such as sitting by a river or lying in a hammock), and 18 neutral images (e.g., clothing). Participants were instructed to indicate as quickly and as accurately as possible if an image was located on the left or right side of the screen by pressing the keys “C” and “M” respectively (Go trials). On 50% of trials, the frame surrounding the picture was bold, which was a signal for participants to withhold their response (No-Go trials). All smoking images were consistently paired with No-Go trials (100% No-Go), all relaxing images were consistently paired with Go trials (100% Go), and 50% of neutral images were paired with No-Go trials (50% Go/No-Go). This was to prevent participants from easily identifying the associative rules of the task and to ensure the task remained challenging and engaging. Each of the 36 images were presented once per block and participants completed a total of six blocks per training session. After each block, participants were provided with feedback (accuracy and mean Go reaction time) and were encouraged to try and beat their own score to increase motivation and task adherence. Time between blocks was self-paced and each training session took approximately 10-minutes.

**Control GNG task.** The control GNG task was identical to the smoking-specific task except there were no smoking and relaxation images. Instead, the smoking and relaxation images were replaced with 18 images of household objects. Go and No-Go trials consisted of an equal mix of neutral and household images (50% Go/No-Go).

**Measures**
Stop-Signal Task (Logan & Cowan, 1984; Verbruggen & Logan, 2008b). All images in the SST were smoking-related and were different from the images used in the smoking-specific GNG task. A total of 16 images (eight pairs) were embedded into the SST, where one image of the pair was a cigarette pointing to the left, and the second image was its mirror image pointing to the right. Using a laptop, participants were presented with a fixation cross (‘+’) in the centre of a white screen for 500ms. Following, a Go stimulus (i.e., one of the 16 cigarette images) appeared on the screen for 1000ms, followed by a blank white screen for 1000ms. Participants were instructed to determine as quickly and as accurately as possible if the lit end of the cigarette was pointing to the left or the right by pressing the computer key “C” and “M” respectively. Participants were also instructed to withhold their response if the Go stimulus was followed by a pair of red lines across the screen (i.e., the stop signal). The stop signal was presented randomly, and on a minority of trials (25%), to prevent participants from predicting when it would occur. The stop-signal also occurred at a variable delay (Stop-Signal Delay; SSD) after the target stimulus appeared, and the length of this delay was contingent upon the participant’s trial accuracy. After a successful stop trial, the SSD increased by 50ms, whereas after a failed stop trial, the SSD decreased by 50ms. This staircase method converges upon a SSD which results in an inhibition success rate of approximately 50%. The Stop Signal Reaction Time (SSRT) was calculated by subtracting the SSD from the mean reaction time to Go stimuli and, a longer SSRT reflects poorer inhibitory control. The SST consisted of one block of 194 trials with each of the 16 images presented 12 times and participants completed one practice block of 10 trials prior to commencing the SST.

The Barratt Impulsiveness Scale-11 (BIS-11; Patton, Stanford, & Barratt, 1995). The BIS-11, consisting of 30 items scored on a 4-point scale, is a commonly used measure which assesses different types of trait impulsivity on three main subscales: motor.
impulsiveness (e.g., “I do things without thinking;”), attentional impulsiveness (e.g., “I concentrate easily;”) and non-planning impulsiveness (e.g., “I plan tasks carefully;”). The Total BIS-11 score is the sum of the subscale scores and showed acceptable reliability ($\alpha = .79$).

**The Fagerström Test of Nicotine Dependence (FTND; (Heatherton, Kozlowski, Frecker, & Fagerström, 1991).** The FTND is a six-item self-report scale which assesses nicotine dependence and scores range from 0 to 10, with higher scores indicating greater dependence. The FTND has been validated in smokers from the general population and in clinical samples and showed acceptable reliability ($\alpha = .72$).

**Timeline Follow-Back (TLFB; (S. M. Robinson, Sobell, Sobell, & Leo, 2014; Sobell & Sobell, 1992).** The TLFB is a calendar-based assessment of daily cigarette use for periods of time ranging from 1 to 12 months prior to assessment. Initially developed to assess alcohol consumption, the TLFB has since been utilised to assess a variety of substance use inclusive of cigarette use (Robinson et al., 2014) and found to be reliable. Memory aids are used to enhance recall of certain time-periods in order to retrospectively estimate number of cigarettes used for each date. The TLFB for cigarettes has shown high test-retest reliability and temporal stability across both clinical and non-clinical participants (Robinson et al., 2014).

**Procedure**

Interested participants were invited to contact the research team via email and were screened via a structured survey over the phone/online to determine their eligibility. Eligible participants were invited to participate and attended a face-to-face meeting at the University. Participants were instructed to abstain from smoking for one-hour prior to the start of the meeting in order to ameliorate the acute effects of nicotine on cognitive performance without introducing withdrawal effects (Houlihan, Pritchard, & Robinson, 1996, 2001). At the outset
of this meeting, the study and its requirements were explained to participants and informed consent was obtained. Participants completed demographic and baseline questionnaires, a one-month retrospective recall diary of daily cigarette consumption and the Stop-Signal Task. Participants were then reminded that they would be required to cease smoking, or reduce towards cessation, at any point during the two-week training program. We did not impose an abrupt cessation target upon participants, unless this was their preference, as research has demonstrated that gradual reduction towards eventual abstinence is an effective method for dependent smokers (Asfar, Ebbert, Klesges, & Relyea, 2011; Ebbert, Hughes, & West, 2015; Hughes & Carpenter, 2006; Klemperer & Hughes, 2015; Wang et al., 2008) and, our two pilot studies indicated that participants wanted flexibility to select their own quit dates (Guo, 2018).

Participants were told that they would be randomly allocated to receive one of two brain training tasks, as the aim of the study was to investigate which was more effective. The types of images included in the training were not specified to prevent participants from identifying if they were in the intervention or control condition. In this respect, the study enabled a reasonable level of blinding as to which task was considered to be the intervention. Participants then began the online task and were automatically randomised to receive either the intervention or control GNG training task via a pre-computed randomisation procedure. Upon finishing the task, participants were instructed to complete the online training task once per day for the next 13 days, totalling 14 sessions, and were requested to abstain from smoking for two-hours prior to each session to reduce the acute effects of nicotine on cognitive performance without introducing withdrawal effects (Houlihan et al., 1996, 2001). Participants were advised that they had 24-hours to complete each of their daily training sessions and could do so at a place and time of their convenience. If participants missed a session, they were not given the opportunity to complete additional sessions. Twice per week,
participants were sent text reminders to complete the task. All data from the online task and outcome measures were securely stored on the University server and linked to an anonymous participant ID number such that only de-identified data were available to researchers. The data was checked for task performance accuracy and participant adherence to the training protocol by a research assistant who was independent from investigators and not involved in data collection or analyses.

Upon completion of the training period (T2), participants were contacted via telephone by a researcher naïve to the group randomisation (i.e., a different researcher to the one who conducted the baseline face-to-face interview). During these phone interviews, participants were asked to provide details about their daily use of cigarettes and nicotine replacement therapies or anti-craving medications during the past 14-days of training. We had two follow-up time points which occurred at one-month (T3) and three-months (T4) after T2. Telephone interviews at T3 and T4 were conducted in the same manner as T2. At the completion of each time point, participants were mailed a $20 gift card. At the conclusion of the data collection period, participants in the control condition were offered the opportunity to complete the smoking-specific ICT program.

Analytic Strategy

All analyses were conducted using IBM Statistical Package for Social Sciences (SPSS, Version 25) unless otherwise stated. An *a priori* power analysis using G*Power (Faul, Erdfelder, Lang, & Buchner, 2007) indicated that a minimum of 92 participants were required to detect a medium effect size ($d = .50$), with an alpha set at 0.05 and power set at .80 (Staiger et al., 2018). Our effect size estimate was drawn from Lawrence et al. (2015) weight-loss reduction outcome as no previous ICT studies have measured abstinence.

To examine if there were any significant differences between conditions on GNG performance and adherence, one-way ANOVAs were conducted. Percent days abstinent was
chosen as the most appropriate outcome measure to assess our primary hypothesis as only five participants reported complete cessation (see protocol for a discussion of the analysis plan of this variable; (Staiger et al., 2018). Given the strong skew, percent days abstinent was analysed using the non-parametric Mann-Whitney U test. Our primary hypothesis relating to reduction in daily cigarette consumption was analysed using a 2 (condition: intervention, control) x 4 (time: baseline, T2, T3 and T4) mixed-design ANOVA. For our primary analyses, Bayes factors were calculated using JASP (2018), using non-informed default priors. Our moderator hypotheses were separately analysed using the SPSS macro PROCESS (Hayes, 2012), with condition as the predictor variable, average daily cigarette consumption at T2, T3 and T4 as separate dependent variables, baseline cigarette consumption as a covariate and trait impulsivity (BIS-11), inhibitory control (SSRT), training dose, gender and age as separate moderator variables. Any significant moderation effects were examined using the Johnson-Neyman (JN) technique. The JN technique determines the values of the moderator where the 95% confidence interval for the expected difference in cigarette consumption between conditions at a particular follow-up point (after adjusting for cigarette consumption at baseline) does not include zero. Thirteen participants reported that they used a smoking cessation treatment at some point during T3 or T4. Results did not significantly differ when we controlled for the use of other treatment or excluded these participants and therefore, they were retained for all analyses.

**Results**

**Participant Flow**

Figure 1 illustrates the flow of participants through each stage of the study.
Figure 1. Recruitment flow diagram showing numbers of participants in each condition at each stage of the study. NRT = nicotine replacement therapy.
A total of 164 participants met eligibility criteria and were invited to participate. Although 110 participants were recruited into the study and randomised to the intervention or control condition, two participants formally withdrew all their data from the study during the training period and one individual was deemed ineligible to participate in the study as they used NRT during the training period. As such, the final intent-to-treat sample was 107.

**Missing Data**

Missing values analysis indicated that a total of four participants (3.8%) had missing TLFB data at T2, six participants (5.6%) at T3 and 13 participants (12.1%) at T4 and all TLFB missing data was due to attrition. One-way ANOVAs were conducted to compare missing and non-missing groups on all baseline characteristics and no significant differences were identified. Missing value analysis indicated that data were consistent with a missing completely at random (MCAR) pattern ($\chi^2 = 36.08, p = .33$) and therefore, a single imputation approach using the expectation maximisation algorithm was used which is considered robust when data is MCAR (Enders, 2010; Schafer & Graham, 2002). Analyses were conducted on the imputed and non-imputed datasets and comparisons yielded no significant differences in the interpretation of the results (i.e., magnitude, directions, statistical significance of effects were consistent). As such, all analyses reported are conducted using the imputed dataset to maximise the sample size available for analysis.

**GNG Training Performance**

Task adherence and accuracy were high, indicating that participants in both conditions were engaged by the training and performed well (see Table 2). As per Lawrence et al. (2015), repeated measures ANOVA were used to examine training performance and learning of stimulus specific Go or No-Go associations for participants in the intervention condition over time (see Supplementary Table 2). Results indicated that participants showed learning of stimulus specific No-Go associations, demonstrated by significantly greater accuracy to the 100% No-Go stimuli (i.e., smoking-related images) compared to the 50% No-
Go stimuli (i.e., clothes). However, reaction time did not significantly differ for 100% Go stimuli (i.e., relaxing images) compared with 50% Go stimuli (i.e., neutral images such as clothes).

Table 2

Mean Task Adherence and Performance Across the Training Period

<table>
<thead>
<tr>
<th></th>
<th>Control (SD)</th>
<th>Intervention (SD)</th>
<th>F / p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICT sessions completed</td>
<td>10.89 (3.20)</td>
<td>10.50 (2.91)</td>
<td>.43 / .51</td>
</tr>
<tr>
<td>Go RT (ms)</td>
<td>516 (66)</td>
<td>547 (91)</td>
<td>4.09 / .05</td>
</tr>
<tr>
<td>Go accuracy (%)</td>
<td>.99 (.13)</td>
<td>.98 (.24)</td>
<td>2.71 / .10</td>
</tr>
<tr>
<td>No-Go accuracy (%)</td>
<td>.97 (.02)</td>
<td>.97 (.02)</td>
<td>.20 / .66</td>
</tr>
</tbody>
</table>

Note. SD = standard deviation; ICT = inhibitory control training; ms = milliseconds; RT = reaction time.

Primary Hypothesis: Percent Days Abstinent

Table 3 shows the percent days abstinent for participants in both conditions. Few participants reported 100 percent days abstinence at T3 (intervention = 6%; control = 2%), or T4 (intervention = 7%; control = 2%). The Mann-Whitney U test indicated that the mean rank for percent days abstinent in the intervention condition did not significantly differ from the control condition at T2 ($U = 1611.00$, $z = 1.86$, $p = .06$, $r = .18$, $BF^{10} = 1.3$), T3 ($U = 1573.50$, $z = 1.40$, $p = .16$, $r = .14$, $BF^{10} = .59$) and T4 ($U = 1583.00$, $z = 1.45$, $p = .14$, $r = .14$, $BF^{10} = .66$).
Table 3

Number of Participants Reporting Percent Days Abstinent at Post-intervention and One-and-
Three-months Follow-up

<table>
<thead>
<tr>
<th>% Days Abstinent</th>
<th>Post-intervention</th>
<th>One-month follow-up</th>
<th>Three-months follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Intervention</td>
<td>Control</td>
</tr>
<tr>
<td>0%</td>
<td>49</td>
<td>43</td>
<td>47</td>
</tr>
<tr>
<td>1-49%</td>
<td>3</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>50-99%</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>100%</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Primary Hypothesis: Cigarette Reduction

A mixed-design ANOVA revealed that the hypothesised time x condition interaction was not significant \(F(3, 103) = .33, p = .80, \eta^2_p = .01, BF^{10} = 0.04\) and there was no main effect of condition \(F(3, 105) = .82, p = .37, \eta^2_p = .01, BF^{10} = 0.31\). However, there was a significant main effect of time \(F(3, 103) = 52.66, p < .01, \eta^2_p = .61, BF^{10} > 99\), indicating that for both conditions, cigarette consumption significantly decreased from baseline to T2 \((t(106) = 12.50, p < .01, d = .83, BF^{10} > 99, \text{mean difference} = 5.43, 95\% \text{CI} [4.57 – 6.30])\), baseline to T3 \((t(106) = 9.64, p < .01, d = .72, BF^{10} > 99, \text{mean difference} = 5.55, 95\% \text{CI} [4.41 – 6.70])\) and baseline to T4 \((t(106) = 7.64, p < .01, d = .62, BF^{10} > 99, \text{mean difference} = 5.04, 95\% \text{CI} [3.63 – 6.18])\). Cigarette consumption did not significantly differ between conditions at T2, T3 or T4 \((p > .05, BF^{10} < .33)\) and the magnitude of group differences in cigarette consumption are displayed in Figure 2.
Secondary Hypotheses: Moderation of Condition by Impulsivity

Separate moderated regression analyses indicated that the relationship between condition and cigarette consumption measured at T2, T3 and T4 was not significantly moderated by SSRT, attentional impulsivity, motor impulsivity and non-planning impulsivity (see Supplementary Table 3).

Exploratory Analyses: Moderation of Condition by Dose, Gender and Age

Separate moderated regression analyses indicated that the relationship between condition and cigarette consumption measured at T2, T3 and T4 was not significantly moderated by training dose or gender (see Supplementary Table 4). However, the magnitude of the difference between the two tasks in daily cigarette consumption at T2, T3 and T4 was significantly moderated by age (see Table 4).
Table 4

**Moderating Effect of Age on the Relationship between Condition and Cigarette Consumption**

<table>
<thead>
<tr>
<th></th>
<th>Post-intervention</th>
<th>One-month follow-up</th>
<th>Three-months follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$b$</td>
<td>$se$</td>
<td>95%CI</td>
</tr>
<tr>
<td>Constant</td>
<td>-.39</td>
<td>1.13</td>
<td>[-2.64, 1.86]</td>
</tr>
<tr>
<td>Condition</td>
<td>.21</td>
<td>.78</td>
<td>[-1.34, 1.76]</td>
</tr>
<tr>
<td>Age</td>
<td>.06</td>
<td>.04</td>
<td>[-0.02, 0.14]</td>
</tr>
<tr>
<td>Condition x age</td>
<td>.19*</td>
<td>.08</td>
<td>[0.03, 0.36]</td>
</tr>
<tr>
<td>Baseline smoking</td>
<td>.73***</td>
<td>.06</td>
<td>[0.62, 0.84]</td>
</tr>
</tbody>
</table>

*Note. Condition x age interaction at post-intervention ($F_{change} = 5.23, p = .024, R^2_{change} = .02$), one-month follow-up ($F_{change} = 5.77, p = .018, R^2_{change} = .03$) and three-months follow-up ($F_{change} = 7.21, p = .008, R^2_{change} = .04$).*

* $p < .05$  
** $p < .01$  
*** $p < .001$.

Figure 3 presents the moderation effects using the JN technique. After adjusting for cigarette smoking at baseline, participants in the intervention condition were found to have significantly lower cigarette consumption when compared to the control condition at T2, T3 and T4 but only for participants aged below 24.83 years (T2), 36.88 years (T3) and 36.44 years (T4). Notably, at T2 and T4, participants in the intervention condition were found to have higher cigarette consumption when compared to the control condition, but only for participants aged above 58.37 years (T2) and 56.95 years (T4).
Figure 3. Johnson-Neyman figures representing the age x condition moderation effects for post-intervention (top), one-month follow-up (middle), and three-months follow-up (bottom). Horizontal lines represent the expected difference in cigarette smoking (and associated 95% CI) between conditions at each time point, after adjusting for baseline cigarette smoking. The green regions represent the ages at which the magnitude of the difference in daily cigarette smoking between conditions was different from zero (i.e., 95% CI does not pass zero; specific ages are presented in each figure). A value below \( y = 0 \) indicates greater reduction in the cue-specific condition (relative to the control condition) at the timepoint. Grey shaded area represent the ages at which there was no difference between the two conditions in reported cigarette consumption at the specific timepoint.
Given the apparent negative consequences of the intervention on cigarette consumption for individuals older than 58 years (T2) and 56 years (T4), we conducted follow-up examinations of participants over 56-years. Notably, given our sample recruited participants between 18 and 60-years, our sample comprised of only 20 participants over this age (~18%). On examination, one participant in the control condition reported a major decrease in cigarette consumption across all three time-points, which we believe was driving the result towards more improvement in the control condition. When this participant was removed, there was no longer a difference between conditions at T2 and T4 for older participants (see Supplementary Figure 1). We also repeated these analyses controlling for nicotine dependence (FTND). The condition x age interaction was robust to covariate adjustment at T2 ($t(101) = 2.70, p = .008, 95\% CI .06 – 0.40$), T3 ($t(101) = 3.14, p = .002, 95\% CI .13 – 0.57$) and T4 ($t(101) = 3.25, p < .001, 95\% CI .16 – .65$).

**Discussion**

This pre-registered clinical trial was the first to examine the real-world effectiveness of ICT on cigarette smoking. It also investigated whether individual differences in impulsivity, training dose, gender or age would moderate the effectiveness of ICT. We found no significant differences between the intervention and control condition on percent days abstinent or daily cigarette consumption although, there was an overall significant decrease in daily cigarette consumption across both conditions. Second, we found no significant moderating effects of impulsivity, gender or training dose on the relationship between cigarette consumption and smoking-specific ICT. However, an exploratory analysis found that the relationship between smoking-specific ICT and cigarette consumption was significantly moderated by age, suggesting that smoking-specific ICT may be effective at reducing daily cigarette consumption for younger participants only.
Across both conditions, the majority of participants reported zero days abstinence, whereas only a minority of participants reported complete abstinence and, analyses indicated that there were no significant group differences in percent days abstinent at any post-intervention time-points. As such, our primary hypothesis that smoking-specific ICT would result in greater percent days abstinent compared to the control task was not supported. However, given the well-established difficulties of achieving abstinence (Hughes et al., 2008; Piasecki, 2006), for ICT to improve cessation rates it may need to be supported by pharmacotherapy to address the cravings and withdrawal symptoms typically associated with early nicotine cessation. Indeed, several recent Cochrane reviews have demonstrated that combining pharmacological and behavioural interventions increase the likelihood of abstinence compared to when each is administered alone (Stead, Koilpillai, & Lancaster, 2015; Stead & Lancaster, 2012; Stead & Lancaster, 2015). Nonetheless, as this is the first study to investigate the effect of ICT on abstinence, it provides initial evidence that smoking-specific ICT, at least as delivered here, may be ineffective as a standalone treatment option to achieve smoking cessation.

With regards to our primary hypothesis concerning smoking reduction, we found that both conditions reported significant reductions in daily cigarette consumption at all post-intervention time points; however, there were no significant differences between conditions. This main effect may be attributable to a variety of features common to both tasks including the requirement to make a quit or reduction attempt (Balmford, Borland, & Burney, 2010; de Vries, Eggers, & Bolman, 2013), or non-specific factors, such as the self-monitoring of daily cigarette consumption or having the motivation to quit/reduce smoking (Curry, Wagner, & Grothaus, 1990; Mcfall & Hammen, 1971). However, a limitation in the design of our study was that we did not include an additional, no-intervention (passive) control group. As such, we are unable to determine whether the reductions in cigarette consumption are attributable
to these aforementioned common features or, whether they relate to features inherent in the two GNG tasks. While it is not expected that a non-smoking specific GNG task would impact smoking behaviour (e.g., Guerrieri et al., 2012; Lawrence et al., 2015; Oomen et al., 2018), additional studies that incorporate passive control groups may assist in disentangling these findings.

However, an important question of this trial was, for whom does ICT work best? Interestingly, exploratory analyses suggested that when age was included as a moderator, smoking-specific ICT led to greater reductions in daily cigarette consumption, relative to the control condition, for younger adults. While we found evidence for the opposite effect (i.e., a greater increase in daily cigarette consumption for the smoking-specific condition relative to the control condition) in older adults at T2 and T4, we believe this was due to one outlying older individual in the control condition who reported large decreases in cigarette consumption. As such, we suggest that exposure to smoking-specific ICT has no increase effect on cigarette consumption in older adults. Although complete abstinence is the preferred outcome in smoking interventions (West, Hajek, Stead, & Stapleton, 2005), our findings may nonetheless have important clinical implications. Reductions in daily cigarette consumption have been shown to yield considerable long-term health benefits (Eliasson, Hjalmarson, Kruse, Landfeldt, & Westin, 2001; Gerber, Myers, & Goldbourt, 2012; P. N. Lee, 2013; Lotan, Goldbourt, & Gerber, 2017) and importantly, can lead to improved cessation outcomes (Asfar et al., 2011; Ebbert et al., 2015; Hughes & Carpenter, 2006; Klemperer & Hughes, 2015; Wang et al., 2008). Therefore, smoking-related ICT may be a promising approach for this sub-group of the population to reduce consumption, which may assist in achieving complete cessation.

With regards to the underlying mechanisms of our age-related finding, one potential explanation may be that younger adults have increased neuroplasticity, and therefore, show
greater benefits from cognitive training compared to older adults (Brehmer, Westerberg, & Bäckman, 2012; Calero & Navarro, 2007; Dahlin, Nyberg, Bäckman, & Neely, 2008; Verhaeghen, Marcoen, & Goossens, 1993). For instance, a series of reviews indicate that cognitive training can lead to greater improvements for younger compared to older adults, and, that younger adults are able to maintain the effects of training over time to a greater extent compared to older adults (S. Jones et al., 2006; Lillard & Erisir, 2011; Lustig, Shah, Seidler, & Reuter-Lorenz, 2009; Noack, Lövdén, Schmiedek, & Lindenberger, 2009; Park & Bischof, 2013). Similarly, parallel literature across executive functions has demonstrated that there are age-related differences in associative learning (Clark, Hazeltine, Freedberg, & Voss, 2018; Kray & Eppinger, 2006) and therefore, younger adults may have been able to form cue-inhibition associations more effectively than older adults. Finally, it is possible that older smokers, who have smoked for a longer period of time and may have more entrenched habits are less sensitive to devaluation of cigarette cues than younger smokers. This idea is potentially consistent with prominent theories of addiction such as the habit-formation theory (Everitt & Robbins, 2005) that suggest that repeated and long-term use of addictive substances leads to a shift in behaviour from being goal-oriented (and sensitive to reinforcer devaluation) to habitual (insensitive to reinforcer devaluation). However, our interaction was robust to covariate adjustment of nicotine dependence and therefore, further investigation into the underlying mechanisms of ICT may shed light on its potential differential effectiveness by age. Nonetheless, it is important to recognise this was an exploratory finding and given the number of moderation effects examined, there is the possibility of Type I error. As such, we look to future studies to replicate this finding before firm conclusions can be reached.

Our secondary hypothesis that impulsivity would moderate the relationship between smoking-specific ICT and daily cigarette consumption was not supported. Given that only
one study (Houben, 2011) has examined the moderating role of inhibitory control on ICT effectiveness, our null findings may indicate that the effectiveness of ICT is not influenced by an individual’s level of pre-existing capacity for inhibitory control or alternatively, could be attributable to differences in methodology between the two studies. For example, Houben (2011) measured unhealthy food consumption immediately following ICT, whereas we assessed cigarette consumption over much longer time periods (i.e, up to three-months). As such, pre-existing levels of inhibitory control may only have an influence on the behavioural outcomes of ICT in the immediate-term, but not in the long-term. Second, Houben (2011) measured baseline inhibitory control using a general SST, whereas we used a smoking-specific SST. While a smoking-specific SST is expected to be a more sensitive measure of inhibitory control relevant to smoking (Houben, Nederkoorn, & Jansen, 2014; Nederkoorn, Coelho, Guerrieri, Houben, & Jansen, 2012; Svaldi, Naumann, Trentowska, & Schmitz, 2014), it is possible that the influence of baseline inhibitory control on outcome is only detected in general SSTs.

Similarly, baseline trait impulsivity had no influence on the effectiveness of ICT. However, our findings are consistent with another study that purports to address impulse control via mindfulness training in those who are substance dependent (Staiger, Dawe, Richardson, Hall, & Kambouropoulos, 2014). In this study, individuals who reported improvements in mindfulness also reported less drug use at follow-up irrespective of their levels of trait impulsivity at baseline. As such, an individual’s level of impulsivity may not influence their capacity to improve inhibitory control via ICT or alternatively, it is possible that ICT exerts its influence on behaviour via devaluation of the smoking stimuli (which will be the focus of an additional paper) rather than changes in impulse control. Given that this is the first study to investigate the role of trait impulsivity on ICT effectiveness further investigation is required.
A number of caveats regarding the methodology are warranted. First, while 12-month outcomes are preferable (West et al., 2005), we wanted to firstly establish whether smoking-specific ICT had any short-term effects before moving to a costly, long-term trial. Additional research is needed to investigate whether reductions in cigarette consumption for participants are maintained beyond three-months post-intervention and, whether this effect remains significant for younger participants only. Second, although self-reports of cigarette consumption are considered reliable, a lack of biochemical verification may have limited the accuracy of our data (Gorber et al., 2009; Hatzianandreou et al., 1989; Patrick et al., 1994). However, as participants were blinded to condition and were also unaware that a control condition existed, any misreporting of data would likely be balanced across both conditions. Third, as we did not impose a specific quit date, nor require abrupt cessation, there was substantial variability as to when participants reduced or ceased smoking. This may explain why the moderating effect of age was weaker at post-intervention compared to subsequent time points and further research is required to examine the importance of abstinence and reduction goals in relation to the effectiveness ICT. Fourth, unlike ICT in Lawrence et al. (2015) where 100% of Go images were towards healthy food, there is no obvious ‘healthy’ opposite of smoking and therefore, our choice of relaxing stimuli as Go images may not have been effective in training a ‘healthy alternative’ to smoking. Furthermore, the training task performance data suggest that smoking-specific participants did not learn to ‘go’ to these relaxing images because they were no faster to respond to them compared to the non-predictive filler images. Given this, future research might consider increasing the proportion of smoking-related No-Go stimuli in lieu of Go stimuli (Chen, Veling, Dijksterhuis, & Holland, 2016; Veling et al., 2014). This is of course an empirical question and warrants further investigation. Finally, our control task did not include smoking-related images as we wanted to avoid the potential confounds associated with executing responses to smoking
images in a control condition (see Adams, Lawrence, Verbruggen, & Chambers, 2017 for a discussion of this issue in relation to food); however, our intervention task did include smoking-related images, and this may have increased craving. Therefore, in addition to passive control groups, future research may want to also investigate the use of a control condition matched for cue-exposure (such as passive viewing of the same images presented in the intervention task).

Future research might also consider allowing participants to select their own smoking-related images, as research has found that when stimuli are more impulse evoking, ICT can be more effective (Chen et al., 2016; Veling et al., 2011; Veling et al., 2013). Although we conducted a pilot study with heavy smokers to ensure that the smoking-related images included in this trial were highly salient and elicited cigarette craving (Guo, 2018), it is possible that if smoking stimuli are personalised for each participant, ICT may be more effective. Indeed, studies have shown that the more similar the stimuli is to the preferred alcoholic beverage the stronger the reactivity and craving to the cue (Staiger & White, 1991). This issue awaits further investigation; however, given the fast pace of technological advancements, future ICT studies delivered via mobile devices may enable participants to personalise their own Go and No-Go images and enhance the ecological validity of the intervention.

To conclude, this study found that smoking-specific ICT did not help smokers achieve abstinence or reduce their cigarette consumption over and above the control task and, impulsivity did not moderate the effectiveness of smoking-specific ICT on daily cigarette consumption. Although analyses indicated that age may be an important factor when considering the effectiveness of ICT, these were exploratory and need to be replicated with a long-term follow-up before any firm conclusions can be reached.
Chapter Six: General Discussion

Smoking is one of the leading preventable causes of illness and premature death worldwide necessitating the development of novel and innovative cessation treatments. It has been highlighted in this thesis that impulsivity is an important risk factor for cigarette use and consequently, targeting this modifiable risk factor may facilitate the cessation of cigarette smoking. In line with this overarching aim, this thesis conducted two studies. The first study was a meta-analytic review of the association between impulsivity and adolescent cigarette smoking and was published in the journal *Drug and Alcohol Dependence* in 2019 (see Appendix E for a copy of the published article). The second study was a pre-registered double-blind randomised controlled trial which investigated the effect of inhibitory control training on cigarette reduction and cessation. This manuscript is currently under its second resubmission in the *Journal of Consulting and Clinical Psychology*. This final chapter will provide an overview of the aims and findings of each study and discuss the relevant implications, limitations and considerations for future research pertinent to each study.

**Study 1: UPPS-P Impulsive Personality Traits and Adolescent Smoking: A Meta-Analysis**

**Summary of aims and findings.**

This meta-analysis aimed to determine the direction and strength of the association between each of the five UPPS-P impulsive traits and adolescent cigarette consumption and nicotine dependence. A secondary aim was to investigate whether age, gender, ethnicity and sample type moderated these associations. Following methods used by previous meta-analyses (Dir et al., 2014; Stautz & Cooper, 2013; VanderVeen et al., 2016), an exhaustive search of extant literature was conducted, yielding a total of 51 studies. Five separate meta-analyses were conducted, and each demonstrated that adolescent cigarette consumption was positively correlated with each of the UPPS-P impulsive traits. In each, the magnitude of the
correlation was in the small range (Cohen, 1988), with \( r \)'s ranging between 0.17-0.20. As only two studies provided effect sizes for the association between the UPPS-P impulsive traits and adolescent nicotine dependence, meta-analyses could not be conducted. Publication bias was assessed via funnel plots and fail-safe-N analyses and both methods indicated that the results are unlikely to be influenced by unpublished studies (see Appendix C). With regards to the secondary aims of this study, results indicated that age, gender, ethnicity and sample type did not moderate any of the associations between adolescent cigarette consumption and the UPPS-P impulsive traits.

This was the first review to provide an assessment of the strength of the relationship between adolescent smoking and the UPPS-P impulsive traits. Overall, findings demonstrated that the relationship between each impulsive trait and adolescent cigarette consumption was significant, albeit small. Second, it highlighted that the relationship between impulsivity and nicotine dependence remains unknown until further data is available. Given that adolescence represents a critical time period regarding the trajectory of nicotine dependence (Backinger et al., 2003; Ernst et al., 2009; Lantz, 2003), findings lend support to the use of impulsivity-targeted prevention and intervention strategies. These are discussed below.

**Clinical implications.**

Thus far, surprisingly few studies have investigated the effectiveness of impulsivity-targeted interventions to prevent or reduce adolescent substance use. For example, one research group examined the effectiveness of tailoring anti-drug messages towards high sensation seeking adolescents and found that these types of communication were effective at reducing adolescent cannabis use (Palmgreen, Donohew, Lorch, Hoyle, & Stephenson, 2001). Another research group investigated the effectiveness of brief, group-based interventions which specifically targeted sensation seeking via psycho-education, motivational interviewing and cognitive behavioural therapy (Conrod et al., 2008; Conrod et
al., 2011; Conrod et al., 2006). Findings indicated that sensation seeking targeted interventions led to significant reductions in adolescent alcohol consumption and binge drinking and importantly, delayed the onset of alcohol consumption by up to six-months. Given the promising nature of these findings, the development of similar mass media and/or group-based interventions which specifically address impulsive tendencies in adolescents who smoke would be important to investigate.

However, results from this meta-analysis demonstrated that each of the five impulsive traits shared similar associations with cigarette consumption (r’s ranging between 0.17-0.20). Therefore, in addition to targeting sensation seeking, which has been the focus of the research discussed above, this thesis suggests that interventions need to be developed that target all of the UPPS-P impulsive traits. For instance, positive and negative urgency, which are more affect driven, can potentially be targeted via emotion regulation strategies (e.g., Sloan et al., 2018), mindfulness (Robinson, Ladd, & Anderson, 2014), or by teaching alternate ways of managing positive and negative moods that are low in risk or do not involve cigarette consumption. Conversely, lack of premeditation, which is more automatic in nature, could potentially be targeted via computerised cognitive training tasks such as cognitive bias modification (e.g., Wiers, Gladwin, Hofmann, Salemink, & Ridderinkhof, 2013) and impulse control training (e.g., Lawrence et al., 2015). In essence, adopting a multidimensional approach towards these interventions may result in enhanced treatment outcomes and reduce the economic and health burden related to adolescent cigarette consumption. Furthermore, developing a suite of impulsivity-targeted strategies enables adolescents to select the interventions that resonate most strongly with their personality, which may enhance the ecological validity and effectiveness of such interventions.

However, this thesis suggests that research efforts should first be directed towards preventing, or at least delaying, the initiation of cigarette smoking for several reasons. First,
research indicates that there is an inverse relationship between the age of smoking onset and subsequent adult consumption and nicotine dependence (Buchmann et al., 2013; Chassin et al., 2000; Jefferis et al., 2003). For example, Buchmann et al. (2013) showed that delaying the age of initiation by as little as one-year among 213 smokers was associated with smoking 33.5 fewer cigarettes per month at age 22 and a decrease of 0.42 in the Fagerström Test for Nicotine Dependence score. Second, studies have demonstrated that nicotine dependence can develop rapidly, and, at low levels of cigarette consumption (DiFranza et al., 2000; Rose et al., 2010) and therefore, once an adolescent is dependent upon nicotine, the likelihood that they will be able to cease smoking significantly decreases (Chatkin et al., 2004; Ferguson et al., 2003; Ong et al., 2005). Finally, exposure to nicotine can induce long-standing neurobiological changes in the adolescent brain which can potentially heighten the risk that they will engage in other substances and risky behaviours (Kandel & Kandel, 2014; Musso et al., 2007; Yuan, Cross, Loughlin, & Leslie, 2015). Therefore, the benefits of smoking prevention strategies may extend beyond cigarette use and positively influence a range of broader substance use and risky behaviours.

**Limitations and considerations for future research.**

Several limitations typically experienced when conducting meta-analyses were discussed in Chapter 2. These include: 1) the potential impact that missing studies could have on results; 2) limitations to the generalisability of findings to clinical populations; 3) the predominant use of self-report smoking data in lieu of bio-chemical verification and; 4) the small number of studies included in the meta-analysis for positive urgency. In addition, several broad limitations are discussed below and considerations for future research are suggested over and above what has been previously discussed.

First, the associations found in the present meta-analysis were in the small range (Cohen, 1988), suggesting that each impulsive trait only accounts for a small portion of the
variance in adolescent cigarette consumption. As has been highlighted throughout this thesis, cigarette smoking is highly addictive and, once dependent upon nicotine, the likelihood that one will achieve complete cessation substantially decreases. Therefore, if the intervention strategies discussed above are to have a significant and long-standing impact on cigarette consumption, it is likely that they will need to be implemented in accordance with other, well-established smoking interventions such as pharmacotherapy or behavioural therapies (e.g., Stead, Koilpillai, & Lancaster, 2015; Stead & Lancaster, 2012; Stead & Lancaster, 2015). For instance, a Cochrane review of 47 studies found that when behavioural support was used as an adjunct to pharmacotherapy, the probability of a successful quit attempt increased by 10 to 25% (Stead et al., 2015). Future research may wish to also investigate whether the inclusion of impulsivity-targeted interventions as an adjunct to well-established cessation treatments enhances their effectiveness.

Second, as we were not able to conduct meta-analyses for nicotine dependence, it remains unknown whether the associations between impulsivity and cigarette consumption become stronger or weaker as adolescents transition from consumption to nicotine dependence. Indeed, previous meta-analyses found differential patterns of association between impulsivity and dependence/problematic use compared to consumption (Kale et al., 2018; Stautz & Cooper, 2013; VanderVeen et al., 2016) and therefore, the impulsivity-targeted interventions discussed above are limited to cigarette consumption and may be ineffective when treating adolescents with nicotine dependence.

Several limitations pertaining to the smoking literature warrants discussion. First, the measurement of cigarette consumption adopted by studies included in the meta-analysis varied. For instance, some studies used the frequency of cigarette consumption (e.g., Baker & Yardley, 2002), whereas others used the quantity of cigarette consumption (e.g., Doran & Trim, 2013). Of those that used frequency, some studies restricted the timeframe to seven
days (e.g., De Leo & Wulfert, 2013), whereas others examined the frequency of consumption over 12-months (e.g., Lynskey et al., 1998). While we used a random effects model and examined demographic and methodological sources of heterogeneity via moderator analysis, the considerable variations between the measurement of cigarette consumption may have reduced the accuracy of our findings (Borenstein et al., 2009). In order to address the inconsistencies regarding the measurement of cigarette consumption, there is a need to develop a standardised questionnaire which separately examines the frequency and quantity of cigarette consumption and includes clearly accepted and defined timelines for cigarette use, ranging from daily to 12-monthly. This would have the potential to significantly improve the comparability of cigarette use across research.

Second, impulsivity is not a unique risk factor for cigarette consumption but also predicts a diverse range of other risk-taking or substance-use behaviours (Kandel & Kandel, 2014; Lai, Lai, Page, & McCoy, 2000; Torabi, Bailey, & Maj-Jabbari, 1993). Therefore, it is possible that many participants in the studies reviewed may have also engaged in other substance-use behaviours in addition to cigarette smoking. Nonetheless, it has been suggested that impulsivity is a transdiagnostic risk factor and therefore, intervening on each impulsive trait may also influence a wide range of other substance and mental-health related behaviours.

**Study 2: A Randomised Controlled Trial of Inhibitory Controlled Training for Smoking Cessation and Reduction**

**Summary of aims and findings.**

The primary aim of this randomised controlled trial was to investigate the effect of internet-delivered inhibitory control training (ICT) on cigarette consumption in community sample of adult heavy smokers. A secondary aim was to investigate whether self-report (i.e., BIS-11) and/or behavioural impulsivity (i.e., SST) moderated the relationship between ICT
and cigarette consumption. In addition, three exploratory analyses were conducted which examined whether age, gender and training dose (i.e., the number of training sessions completed) moderated the relationship between ICT and cigarette consumption.

It was hypothesised that participants who received smoking-specific ICT would report higher rates of abstinence and lower daily cigarette consumption compared to participants in the active control condition at post-intervention and one-month and three-months follow-up. Second, it was hypothesised that participants with elevated self-report and behavioural impulsivity would report greater reductions in cigarette consumption following smoking-specific ICT compared to participants with low self-report and behavioural impulsivity at post-intervention and one-month and three-month follow-up.

One-hundred and seven adult smokers were randomly allocated to receive ICT in which either smoking stimuli (intervention) or non-smoking stimuli (control) were paired with No-Go signals. All participants were instructed to complete one training session per day over a two-week period. Contrary to expectations, no significant differences between conditions on abstinent rates or daily cigarette consumption at post-intervention and one-month and three-months follow-up were found; however, both conditions reported significant reductions in daily cigarette consumption across all time points. Impulsivity, gender and dose did not moderate the relationship between condition and cigarette consumption. However, exploratory analyses revealed that age significantly moderated the relationship between condition and cigarette consumption whereby younger participants in the intervention group reported significantly less cigarette consumption than older participants at one and three-months post-intervention.

**Clinical implications.**

Findings suggest that ICT may be an effective method to help younger adults reduce cigarette smoking. Importantly, gradual reductions in cigarette consumption have been shown
to be an effective method to achieve eventual cessation (Asfar et al., 2011; Ebbert et al., 2015; Hughes & Carpenter, 2006; Klemperer & Hughes, 2015; Wang et al., 2008) and, have been shown to yield considerable long-term health benefits (Eliasson et al., 2001; Gerber et al., 2012; Lee, 2013; Lotan et al., 2017). While it is acknowledge that even low rates of cigarette consumption can be harmful (Schane, Ling, & Glantz, 2010), findings suggest that smoking-related ICT may be a worthwhile approach for young adults to initially reduce consumption, which may assist in achieving complete cessation. This has considerable promise given that a longitudinal study which examined data on 21,000 participants aged 50-years and older found that if smokers quit before the age of 35-years, they were likely to regain two-years lost to smoking and were comparable to never-smokers on a variety of health-related measures (Østbye & Taylor, 2004).

Replication of this age-related finding is needed before any firm conclusions can be drawn. However, if it is successfully replicated, future research may wish to examine the underlying mechanisms in greater detail. As discussed in Chapter Five, it is possible that younger participants experienced greater benefits from ICT compared with older participants due to an increased capacity for neuroplasticity (Brehmer et al., 2012; Calero & Navarro, 2007; Dahlin et al., 2008; Verhaeghen et al., 1993). Second, as per the habit-formation theory (Everitt & Robbins, 2005), it is possible that heavy, long-term smokers, who have more entrenched habits, may be less sensitive to the devaluing effects of ICT (Veling et al., 2008) compared to younger smokers. Third, parallel literature across executive functions has demonstrated that there are age-related differences in associative learning (Clark, Hazeltine, Freedberg, & Voss, 2018; Kray & Eppinger, 2006) and therefore, younger adults may have been able to form cue-inhibition associations more effectively than older adults. Finally, an additional suggestion worthy of investigation concerns the incentive sensitisation theory (Berridge & Robinson, 2016; Everitt & Robbins, 2005). According to this theory, repeated
and long-term use of addictive substances can produce lasting changes in the mesocorticolimbic dopamine systems, which are involved in the process of wanting. Through prolonged substance use, wanting for substances increases while liking either decreases or is no longer associated with substance-use. Therefore, if devaluation of smoking-stimuli is indeed the mechanism by which ICT reduces cigarette consumption, this theory suggests that ICT would be less effective for older, long-term smokers who may be less prone to ‘like’ smoking.

**Considerations for future research.**

Despite the potential promise of this age-related reduction finding, results from this RCT suggest that ICT is not an effective treatment for smoking cessation. Importantly, it is possible that this study was inadequately powered to detect abstinence, as our a priori power analyses were based upon previous research which has examined reduction (i.e., as per Lawrence et al., 2015). Nonetheless, as has been highlighted throughout this thesis, achieving cessation is extremely challenging, especially for heavy, nicotine dependent smokers (Hughes et al., 2008; Piasecki, 2006). Therefore, as suggested in Chapter Five, for ICT to improve cessation rates, it may need to be supported by pharmacotherapy to address the cravings and withdrawal symptoms that are the among the strongest predictors of relapse (Allen, Bade, Hatsukami, & Center, 2008; Killen & Fortmann, 1997). Indeed, several recent Cochrane reviews have demonstrated that combining pharmacological and behavioural interventions increase the likelihood of abstinence compared to when each is administered alone (Stead et al., 2015; Stead & Lancaster, 2012a, 2012b) and we suggest that future research examines whether the use of ICT as an adjunct to these existing treatments augments treatment success. However, our low cessation rates may also be influenced by other factors which future ICT research may want to consider. These are discussed below.
**Targeted versus flexible quit dates**

This RCT did not impose a quit date upon participants but rather, allowed them to select their own quit date and/or reduce towards cessation during the two-week training period. This flexible approach to quitting was informed from our two pilot studies (Guo, 2018) and also, by previously published research which has demonstrated that flexible quit dates are an effective method for cessation (Asfar et al., 2011; Ebbert et al., 2015; Hughes & Carpenter, 2006; Klemperer & Hughes, 2015; Wang et al., 2008).

However, allowing a flexible approach to cessation introduced considerable variability regarding how participants approached cessation. For instance, some participants chose to cease smoking on the first day of training, other participants chose to complete all 14 training sessions and then cease and finally, some participants chose to reduce their smoking across the training period and then cease. Such variations meant that we were unable to answer several important questions regarding the most effective way to deliver ICT. For instance, is ICT most effective if participants firstly strengthened their inhibitory control capacities via training and then make a quit attempt? Or conversely, is ICT most effective if participants firstly make a quit attempt and then use the training sessions to maintain cessation?

Due to our methodology, these questions remain unknown and therefore, allowing a flexible quit date may have meant that for a portion of participants, treatment delivery was suboptimal. As this was the first study to examine ICT on smoking cessation, future studies are needed to elucidate the most effective way to deliver ICT and examine the impact that a targeted versus flexible quit date has on cessation rates following ICT.

**Dose of ICT**

Another factor which may have contributed to the low cessation rates relates to the quantity and frequency of ICT sessions (i.e., dose). In this study, participants were instructed...
to complete one session per day across 14 days, which is the equivalent highest number of training sessions delivered across all ICT research to date. However, there are no clear guidelines regarding the optimal number of ICT sessions needed to elicit a positive and long-lasting behavioural change and future research is needed to directly examine this issue. For example, future studies could compare the effects of a set number of ICT sessions (e.g., 8 and 12) on smoking cessation outcomes or alternatively, allow participants to use ICT as frequently as needed and examine whether cessation rates improve as a result of increased dosage. This latter approach, where participants can use the training as often needed, appears to align more closely with well-established smoking cessation interventions, such as nicotine replacement therapy. For instance, guidelines from the Royal Australian College of General Practitioners (2011) on the usage of nicotine replacement therapy advise smokers to use 8-12 pieces of gum per day (approximately once per hour) for a minimum of eight weeks. However, as Jones et al. (2016) demonstrated in their meta-analysis of ICT research, the effectiveness of ICT appears to be contingent upon the number of successful inhibitions and therefore, dose-related enquiries may be less important than ensuring participants understand the task so that they correctly inhibit responses to cue-specific stimuli. Overall, ICT is still an emerging research and therefore, many important questions regarding its optimal delivery should be the focus of future research.

Clinical versus non-clinical samples

Participants in this study were heavy, nicotine dependent smokers who met criteria for a Tobacco-Use Disorder as per the DSM-5 (APA, 2013) and therefore, this sample can largely be classified as ‘clinical’. Conversely, much ICT research has been conducted using non-clinical samples, such as students, social drinkers or participants who are overweight. This gives rise to the question as to whether many of the promising ICT findings can be transferred to populations with a diagnosed clinical disorder and/or entrenched habit. Indeed,
Adams et al. (2017) recruited nicotine dependent smokers and found no significant effect of ICT on subsequent cigarette consumption. Similarly, Jones et al. (2018), recruited a community sample of problem drinkers and found no significant effect of ICT on alcohol consumption. Although food-related ICT research has been conducted using obese participants (Chen et al., 2018; Lawrence et al., 2015), no research has investigated the effectiveness of ICT on unhealthy food consumption and/or weight loss in clinical populations, such as those with a diagnosed Binge Eating Disorder. Continued research using participants with clinical disorders/entrenched habits are needed to disentangle these findings and determine, which population group derives the greatest benefit from ICT.

**The role of impulsivity in ICT**

A final consideration for future research involves clarifying whether the effectiveness of ICT is contingent upon one’s pre-existing level of impulsivity. In what was the first trial to examine the moderating effect of both behavioural (i.e., SST) and self-report (i.e., BIS-11) impulsivity, results from this RCT demonstrated that training was not particularly effective for participants with elevated levels of impulsivity. Several possibilities for these null findings were offered in Chapter Five; however, an additional factor is worthy of consideration. As impulsivity is a multidimensional construct, it is possible that this study did not measure the facet of impulsivity that is responsible for moderating the effectiveness of ICT. For example, the UPPS-P measure could have been administered in lieu of, or in addition to, the BIS-11, which may have provided a more widespread and comprehensive assessment of trait impulsivity. Similarly, the SSRT is only one behavioural measure of impulsivity that can be derived from the SST and, future research might want to examine whether other derivatives, such as response monitoring (i.e., adjustments in reaction time following unsuccessful versus successful inhibitions), are effective moderators (see Bø, Aker, Billieux, & Landrø, 2016 for a discussion of this in relation to binge drinking). Given the vast
and multifaceted nature of impulsivity, much research is still required to clarify its role in ICT.

**Concluding Remarks**

Cigarette smoking is one of the leading preventable cause of illness and death worldwide. Despite a range of effective treatments, relapse rates remain at unacceptably high levels and novel, innovative interventions are needed to improve cessation rates. The broad construct of impulsivity has been implicated in all stages of cigarette use and consequently, targeting this modifiable risk-factor may increase the likelihood of achieving abstinence. The first study of this thesis synthesised extant literature and demonstrated that there is a significant, albeit small, association between impulsivity and adolescent cigarette consumption. These findings lend support to the use of impulsivity-targeted strategies to prevent and intervene on adolescent smoking. The second study was the first double-blind randomised controlled trial investigating the effect of ICT on adult smoking. Although ICT was not found to be an effective treatment for abstinence, exploratory moderator analyses demonstrated that ICT was particularly effective in helping younger participants reduce their cigarette consumption. While replication is needed before any firm conclusions can be drawn, ICT may be a promising approach for this sub-group of the population to reduce consumption, which may assist in achieving eventual cessation. Overall, it is the hope that the two studies presented in this thesis stimulate further enquiry into impulsivity-targeted smoking interventions as they may have the potential to reduce the morbidity and mortality rates associated with smoking.
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Appendix A

Published Protocol Paper
STUDY PROTOCOL

A randomised controlled trial examining the efficacy of smoking-related response inhibition training in smokers: a study protocol

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Abstract

Background: Smoking is one of the leading preventable causes of illness and premature death worldwide. Despite a variety of effective treatments, relapse rates remain high, and novel, innovative interventions are needed in order to reduce the global prevalence of smoking. Research has indicated that deficits in the ability to inhibit a response (referred to as response inhibition) is a predictor of relapse and subsequently, targeting this potentially modifiable risk factor may lead to improvements in smoking outcomes. Indeed, in recent years, stimulus-specific response inhibition training has emerged as a potentially efficacious intervention to reduce unwanted/ unhealthy behaviours such as alcohol and unhealthy food consumption. As such, the present trial is the first to evaluate the real-world efficacy of response inhibition smoking training (INST) in a sample of adult heavy smokers.

Methods/design: This randomised controlled trial will recruit nicotine dependent smokers aged between 18 and 60 using social media and advertisements in Victoria, Australia. The sample target was 150 to account for drop out and non-adherence. Once informed consent has been obtained, participants complete a range of baseline measures during a face to face interview. Participants are randomly allocated to one of two online training conditions: an intervention training group (INST), which requires participants to exercise response inhibition towards smoking-related stimuli; or an active control group, which requires participants to exercise response inhibition towards household items and does not include any smoking-related stimuli. They complete the first training session during the interview to ensure the training protocol is clear. Both groups are instructed to complete a further 13 training sessions (1 per day) at home on their computer and follow-up phone calls will be conducted at three time points: post-intervention, one-month and three months. The primary outcomes are: a) rates of smoking cessation and; b) reduction in the quantity of average daily smoking at post-intervention, one and three months follow-up.

Discussion: There is a pressing need to develop novel and innovative smoking interventions. If proven to be effective, INST could make a highly cost-effective contribution to improvements in smoking intervention outcomes.

Trial registration: The trial was prospectively registered with the Australian New Zealand Clinical Trials Registry 17th February 2017. Trial ID: ACTRN12617000252314.

Keywords: Smoking cessation, Response inhibition, Inhibitory control, Cognitive training, Devaluation, eHealth, Craving, Intervention

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Background
Tobacco smoking is one of the leading preventable causes of illness and premature death worldwide. It is the second largest contributor to the burden of disease globally, with 134.2 million years lost to disability, illness and premature death [1]. In 2013, 6.1 million people died globally as a result of tobacco use [1], and, if trends persist, this number will exceed 8 million by the year 2030 [2]. Furthermore, tobacco use has been found to cost the global economy more than US$1 trillion each year in healthcare expenditures and lost productivity [3]. As smoking remains at unacceptable levels across the world [4, 5], examinations of effective and accessible smoking cessation treatments are crucial in reducing the global burden of smoking on public health.

Currently, pharmacological and psychosocial interventions have the most support as efficacious treatments for the cessation of smoking [6–10]. However, despite the positive outcomes associated with these interventions, most smokers do not seek formal treatment to reduce smoking [11] and existing treatments can entail several limitations. First, smokers have reported concerns regarding adverse side-effects of pharmacological treatments which have impacted treatment uptake and long-term adherence [12–14]. Second, the long-term cost of pharmacological and psychosocial interventions, which can be more expensive than cigarettes themselves, often prohibit individuals from accessing smoking cessation treatments. This is particularly relevant given that: 1) the financial costs of tobacco are one of the primary reasons underpinning quit intentions and attempts [4, 15, 16] and; 2) the incidence of smoking is increasing most rapidly in developing nations who have the lowest levels of disposable income [5]. Therefore, there is a critical need for accessible and cost-efficient interventions for smoking cessation. Third, relapse rates remain consistently high following treatment [17] and, the vast majority will relapse within five to 10 days of treatment cessation [18, 19]. Thus, a substantial proportion of individuals attempting to quit smoking fail to achieve long-term abstinence, inviting the question: what modifiable risk factors for smoking relapse may be targeted to increase abstinence rates or at the very least result in reduction of level of smoking?

Previous research indicates that deficits in response inhibition are a strong predictor of relapse for smokers following a quit attempt [20, 21]. Research suggests that recently abstinent smokers experience heightened difficulties with response inhibition [22, 23], indicating that targeting this may assist in preventing relapse. Importantly, a meta-analysis [23] supports evidence showing that individuals dependent on substances such as cocaine and alcohol may experience deficits in response inhibition. Furthermore, Yin and colleagues [24] found that a group of smokers reported response inhibition deficits on the GNG task. Taken together this provides some evidence that smokers may experience difficulties with response inhibition. Of significance is that individuals who reported higher nicotine dependence experienced greater deficits in response inhibition than those of lower use or dependence [25, 26]. Given that heavier smokers find it more difficult to quit [27, 28], response inhibition deficits may be an effective target for treatment in these individuals.

Indeed, response inhibition training interventions utilising tasks such as the go/no-go (GNG) task and stop signal task (SST) focus on training successful inhibition of a habitual or pre-potent response by pairing pictorial cues of the targeted behaviour with stop signals or no/go cues [29]. The GNG task targets automatic bottom-up response inhibition (or action restraint) by consistently pairing no-go cues with the target stimuli [30, 31], while the SST targets top-down inhibitory control (or action cancellation) as stop signals occur after an initiated response and are mapped only to a proportion of target stimuli [32]. These tasks have recently been examined to reduce alcohol and food intake, yielding efficacious results [33]. For example, Houben, Havermans, Nederkoorn, and Jansen [34] randomly assigned 57 heavy alcohol drinkers to receive one of two training conditions: a beer/no-go condition, where alcohol-related stimuli were consistently paired with a stopping response, or a beer/go condition, where participants always responded to alcohol-related stimuli. Compared to participants in the beer/go condition, those who were trained to inhibit their response towards alcohol-related stimuli (beer/no-go) reported significantly less alcohol intake. Similar findings were reported by Jones and Field [35]. In their study, following motor inhibition training utilising a modified SST, heavy social drinkers were found to consume significantly less alcohol in a subsequent ad libitum taste test.

More recently Lawrence et al. [36] implemented an internet-delivered response inhibition training intervention for food among 83 overweight and obese adult participants. Participants were randomly allocated to receive four 10-min training sessions completed online. In the intervention group, high-calorie foods were consistently paired with no-go signals and in the control group, non-food stimuli were consistently paired with no-go signals. At one-week follow-up, participants in the food no-go condition consumed significantly less food, showed significant weight loss, and had decreased positive evaluations towards high calorie foods compared to controls. At 6 month follow-up, participants in the intervention group displayed significantly higher average weight loss (2.21 kg) compared to controls (0.36 kg). These findings are consistent with a previous trial [37].
that compared two interventions for losing weight: an implementation intention intervention that instructed participants to plan reminders for dieting and a response inhibition intervention that paired no-go responses with food-related stimuli. Findings indicated that participants who completed only the response inhibition training reported significant weight loss after four training sessions. Together, these results indicate that response inhibition training can be effectively delivered online, promoting greater accessibility and cost-efficiency of these types of interventions.

Two meta-analyses have found that inhibitory control training resulted in an overall significant effect (albeit a small effect size), with GNG training yielding larger (medium) effect sizes than SST training [29, 33]. According to the Behaviour Stimulus Interaction (BSI) theory [38] behavioural changes induced by the GNG training are mediated by changes in evaluations of the stimuli used in the task. That is, positively regarded stimuli will become associated with negative affect as a result of consistently being paired with no-go cues. This is thought to devalue the stimuli and minimise the likelihood of approach behaviours occurring towards the stimuli in real life. This theory has been supported by evidence in studies targeting alcohol consumption that suggest a mediating effect of changes in implicit attitudes on alcohol intake [34, 39]. In the food domain, there is evidence of devaluation of trained no-go food stimuli as assessed by visual analogue scales [36, 40, 41]. Another proposed mechanism of response inhibition training is the automatic inhibition hypothesis (AIH) [32], which posits that automatic response inhibition can develop over practice if stimuli are consistently associated with stopping [42, 43]. These two potential mediating hypotheses will be investigated in this trial.

In summary, given that significant effects of the GNG task were found despite the use of non-clinical samples, it was expected that these interventions would be particularly effective with smokers as smoking receives the most frequent reinforcement compared with other dependent populations, with multiple smoking sessions each day. Furthermore, we hypothesise that it will be particularly beneficial for heavy smokers who report the greatest difficulty with impulse control [4]. This is suggested by findings that stronger nicotine dependence is associated with poorer inhibitory control [44]. Thus, this is the first study to use the GNG task in a sample of individuals who have a Tobacco Use Disorder according to DSM-5 criteria and who wish to quit/reduce smoking.

As previous studies have found response inhibition training to be effective even when administered over the internet [36, 37], this study delivered the training paradigm online. This enabled the intervention to be accessible, convenient and cost-efficient for individuals and further contribute to reducing the burden on other treatment services and resources. The study is a randomised controlled trial (RCT) examining the efficacy of response inhibition training in reducing smoking in heavy dependent smokers. It is implemented in accordance with CONSORT guidelines, and involves collecting follow-up data from participants at 1 month and 3 months post-intervention.

Primary hypotheses

1. Smokers who received smoking-related response inhibition training (INST program) would report significantly higher cessation rates compared to those in the active control condition at the end of the intervention, 1 month and 3 months post-intervention.
2. Smokers who received smoking-related response inhibition training (INST program) would report significantly less cigarette consumption compared to smokers in the active control condition at the end of the intervention, 1 month and 3 months post-intervention.

Secondary hypotheses

1. Smokers who received smoking-related response inhibition training (INST program) would report significantly less craving for cigarettes compared to smokers in the active control condition at the end of the intervention and 1 month and 3 months post-intervention.
2. Smokers who received smoking-related response inhibition training (INST program) would report significantly lower levels of nicotine dependence compared to smokers in the active control condition at the end of the intervention and 1 month and 3 months post-intervention.

Predictor/moderator hypotheses

1. Individuals reporting high levels of impulsivity would report significantly improved outcomes from the intervention training compared to those with lower levels of impulsivity.
2. Individuals who completed a greater number of sessions (i.e., dose) would report significantly improved outcomes from the intervention training compared to those who completed less sessions.

Mediator hypotheses

1. The effects of INST training on level of smoking would be mediated by devaluation of smoking...
stimuli as measured by a devaluation of smoking images task.

2. The effects of INST training on level of smoking would be mediated by an independent measure of response inhibition (SST).

The following exploratory question was proposed:

1. Do smokers who receive smoking-related response inhibition training (INST program) report significantly higher levels of self-confidence and motivation to quit smoking compared to smokers in the active control condition at the end of the intervention, 1 month and 3 months post-intervention.

Methods/design

Design

This is a 2-group parallel-block double-blind randomised controlled trial testing the efficacy of an intervention compared to an active control training. The intervention training is a smoking version of the food GNG training task in Lawrence et al. [36]. The active control training is similar to the control training in Lawrence et al. [36], with no-go training to household items. The Deakin University Human Research Ethics Committee (DUHREC) reviewed and approved all relevant study materials (Project ID: 2015–298). The trial was registered with the Australian New Zealand Clinical Trials Registry (Trial ID: ACTRN12617000252314; see Additional file 1: Table S1 for items from the World Health Organisation Data Set as per Spirit Guidelines). No study protocol amendments were made once the trial commenced and this protocol was originally submitted to this journal 1 November 2017.

Procedure

The following sections describe the study procedure. See Table 1 for an overview.

Initial screening

Participants were adult smokers aged between 18 and 60 years, recruited through social media and advertisements in Victoria, Australia who had a desire to quit smoking.

Inclusion criteria

- Aged between 18 and 60 years.
- Smoke, on average, a minimum of 10 cigarettes per day for the last 12 months.
- Meet criteria for moderate or above Tobacco Use Disorder defined by the DSM-5 [45].
- Be motivated to make a quit attempt during the training stage of the intervention.
- Completed at least Year 9 (or equivalent) schooling.
- Have computer and internet access during the intervention phase of the study.

Exclusion criteria

- Primarily uses electronic cigarettes on a daily basis.
- Non-smoking period of 2 weeks or more in the past 3 months.
- Currently using anti-craving medication.
- Using nicotine-replacement therapy during the intervention period.
- Self-reported problematic alcohol or drug(s) use other than tobacco.
- Reported a traumatic or acquired brain injury or a loss of consciousness for more than 30 min.
- Reported current use of psychotropic medication such as anti-depressant, anti-psychotic and/or anxiolytic medication.

Interested participants were invited to contact the research team via email. They were screened over the phone/on-line to determine their eligibility. Participants who met the inclusion criteria were invited to participate in the study and attended a face to face interview in order to sign the consent form, collect baseline measures and participate in the first online training session.

Baseline assessment (T1)

At the beginning of the baseline interview session, participants read the plain language statement and if in agreement signed the consent form. They were requested to report any adverse events or consequences which will be reported in the flow chart of the primary outcomes paper. They were informed that they were able to withdraw from the study at any time. They were asked to indicate whether they would like to receive a summary of the trial findings following completion of data analyses. Participants were informed that they would receive one of two brain training tasks as the aim of the study was to investigate which one was more effective. While they were informed that the task incorporated a “variety of visual images”, the types of images were not specified to prevent participants from identifying if they were in the control group and hence we propose that participants were likely blind to the nature of the intervention and whether they were randomised to an active condition.

Participants completed a battery of questionnaires (outlined in Table 1), and completed ratings of their craving, motivation and self-efficacy. Following the completion of the questionnaires, participants completed ratings of stimulus evaluation test and a smoking stop signal task (SST), an independent measure of response inhibition separate to the response inhibition training.
Randomisation
Immediately following the completion of the baseline assessment, participants began the online training task. Participants were automatically randomised to either the intervention or the control training task via a pre-computed randomisation procedure. A permuted block randomisation procedure was utilised [46] whereby participants were allocated to the intervention or control group through the use of a randomly generated number. The permuted blocks were organised in groups of ten, the details of which were not known by investigators involved with the administration of the trial. The use of the permuted block randomisation process ensures that intervention group numbers will be balanced at the end of each block and is thus the recommended process in studies with smaller samples.

Upon finishing this task participants were instructed to complete the online training task once per day for the next 13 days, totalling 14 sessions. They were asked to rate their smoking craving level before and after each training session. Twice per week, participants were sent text reminders to complete the training. All data from the online training task and outcome measures were securely stored on the Deakin University server and linked to an anonymous participant ID number such that only de-identified data were available to researchers. The data was checked for training task performance accuracy and
participant adherence to the training protocol by a research assistant who was independent from investigators and not involved in data collection or analyses.

**Inhibition training task**
The intervention is an online GNG training task as developed by Lawrence et al. [36], modified to incorporate images of smoking. The task included nine smoking images (or household items in the control group), nine relaxation images (or household items in the control group) and 18 neutral filler images presented on the left or right of the computer screen (see Fig. 1). Each image was presented for 1250 ms followed by a 1250 ms inter-stimulus interval. Participants were instructed to indicate whether the image is located to the left or the right of the screen using the keys “C” and “M” respectively on their keyboard. On half of the trials, the frame around the picture was bolded and the participants were required to not respond (no-go trials). On the other half of the trials the frame was not bolded (go trials) and the participant were required to respond as quickly as possible. During each training session participants completed 6 training blocks, with each of the 36 images presented once per block. At the end of each block, participants were provided with feedback on their accuracy and mean correct go reaction time and will be encouraged to continue trying to beat their own score. Each training session will last for approximately 10 min. Participants were asked to complete the training at home in a quiet place and preferably, when they experienced craving for a cigarette.

**Intervention group**
The intervention consisted of nine smoking-related images, nine relaxing images, (i.e. depicting relaxing/enjoyable activities), and 18 neutral filler pictures (e.g. clothing). For the intervention group, the smoking-related pictures were always “no-go” trials and the non-smoking pictures were always “go” trials. The neutral pictures were equally “go” and “no-go” trials (see Fig. 1). The neutral filler pictures were incorporated to prevent participants from easily identifying the associative rules of the task and to ensure the task remains challenging and engaging.

**Control group**
In the control group, participants complete a similar task to the smoking intervention group except that randomly presented 18 images of household objects replace the 18 smoking and relaxation images. The household images were presented equally as “go” and “nogo” trials.

**Post-intervention (T2)**
At the completion of the two-week intervention period, participants are contacted via phone by a researcher naïve to the group randomisation (i.e. a different researcher to the one who conducted the baseline interview). They receive a text message reminder 24-h prior to confirm the time of the phone call. During these phone interviews, participants are asked to provide details about their use of cigarettes and nicotine replacement therapies or anti-craving medications over the previous 2 weeks. At the conclusion of this interview, participants are emailed a link to complete the same battery of questionnaires, ratings of their craving, motivation and self-efficacy and SST (completed last) as completed at baseline (T1).

**One-month and three-months follow-up (T3 and T4)**
Follow-up at 1 month (T3) and 3 months (T4) are conducted in the same manner as T2. The two follow-up time points are identical with the exception that the SST was not completed at T3 only in T4 to reduce participant burden. At the completion of each time point, participants were mailed a $20 gift card. At the conclusion of the data collection period, participants in the control group are offered the opportunity to complete the smoking-related response inhibition training.

**Measures**
This study used information from a face-to-face interview session (T1) and phone interviews (T2, T3 and T4), in addition to self-report questionnaires, a cognitive task and a stimulus evaluation test. A list of measures used at each assessment point is provided in Table 1. Demographic information, such as age, gender, socioeconomic status and number of years of smoking, were collected at baseline.

**Researcher-administered measures**

**Timeline Follow-Back (TLFB)** [47, 48]
The TLFB is a calendar-based assessment of daily cigarette use for periods of time ranging from 1 to
12 months prior to assessment. Initially developed to assess alcohol consumption, the TLFB has since been utilised to assess a variety of substance use inclusive of cigarette use [47]. Memory aids are used to enhance recall of certain time-periods in order to retrospectively estimate number of cigarettes used for each date. The cigarette TLFB has shown high test-retest reliability and temporal stability across both clinical and non-clinical participants [47].

**Self-report measures**

*Fagerström Test for Nicotine Dependence (FTND)* [49]
The FTND is a six-item self-report questionnaire of nicotine dependence. Dichotomous items (yes or no) are scored as 0–1, and options for categorical items are scored 0–3. The FTND has a maximum score of 10, with higher scores indicating greater nicotine dependence. The FTND demonstrates moderate internal consistency (α = .61) and has been validated in smokers from the general population [48] and in a clinical sample [50].

*Craving for cigarettes*
A one-item question utilising a 100 mm slider scale measures craving from “not at all” to “extremely”. Participants respond to the question “How much are you currently craving a cigarette”. A slider bar is presented at the left end of the scale and participants will click and drag the bar along the scale to indicate their response. It has been found that a single measure of craving is just as reliable and sensitive as self-report questionnaires for measuring craving for smoking [51, 52]. Slider scales are considered to be an engaging type of interface [53] and are regarded as a psychometrically acceptable measurement [54].

*Depression, Anxiety and Stress Scale (DASS-21)* [55]
The DASS-21 is a 21-item measure consisting of three subscales: depression, anxiety, and stress. Participants are asked to use a four-point Likert scale to rate the extent to which they have experienced the state described over the past week. The DASS has excellent internal consistency for the total scale (α = .97), and each subscale (Depression = .96; Anxiety = .92; Stress = .95) has high test-retest reliability and acceptable construct and convergent validity [56].

*Alcohol Use Disorders Identification Test (AUDIT)* [57]
The AUDIT is a 10-item measure of alcohol problems. Questions relate to frequency and quantity of consumption, and alcohol-related problems. Participants are asked to rate items from 0 to 4 and can receive a maximum possible score of 40, with higher scores indicative of more hazardous drinking, AUDIT is highly reliable and valid for use across a range of populations [58].

*Barratt Impulsiveness Scale (BIS-11)* [59]
The BIS-11 is a 30-item questionnaire assessing trait impulsivity. Each item is scored on a four-point Likert scale that ranges from “rarely/never” to “almost always”. Scores are summed to yield an overall total score ranging from 30 to 120, with higher scores indicating greater trait impulsivity. The BIS-11 also provides scores on three subscales: attentional impulsiveness, motor impulsiveness, and non-planning impulsiveness. The BIS-11 is widely used in research and clinical contexts and has been shown to demonstrate good reliability [59, 60].

**Ratings of motivation and self-efficacy**
Participants are asked to rate their motivation (“currently, how motivated are you to reduce or quit smoking?”) and self-efficacy (“currently, how confident are you in your ability to quit or reduce smoking?”) on slider scales. The scale is a 100 mm line with the left anchor labelled “not at all” and the right anchor labelled “extremely”. Similar to the craving slider scale, participants indicate their response by clicking and dragging the slider bar along the scale.

**Stimulus evaluation test (ratings of likeability of smoking and relaxing images)**
Slider scales are used for the likeability ratings of the smoking and relaxing images used in the inhibition training task (INST). Participants are presented with the question, “how much would you like to do this activity right now?” and rate the images from “not at all” to “extremely”. The slider bar is presented in the middle of the scale and participants click and drag the slider bar to indicate their response.

**Cognitive task**

*Stop Signal Task (SST)* [32, 61, 62]
A smoking-specific version of the SST [30, 32, 61–63] is utilised. The SST contains images of smoking-related stimuli that are different images from those used in the intervention task. Participants are presented with a fixation cross in the centre of a screen on a white background for 500 ms. A smoking-related image (go-stimulus) then appears for 1000 ms, followed by a blank white screen for 1000 ms (inter-stimulus interval). The 16 images used in the SST are comprised of 8 pairs of images, where one image of the pair is a cigarette pointing to the left, and the second image is its mirror image pointing to the right. As such, the presentation of stimuli pointing left or right will be equally balanced. Each of the 16 images is presented a total of 12 times.

Participants are instructed to indicate whether the cigarette is pointing left or right by pressing the computer keys “C” or “M” respectively (Fig. 2). The stop signal is a pair of red lines across the image and will appear
on 25% of trials. It appears at a short delay (Stop Signal Delay or SSD) after the onset of the go stimulus and stays on screen until the inter-stimulus interval. Participants are instructed to respond as quickly as possible but to not respond when the red lines appear. This delay between the onset of the go signal and the stop signal begins at 250 ms on the first stop trial, and then adjusted by 50 ms in a staircase manner. Successful inhibition on stop trials results in the SSD increasing for the next stop trial, while unsuccessful inhibition, where the participant responds on a stop trial, will shorten this delay by 50 ms. The SST consists of one practice block of 10 trials followed by the experimental block of 192 trials. The SSD will be used to calculate the stop signal reaction time (SSRT) as a measure of response inhibition and the reaction time on go trials will be a measure of behavioural impulsivity [62].

Analysis plan
All participants will be included in the intent-to-treat analyses for the primary and secondary hypotheses. If relevant, per protocol analysis will include those who complete at least four sessions of the training (as per Lawrence et al. [36]) and achieve a training accuracy of at least 70%. SST data will be included for those who yield an accuracy of 40–60% on stop trials and at least 70% on go trials. Prior to analyses, all variables will be examined through IBM Statistical Package for Social Sciences (SPSS Version 25) for accuracy of data entry, missing values and fit between their distributions and the assumptions of multivariate analysis. Any violations will be addressed as per standard protocols [64].

Missing data will be managed using SPSS. First, a missing value analysis will be conducted to determine the percentage and pattern of missing data. If missing data are found to relate to a measured participant variable, those variables will be included as covariates in the analyses. If appropriate, multiple imputation will be used to replace missing values and the imputation model will include baseline covariates and outcome data. Missing data will be imputed using the Markov Chain Monte Carlo method or the Monotone method, contingent upon the pattern of missing data. A minimum of five imputed datasets will be produced [65]; however, depending on the percentage of missing data, a minimum of 20 imputed datasets may be required [66]. Wherever possible, results from the complete case analysis will be compared with results based on imputed data. If there are important differences, explanations will be offered.

The primary and secondary hypotheses will be assessed using separate mixed-design ANOVAs and a Chi-square analysis for the binary outcome. Depending on the rate of smoking abstinence at follow up, the outcome variable will be calculated as either binary (smoking abstinence: yes/no) or percent days abstinence if Chi-square analysis is contraindicated due to low numbers in each cell. For all other mixed design ANOVAs group (i.e., intervention or control) will be included as the between-subjects factor and time (survey time points) is the within-subjects factor. For the smoking reduction primary hypothesis, the repeated-measures factor will be the average number of cigarettes smoked per day at each timepoint (i.e., baseline, post-intervention, 1 month and 3 months post intervention). For the secondary hypotheses, the repeated-measures factor will be craving or nicotine dependence at each time-point. The predictor hypotheses will be examined using separate moderated regression analyses, with group as the predictor variable, impulsivity and dose as the moderator variable and change in smoking as the dependent variable.

The two mediation hypotheses will be assessed using a linear mixed model approach to examine whether the effects of INST training on level of smoking will be mediated by devaluation of smoking stimuli or an independent measure of response inhibition (SSRT).

The exploratory questions related to self-confidence and motivation will be examined using a separate mixed-design ANOVA, with group included as the between subjects factor and self-confidence and motivation at each timepoint included as the repeated-measures factor.

Repeated measures ANOVAs will be performed on “go” reaction times and “no-go” accuracy to examine stimulus-specific learning effects (100% stimuli vs. 50% stimuli) over time (first vs. fourth training session as per the analysis by Lawrence and colleagues to allow comparability). Evidence of learning across the two time points will be indicated by faster reaction time on 100% go stimuli and fewer errors on 100% no-go stimuli. Any further exploratory analyses will be labelled as such in the publication.

Power analysis
As previous ICT studies have not targeted abstinence the current study was powered on smoking reduction based on Lawrence et al., [36] weight reduction ICT outcome data. Power analysis conducted via G*power indicated that an overall sample size of 92 is required to detect a medium effect size (approximately .50 cohen’s d based on Lawrence et al.) at the .05 alpha level using linear.
techniques (power = .80). Given that it is expected that approximately 25% will be lost to follow-up and up to 30% would not complete a minimum of 4 sessions, the target of the current study was set at 150 at the time of trial registration. However, estimated target sample may be amended if attrition is better than expected.

Discussion
Despite a decline in smoking rates prevalence of tobacco smoking still remains unacceptably high. Many pharmacological and psychosocial interventions for smoking are restricted in accessibility due to barriers such as cost and easy access. This trial has been designed to deliver internet-based response inhibition training in order to offer a simple, low-cost, and easily accessible smoking cessation/reduction intervention. As such, even small effect sizes of the intervention may translate to cumulatively large gains to public health. The current study protocol has been designed to examine the efficacy of response inhibition training to assist dependent smokers to cease or reduce cigarette use.

The intervention has several strengths regarding its timing, delivery and content. Firstly, the intervention maximises the use of being an internet-based program, which capitalises on the ability to have a wide reach within the community at a relatively low cost. This ensures that the intervention is both convenient and highly accessible given that the majority of the population have access to a computer. Secondly, while there is currently limited evidence to suggest that training response inhibition to smoking cues reduces cigarette use or craving [67], previous studies suggest that online response inhibition training to energy-dense food images helps individuals reduce their food intake, weight and food liking [36, 37, 68]. Thirdly, it has been suggested [69] that the best test of stimulus-specific response inhibition training is to use real-world studies that adopt a mixed between- and within-subjects design with repeated-measures (pre to post-intervention). This allows changes from baseline to be computed for meaningful/ecologically valid outcome measures.

While the usual process in translational research is to conduct “proof of concept” studies in the lab before attempting trials in the real-world, we decided to proceed straight to a real-world RCT of smoking-related response inhibition training based on the promising findings in eating behaviour and weight change. This is because laboratory studies can only measure acute training effects that may have little application or predictive value for real-world effects, and because laboratory studies typically adopt a single-session, between-groups design with the dependent variable often being measured only once post-training. This design is limited by confounds such as only one group being exposed to smoking cues during training. Furthermore, if the training relies on changing stimulus-response associations [43], it may be more effective at inducing behavioural change when conducted in real-world contexts associated with smoking (such as the home or workplace) than when conducted in a neutral laboratory setting.

A number of limitations need to be considered. Ongoing studies need to include an objective measure of nicotine use and larger samples in order to adequately power mediation analyses.

Considerations for future research
If this trial suggests positive effects of smoking-related response inhibition training, future research will need to determine how to optimise outcomes for smokers. Furthermore, research could include examining which aspects of the intervention will produce particular effects. This is both in terms of the training schedule (frequency, duration, timing and location of the training) and the mode of delivery (e.g. online vs. smartphone delivery). Smartphone apps and digital interventions to assist with smoking cessation are very popular but are largely lacking in evidence [70]. This RCT aims to contribute to the evidence-base for the development of new innovative eHealth interventions for smoking cessation.

Additional file

Additional file 1: Table S1. Items from the World Health Organisation Trial Registration Data Set as per SPIRIT guidelines. (DOCX 15 kb)

Abbreviations
AIH: Automatic Inhibition Hypothesis; ANOVA: Analysis of Variance; AUDIT: Alcohol Use Disorders Identification Test; BIS-11: Barratt Impulsiveness Scale; BS: Behavioural Stimulus Interaction; CONSORT: Consolidated Standards of Reporting Trials; DASS-21: Depression, Anxiety and Stress Scale; DSM-5: Diagnostic and Statistical Manual of Mental Disorders; FTND: Fagerström Test for Nicotine Dependence; GNG: Go/No-go; ID: Identification; INST: Inhibition Smoking Training; NRT: Nicotine Replacement Therapy; RCT: Randomised Controlled Trial; SSD: Stop Signal Delay; SSRT: Stop Signal Reaction Time; SST: Stop Signal Task; T1: Time 1 (baseline assessment); T2: Time 2 (post-intervention); T3: Time 3 (one month follow-up); T4: Time 4 (three months follow-up); TLPB: Timeline Follow-Back

Acknowledgements
The authors would like to thank the following people for their expertise and input: Ron Borland, Robert Dvorak, Frederick Verbruggen, Peter Enticott, Denise Foley, Sasha Davies, Ben Richardson, and Adrian Shatte. Thank you to the participants for participating and providing the feedback on this program.

Funding
This research is wholly funded by Deakin University. This funding source had no role in the design of the study and collection, analysis, interpretation of data or writing of the manuscript.

Availability of data and materials
The syntax and full analysis plan will be made available on the Open Science Framework and the dataset made available by contacting the first author.
Consent for image reproduction


Authors’ contributions

PS is the project lead who has overall responsibility for the design and content of the intervention, and wrote the draft of the manuscript. MH is co-lead on this project and has shared responsibility for the design and content of the intervention and wrote the discussion section. KG is a Doctorate of Clinical Psychology candidate and led the piloting of the intervention. LH is a PhD student and along with JB, who is a Doctorate of Clinical Psychology candidate, contributed to the intervention design, the trial design, and will collect and analyse the data and write the first draft of the main papers. NL is the expert advisor on the response inhibition training intervention and provided all aspects of the control intervention and had input into the design. All authors contributed to the development of the protocol and writing of this paper, and have read and approved the final manuscript.

Ethics approval and consent to participate

Ethics for this study was approved by the Deakin University Human Research Ethics Committee (DUHREC) on 2nd February 2016 (Project ID: 2015 Ethics approval and consent to participate have read and approved the final manuscript.

Consent for publication

All participants provided written consent.

Consent for image reproduction


Competing interests

The authors declare that they have no competing interests.

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44. Pettiford J, Kozink RV, Lutz AM, Kollins SH, Rose JE, McClernon FJ. Increases in impulsivity following smoking abstinence are related to baseline nicotine intake and boredom susceptibility. Addict Behav. 2007;32:2351–7.
Appendix B

Authorship Statements
# AUTHORSHIP STATEMENT

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<tr>
<td>As above</td>
<td>As above</td>
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</tbody>
</table>

I was involved in the conceptual development of the study, drafted the initial manuscript, reviewed the selected articles and extracted all data from the studies. I conducted all analyses, made alterations to the manuscript based on reviewers’ comments, responded to comments from the editor and reviewers and prepared the final manuscript for submission.

I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.

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<tr>
<td>Melissa Hayden</td>
<td>Melissa contributed to the conceptual development of the research question, was the second independent reviewer for a portion of articles for data extraction and contributed to subsequent drafts of the manuscript.</td>
</tr>
<tr>
<td>Jarrad Lum</td>
<td>Jarrad contributed to the methodology, supervised and contributed to data analyses and contributed to subsequent drafts of the manuscript.</td>
</tr>
<tr>
<td>Petra Staiger</td>
<td>Petra was involved in the conceptual development of the research question, was the second reviewer of a portion of articles for screening, contributed to the revisions document and drafts of the manuscript.</td>
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*I declare that the above is an accurate description of my contribution to this paper, and the contributions of other authors are as described below.*

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<td>George Youssef</td>
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## Appendix C

### Supplementary Material for Study 1

### Supplementary Methods

Supplementary Table 1

**UPPS-P Impulsive Trait Categories and Measures Modified from Stautz and Cooper (2013)**

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<td>Zuckerman–Kuhlman Personality Questionnaire — Impulsivity</td>
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<tr>
<td>Lack of perseverance</td>
<td>Sensation Seeking Scale — Boredom susceptibility, Disinhibition</td>
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<td>UPPS — Lack of perseverance</td>
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<tr>
<td>Sensation seeking</td>
<td>BIS/BAS Scales — Fun Seeking</td>
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<td>JTCI — Novelty Seeking</td>
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<td>TCI — Novelty Seeking</td>
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<td>Sensation Seeking Scale — Thrill and adventure seeking</td>
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<td>aSensation Seeking Scale — Total score</td>
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<td>Sensation Seeking Scale for Children</td>
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<td>Substance Use Risk Profile Scale — Sensation seeking</td>
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<td>UPPS — Sensation Seeking</td>
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<td>Zuckerman–Kuhlman Personality Questionnaire — Sensation seeking</td>
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<td>Negative urgency</td>
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<td>NEO-PI-R Impulsiveness</td>
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<td>UPPS — Positive urgency</td>
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*a Only used if the subscale score was unavailable.
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<th>Statistics for each study</th>
<th>Correlation and 95% CI</th>
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<tr>
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<td>Batsche, Wain &amp; Fiory (2013)</td>
<td>0.16</td>
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</tr>
<tr>
<td>Capone &amp; Wood (2006)</td>
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</tr>
<tr>
<td>Dinn et al. (2004)</td>
<td>0.27</td>
<td>0.18</td>
</tr>
<tr>
<td>Dorn et al. (2011)</td>
<td>0.07</td>
<td>0.06</td>
</tr>
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<td>Kuo et al. (2002)</td>
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<td>Laucht et al. (2005)</td>
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<td>Schmid et al. (2007)</td>
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<tr>
<td>RE Model</td>
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Supplementary Figure 1. Forrest plot of effect sizes of relationship between sensation seeking and cigarette consumption.
### Supplementary Figure 2.

Forrest plot of effect sizes of relationship between lack of premeditation and cigarette consumption.

<table>
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<tr>
<th>Study name</th>
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<th>Upper Limit</th>
<th>Z-Value</th>
<th>p-Value</th>
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Supplementary Figure 3. Forrest plot of effect sizes of relationship between lack of perseverance and cigarette consumption.
Supplementary Figure 4. Forrest plot of effect sizes of relationship between negative urgency and cigarette consumption
Supplementary Figure 5. Forrest plot of effect sizes of relationship between positive urgency and cigarette consumption. It should be noted this meta-analysis consisted of three effect sizes.
Supplementary Figure 6. Funnel plot assessing publication bias for the meta-analysis examining the relationship between cigarette consumption and lack of premeditation. The result of Egger’s test was found to be significant (p < .001) suggesting an asymmetrical funnel plot and potential publication bias. However, the impact of potential missing studies on the average effect size reported in Table 2 appears to be minimal. Duval and Tweedie’s trim and fill method were used to assess the impact of potentially missing studies on the average effect size. The adjust value was found to be 0.137 and was still statistically significant (p < .05). As a comparison the observe average effect size was found to be 0.184.
Supplementary Figure 7. Funnel plot assessing publication bias for the meta-analysis examining the relationship between cigarette consumption and lack of perseverance. The results of Egger’s test was not significant ($p = .293$) suggesting publication bias is unlikely.
Supplementary Figure 8. Funnel plot assessing publication bias for the meta-analysis examining the relationship between cigarette consumption and sensation seeking. For this funnel plot, Egger’s test was significant ($p < .001$). The impact of potential missing studies on the average effect size reported in Table 2 was found to be negligible when assessed using Duval and Tweedie’s trim and fill method. The estimated average effect size, which imputes missing studies was found to be .199, which was the same as the observed average effect size.
Supplementary Figure 9. Funnel plot assessing publication bias for the meta-analysis examining the relationship between cigarette consumption and negative urgency. For this funnel plot, Egger’s test was significant ($p = .015$). However, when assessing the source of asymmetry using Duval and Tweedie’s trim and fill method, missing studies appeared to be on the right of the funnel plot. That is, studies may be potentially missing that have larger correlations than those identified in this report. For example, after imputing missing studies assumed to be on the left of the funnel plot (i.e., studies with small or negative correlations) there was no difference between the observed and imputed average effect size (both 0.191). However, after imputing missing studies that are assumed to be on the right of the funnel plot (i.e., studies with larger positive values), the imputed correlation coefficient was found to be 0.210. In either case, the analysis of publication bias indicates publication does not appear to have led to an overestimation of the correlation coefficient for this meta-analysis.
Supplementary Figure 10. Funnel plot assessing publication bias for the meta-analysis assessing the relationship between cigarette consumption and positive urgency. For this funnel plot, Egger’s test was not significant ($p = .587$) suggesting publication bias is unlikely for this meta-analysis. However, it should be noted this meta-analysis consisted of three effect sizes.
Appendix D

Supplementary Material for Study 2

Supplementary Methods

*Participant screening:* We received a total of 994 expressions of interest. Three-hundred and forty-one individuals were screened for eligibility and 176 individuals were excluded from participating in the present study, as they did not meet the eligibility criteria (see Table 1). Recruitment took placement between 22\(^{nd}\) February and 22\(^{nd}\) December 2017 (see Clinical Trials Registry: [ACTRN12617000252314](https://clinicaltrials.gov/ct2/show/ACTRN12617000252314))

Table 1

<table>
<thead>
<tr>
<th>Inclusion/Exclusion Criteria</th>
<th>n</th>
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</thead>
<tbody>
<tr>
<td>Was not aged between 18-60 years-old</td>
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<tr>
<td>Smoked less than 10 cigarettes per day for the past 12 months</td>
<td>24</td>
</tr>
<tr>
<td>Did not meet criteria for a moderate Tobacco Use Disorder as per the DSM-5</td>
<td>23</td>
</tr>
<tr>
<td>Was not motivated to make a quit attempt in near future</td>
<td>3</td>
</tr>
<tr>
<td>Did not complete at least Year 9 (or equivalent) of schooling</td>
<td>2</td>
</tr>
<tr>
<td>Did not have daily access to a computer and internet</td>
<td>4</td>
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<tr>
<td>Primarily used electronic cigarettes</td>
<td>6</td>
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<tr>
<td>Reported a period of abstinence for more than two-weeks over the past three months</td>
<td>16</td>
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<tr>
<td>Used anti-craving medication</td>
<td>3</td>
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<tr>
<td>Would not cease NRT during the training phase of the intervention</td>
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<tr>
<td>Self-reported problematic AOD use</td>
<td>38</td>
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<tr>
<td>Self-reported ABI, or LOC for more than 30 minutes</td>
<td>12</td>
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<tr>
<td>Self-reported use of psychotropic medications</td>
<td>71</td>
</tr>
</tbody>
</table>

*Notes.* \(n\) = number of individuals; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; NRT = nicotine replacement therapy; AOD = alcohol and other drug; ABI = acquired brain injury; LOC = loss of consciousness. The sum of ineligible individuals per criterion (\(n = 213\)) is greater than the total number of ineligible individuals (\(n = 176\)) as some were excluded based on more than 1 criterion.
Supplementary Results

Statistical analysis of inhibitory control training performance over time for the smoking-specific training condition: Repeated measures ANOVAs were conducted to examine stimulus-specific learning effects (100% stimuli vs. 50% stimuli) over time (first vs. fourth training session) as per Lawrence et al. (see Table 2). Results indicated that accuracy significantly improved over time ($F(1, 52) = 17.29, p < .001, \eta_p^2 = .25$) and there was a main effect of stimulus ($F(1, 52) = 16.73, p < .001, \eta_p^2 = .24$), with greater accuracy towards the 100% No-Go stimuli (i.e., smoking) compared with the 50% No-Go stimuli (i.e., neutral). However, there was no stimulus x time interaction ($F(1, 52) = 2.47, p = .12, \eta_p^2 = .05$). For reaction time, analyses indicated that reaction time decreased over time ($F(1, 52) = 6.43, p = .014, \eta_p^2 = .11$), however; there was no main effect of stimulus ($F(1, 52) = 1.04, p = .312, \eta_p^2 = .02$) or time x stimulus interaction ($F(1, 52) = 4.00, p = .051, \eta_p^2 = .07$).

Table 2

Mean Go reaction time and mean No-Go accuracy at ICT session 1 and 4

<table>
<thead>
<tr>
<th></th>
<th>ICT Session 1 (SD)</th>
<th>ICT Session 4 (SD)</th>
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<tbody>
<tr>
<td>Go reaction time ms (N)</td>
<td>599 (109)</td>
<td>552 (142)</td>
</tr>
<tr>
<td>Go reaction time ms (R)</td>
<td>600 (105)</td>
<td>546 (137)</td>
</tr>
<tr>
<td>No-Go Accuracy (N)</td>
<td>.95 (.04)</td>
<td>.97 (.03)</td>
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<tr>
<td>No-Go Accuracy (S)</td>
<td>.98 (.03)</td>
<td>.98 (.03)</td>
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</tbody>
</table>

Notes. ms = milliseconds; N = neutral stimuli; R = relaxing stimuli; S = smoking stimuli; ICT = inhibitory control training.
Table 3

**Moderation Effect of Impulsivity on the Relationship between Condition and Cigarette Consumption**

<table>
<thead>
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<tr>
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<td>b</td>
<td>se</td>
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<td>(analysis 1)</td>
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<tr>
<td>Group x BIS-A</td>
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<tr>
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<tr>
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<td>.18</td>
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**Notes.** T2 = post-intervention; T3 = one-month follow-up; T4 = three-month follow-up; CI = confidence interval; SSRT = stop signal reaction time; BIS-A = Barratt Impulsiveness Scale – Attentional; BIS-M = Barratt Impulsiveness Scale – Motor; BIS-NP = Barratt Impulsiveness Scale – Non-Planning. Effect size for Group x SSRT at T2: $R^2_{change} = .000$; at T3: $R^2_{change} = .002$; at T4: $R^2_{change} = .004$. Effect sizes for Group x BIS-A at T2: $R^2_{change} = .008$; at T3: $R^2_{change} = .011$; at T4: $R^2_{change} = .017$. Effect sizes for Group x BIS-M at T2: $R^2_{change} = .001$; at T3: $R^2_{change} = .000$; at T4: $R^2_{change} = .004$. Effect sizes for Group x BIS-NP at T2: $R^2_{change} = .001$; at T3: $R^2_{change} = .002$; at T4: $R^2_{change} = .003$.

Table 4

**Moderation effect of Dose and Gender on the Relationship between Condition and Cigarette Consumption**

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<th>T4</th>
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<tbody>
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<td>se</td>
<td>95%CI</td>
</tr>
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</tbody>
</table>

**Notes.** T2 = post-intervention; T3 = one-month follow-up; T4 = three-months follow-up. Effect sizes for Group x Dose at T2: $R^2_{change} = .004$; at T3: $R^2_{change} = .010$; at T4: $R^2_{change} = .004$. Effect size for Group x Gender at T2: $R^2_{change} = .000$; at T3: $R^2_{change} = .011$; at T4: $R^2_{change} = .009$. 

*IMPULSIVITY AND CIGARETTE SMOKING* 180
Figure 1. Johnson-Neyman (JN) figures representing the age x condition moderation effects for post-intervention (T2; top), one-month follow-up (T3; middle), and three-months follow-up (T4; bottom) with one participant removed (N = 106). Horizontal lines represent the expected difference in cigarette smoking (and associated 95% CI) between conditions at each follow-up point, after adjusting for baseline cigarette smoking. The green regions represent the ages at which the magnitude of the difference in daily cigarette smoking between conditions was different from zero (i.e., 95% CI does not pass zero; specific ages are presented in each figure). A value below $y = 0$ indicates greater reduction in the smoking-specific condition (relative to the control condition) at the time point. Grey shaded areas represent the ages at which there was no difference between the two conditions in reported cigarette consumption at the specific time point.
Appendix E

Published Meta-Analysis
UPPS-P impulsive personality traits and adolescent cigarette smoking: A meta-analysis

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ABSTRACT

Background: Adolescence is a critical developmental period in the trajectory of nicotine dependence, highlighting the need for a greater understanding of the modifiable risk factors. An extensive body of research has found that trait impulsivity is associated with higher levels of adolescent smoking; however, findings have been mixed. The present study aimed to synthesise existing literature to determine the strength and nature of the relationship between the UPPS-P impulsive traits and both adolescent cigarette consumption and nicotine dependence.

Methods: Fifty-one studies were meta-analysed using a random effects model to determine the association between each UPPS-P impulsive trait and both adolescent cigarette consumption and nicotine dependence. Age, gender, ethnicity and sample type were examined as potential moderators.

Results: Cigarette consumption was positively associated with each UPPS-P impulsive trait (r's ranging from 0.17-0.20). There were an insufficient number of studies to meta-analyse the association between nicotine dependence and the UPPS-P impulsive traits. There were no significant moderation effects of age, gender, ethnicity or sample type.

Conclusions: Findings suggest that each UPPS-P impulsive trait shares similar associations with adolescent cigarette consumption. Additional studies are needed to determine the relationship between adolescent nicotine dependence and impulsivity. As most adult smokers initiate during adolescence, targeting these impulsive traits via novel prevention and intervention strategies may assist in reducing the prevalence of smoking.

1. Introduction

Despite the well-established health risks, cigarette smoking remains one of the leading preventable causes of premature death worldwide (World Health Organisation [WHO], 2015). In 2015, over six million people died globally as a result of smoking and, if current trends persist, this number will exceed eight million by the year 2030 (WHO, 2015). Adolescence is a critical developmental period where increases in risk-taking behaviours and experimentation with a variety of substances, such as cigarette smoking, emerge (Backinger et al., 2003; Ernst et al., 2009; Lantz, 2003). Research has demonstrated that smoking initiation predominantly begins during adolescence (U.S Department of Health and Human Services, 2012), and, longitudinal research has indicated that cigarette consumption (i.e., the quantity and frequency of cigarette use) during adolescence is associated with levels of consumption and dependence in adulthood (Buchmann et al., 2013; Chassin et al., 2000; Jefferis et al., 2003). For instance, a one-year increase in age at initiation among 213 ever-smokers, was associated with smoking 33.5 fewer cigarettes per month at age 22 and a decrease of 0.42 in the Fagerström Test for Nicotine Dependence score (Buchmann et al., 2013). Furthermore, adolescent cigarette smokers are more likely to engage in other addictive behaviours (Kandel and Kandel, 2014; Merline et al., 2004; Moss et al., 2014) and, are at an increased risk of experiencing a range of negative outcomes, such as anxious and depressed mood and poor academic achievement (Leventhal and Zvolensky, 2015; Morin et al., 2012). As such, research into the modifiable risk factors associated with adolescent cigarette smoking is critically important to effectively reduce the global prevalence of smoking. Doing so will enable the identification of adolescents who are at the greatest risk of smoking, and, importantly, allow for the development of tailored prevention and intervention strategies to be directed towards those who would yield the greatest benefits.
1.1. Trait Impulsivity and Adolescent Cigarette Smoking

An increasing amount of attention has been placed on trait impulsivity and its role in the development and maintenance of cigarette smoking (Bloom et al., 2013). Research has generally demonstrated that adolescent smokers are more impulsive than their non-smoking counterparts and, that trait impulsivity is associated with smoking initiation, cigarette consumption, poor cessation outcomes and nicotine dependence (Burris et al., 2017; Fields et al., 2009; Lee et al., 2015; Pang et al., 2014; Reynolds et al., 2007; Spillane et al., 2010; Weckler et al., 2017). Yet, despite this well-examined relationship, no attempt has been made to systematically meta-analyse these studies. One potential reason is that quantifying the overall association between adolescent cigarette smoking and trait impulsivity poses challenges, largely because impulsivity is a multidimensional construct with varying definitions. For example, commonly used trait impulsivity variables such as novelty seeking, fun seeking, disinhibition and boredom susceptibility have all been subsumed under the construct of impulsivity; however, research has shown that these variables are both unique, and related, components of impulsivity (Lynam et al., 2006; Whiteside and Lynam, 2001). Specifically, Whiteside and Lynam (2001) used factor analysis on a number of frequently used trait impulsivity measures and demonstrated that impulsivity comprises five distinct, yet interrelated, impulsive traits, including: 1) sensation seeking, defined as the tendency to seek sensory pleasure, excitement and novel experiences; 2) lack of premeditation, defined as the tendency to act without forethought; 3) lack of perseverance, defined as the tendency to not finish tasks, or heightened susceptibility to boredom; 4) negative urgency, defined as the tendency to act rashly in negative emotional states, and; 5) positive urgency, defined as the tendency to act rashly in positive emotional states (UPPS-P; Lynam et al., 2006; Whiteside and Lynam, 2001).

Studies have shown that the UPPS-P impulsive traits share between 6% and 27% of their variance, with negative and positive urgency sharing the largest proportion of variance (Cyders and Smith, 2007).

In recent years, several meta-analyses have utilised the UPPS-P model when quantifying the association between trait impulsivity and adolescent risky behaviours, including alcohol use (Stautz and Cooper, 2013), marijuana use (VanderVeen et al., 2016) and risky sexual behaviours (Dir et al., 2014). For example, Stautz and Cooper (2013) meta-analysed 87 studies to examine the relationship between impulsivity and adolescent alcohol consumption and found that sensation seeking and positive urgency were most strongly associated with alcohol consumption, whereas positive and negative urgency showed the largest associations with alcohol dependence. Similar meta-analyses have been conducted using adult samples, with results demonstrating that the UPPS-P impulsive traits share distinct associations with nicotine dependence (Kale et al., 2018) and alcohol consumption (Coskunpinar et al., 2013). As such, utilising the UPPS-P model of impulsivity allows for clarification of discrete relationships that might otherwise be hidden when impulsivity constructs are combined (Smith et al., 2003).

Indeed, research has demonstrated that the UPPS-P traits share unique associations with adolescent smoking outcomes. Sensation seeking has been the most widely studied impulsivity-related trait and it has been shown to positively associate with cigarette consumption (Kraft and Rise, 1994; Pokhrel et al., 2010; Urbán and Urbán, 2010), status as a smoker (Tercyak and Audrain-McGovern, 2003; Thrasher et al., 2006) and the initiation of smoking (Spillane et al., 2012; Wellman et al., 2016). There is initial evidence that positive and negative urgency are associated with cigarette consumption (Balevich et al., 2013; Lee et al., 2015) and nicotine dependence (Ryan et al., 2013; Spillane et al., 2010), whereas lack of perseverance has been found to relate to cigarette consumption (Frankenberg, 2004; Pedersen et al., 1989), though with varying degrees of association, as well as smoking status (Balevich et al., 2013; Spillane et al., 2010). Lack of premeditation has been found to be strongly related to cigarette consumption in some studies (Cavalca et al., 2013; Reynolds et al., 2007), but weakly related in others (Leeman et al., 2014; White et al., 2011), and there is mixed evidence regarding its association with the severity of nicotine dependence (Ryan et al., 2013; Spillane et al., 2010). Such variations and inconsistencies in the relationships between impulsivity and adolescent cigarette smoking warrants a more comprehensive systematic review of current literature.

1.2. Present Study

The aim of the present study is to summarise and synthesise existent literature to determine the direction and magnitude of the relationship between each UPPS-P impulsive trait and both adolescent cigarette consumption and nicotine dependence. In addition, this review will investigate whether age, gender, ethnicity, and sample type moderate any relationships. To the best of our knowledge, this is the first meta-analysis to examine the association between the UPPS-P impulsive traits and adolescent cigarette smoking. It is our hope that improved understanding of the modifiable risk factors associated with adolescent cigarette consumption and nicotine dependence may enable the development of tailored prevention and intervention strategies, and ultimately, reduce the prevalence of smoking.

2. Materials and Methods

2.1. Study Design

We followed methods used by previous meta-analyses examining the association between adolescent risky behaviours and UPPS-P impulsive traits (Dir et al., 2014; Stautz and Cooper, 2013; VanderVeen et al., 2016). Relevant articles were identified following searches in PsycINFO, MEDLINE, CINAHL and Embase electronic databases to October 2018. Searches were conducted based on all keyword combinations of terms for adolescence (adolesc* OR youth OR teen*), impulsivity (impuls* OR disinhibit* OR premedit* OR “sensation seek*” OR “novelty seek*” OR “behavi* approach” OR “behavi* activation” OR BAS OR “reward sensitivity” OR “reward drive” OR “negative urgency” OR “positive urgency” OR perseverance OR (boredom N3 (prone* OR suscep*))) and smoking-related behaviours (cigarette* OR tobacco OR smoke* OR nicotine). The reference sections of all included articles were also examined to identify further studies that could be included.

2.2. Inclusion and Exclusion Criteria

Studies included in the final meta-analysis met the following criteria: 1) published in a peer-review journal reporting on an original piece of research; 2) measured self-report impulsivity and cigarette consumption (and not any other forms of tobacco such as cigars, hookah, e-cigarettes etc.) and/or severity of nicotine dependence; 3) included a sample of adolescents with a mean age between 10.0 and 19.9 years, a range of adolescence provided by the World Health Organisation (WHO, 2011) and; 4) published in English. Studies were excluded if they: 1) used a composite measure of substance use that combined cigarette and other drug use; 2) used a measure of impulsivity that was unable to be coded onto the UPPS-P model and; 3) were review studies, case studies, commentaries, systematic reviews or meta-analyses. Fig. 1 summarises the studies removed following application of each criterion according to PRISMA guidelines (Moher et al., 2009).

2.3. Study Selection

Following the removal of duplicate entries, one reviewer (JB) assessed all records. Twenty percent of title and abstracts were assessed by PS and 10% of full-text articles were assessed by MH. For 19 out of the 20 full-text articles (Cohen’s-kappa = 0.90), the reviewers
independently agreed upon the appropriateness of each article for inclusion. Fifty-five studies did not include sufficient data to calculate effect sizes. For studies in the previous ten years, first authors were contacted with a request for data. A total of 35 authors were contacted and six provided the requested data. A total of 51 published studies were included and their data was extracted for the five separate meta-analyses.

2.4. Data Extraction and Effect Size Calculation

All studies were coded by the first author. Five randomly selected studies were coded by a second author (MH) to assess reliability. There was a 97% agreement between coders. The following information was extracted from each of the included studies: Author(s) and year of publication, study design (longitudinal or cross-sectional), sample size, sample type (normative, which included high school, university or community samples and non-normative, which included clinical or incarcerated samples), mean age of the sample (when the age range was reported and not the mean, the median value of the range was extracted), gender (percentage male), ethnicity (percentage Caucasian, as most studies reported samples of Caucasian ethnicity), trait impulsivity scale used and effect sizes reported.

Two variables were extracted from each study. The first was a measure of trait impulsivity and the second was a measure of cigarette use. The data extracted to measure trait impulsivity was categorised into one of the five relevant UPPS-P traits based on previous categorisation developed by Stautz and Cooper (2013) \(^1\). The data extracted to measure cigarette use was the quantity, frequency or lifetime use of cigarettes consumed (i.e., consumption) and/or nicotine dependence.

The relationship between the UPPS-P impulsive traits and both cigarette consumption and nicotine dependence was Pearson’s \(r\) correlation coefficient. Using this effect size permits our results to be compared with previous meta-analyses on this topic (Coskunpinar et al., 2013; Dir et al., 2014; Kale et al., 2018; Stautz and Cooper, 2013; VanderVeen et al., 2016). For studies that did not report a correlation, \(r\) was converted from Cohen’s \(d\), \(F\), odds ratios using Comprehensive Meta-Analysis (CMA; Borenstein et al., 2005). Several studies provided more than one effect size for the association between the UPPS-P impulsive traits and cigarette consumption. In these cases, CMA was used to generate one effect size across all measures, ensuring each study contributed only one effect size to any one meta-analysis. Multiple effect sizes from longitudinal studies were averaged using CMA. Effect sizes were coded such that higher positive values indicated higher levels of trait impulsivity.

2.5. Meta-Analytic Procedure

Study level Pearson’s \(r\) values were pooled, and an average value was computed using a random effects model. This model assumes that variability in effect sizes reflects both random error and true heterogeneity/non-random error (Borenstein et al., 2011). An alpha level of 0.05 was used for all statistical tests. The values of the \(r\) coefficients were interpreted according to Cohen’s (1988) guidelines: Small (\(r = 0.10\)), Medium (\(r = .30\)) and Large (\(r = .50\)). Forrest plots were calculated to illustrate the heterogeneity of included studies in each meta-analysis (see Supplementary Figures 1–5) \(^1\).

For all meta-analyses, the \(I^2\) statistic was computed. The \(I^2\) statistic measures, as a percent, the variability between effect sizes that is due to true heterogeneity. \(I^2\) values of 25%, 50% and 75% correspond to low, moderate and high levels of heterogeneity between effect sizes respectively (Higgins et al., 2003). When \(I^2\) values exceeded 50%, meta-regression (Greenland, 1987) was conducted. Meta-regression examined whether participants’ age, gender and ethnicity were significant predictors of the effect sizes. Sub-group analysis using CMA examined whether sample type (i.e., normative versus non-normative) moderated effect sizes. Publication bias was assessed by computing fail-safe N (FSN) analyses (presented in Table 2) and funnel plots (see Supplementary Figures 6–10) \(^1\).

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\(^1\) Supplementary material can be found by accessing the online version of this paper at https://doi.org/10.1016/j.drugalcdep.2019.01.018.
Table 1
Studies included in the meta-analyses.

<table>
<thead>
<tr>
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<th>N</th>
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<th>Gender (% Male)</th>
<th>Ethnicity (%Caucasian)</th>
<th>Sample Type</th>
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<th>Smoking Measure</th>
<th>Impulsivity Measure</th>
<th>UPPS-P Trait</th>
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<td>107</td>
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<td>Tercyak and Audrain-McGovern (2005)</td>
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5. Results

5.1. Study Characteristics

A total of 51 studies, published between 1973 and 2017, were eligible for inclusion (see Table 1). The mean sample size was 645 (SD = 866.03; range 23–3783), and the mean age was 16.05 (SD = 2.00; range 10.30–19.44). On average, samples were 48.77% male (SD = 11.40, range 28.20–100), and 55.70% Caucasian (SD = 29.75; range 0–100). The majority of samples were from high school (n = 25, 49%), followed by community (n = 14, 28%), university (n = 8, 16%), clinical (n = 2, 4%) and incarcerated (n = 2, 4%), and most studies used a cross-sectional design (n = 48, 94%).

5.2. Meta-Analysis

3.2.1. The Relationship between UPPS-P Impulsive Traits and Adolescent Cigarette Consumption

Five meta-analyses examined the association between the UPPS-P impulsive traits and adolescent cigarette consumption (see Table 2). Results from all meta-analyses showed impulsive traits to be significantly correlated with adolescent cigarette consumption. In each, the magnitude of the correlation can be considered small according to Cohen’s (1988) guidelines. All five meta-analyses showed similar weighted correlations, ranging between r = 0.17 and r = 0.20. FSN analyses revealed that the significant results observed in each meta-analysis is unlikely to be due to missed publications. The smallest number of missed studies was 23 and this was more than seven times the number studies found (i.e., for positive urgency). Funnel plots indicated that publication bias is unlikely to have influenced the results (see Supplementary Figures 6–10). Calculation of the I² statistic indicated that the percentage of true heterogeneity between effect sizes was high for sensation seeking and lack of premeditation. For lack of perseverance and positive urgency the I² value was moderate (see Table 2).

3.2.2. The Relationship between UPPS-P Impulsive Traits and Adolescent Nicotine Dependence

Only two studies provided effect sizes for the association between the UPPS-P impulsive traits and adolescent nicotine dependence and therefore, meta-analyses could not be conducted. Bivariate correlations are presented in Table 1.

3.2.3. Moderator Analysis

Moderator analyses examines systematic influences for the association between cigarette consumption, and sensation seeking, lack of...
premeditation and lack of perseverance.

Meta-regression was used to assess the potential moderating effects of the continuous variables of age, gender and ethnicity (%Caucasian). No significant moderating effects were found for any of the continuous variables on the relationship between each UPPS-P impulsive trait and adolescent cigarette consumption. Following, sample type (i.e., normative vs non-normative) was considered as a potential categorical moderating variable. Similarly, no significant moderating effects were found for sample type on the relationship between each UPPS-P impulsive trait and adolescent cigarette consumption.

4. Discussion

A systematic review of relevant research literature was conducted to determine the strength and nature of the relationship between the UPPS-P impulsive traits and both adolescent cigarette consumption and nicotine dependence. Results from a review of 51 studies, comprising over 50,000 participants, found that adolescent cigarette consumption was positively related to impulsivity. Specifically, five separate meta-analyses demonstrated that each UPPS-P impulsive trait shared a small, positive association with cigarette consumption. Meta-analyses for the association between adolescent nicotine dependence and the UPPS-P impulsive traits could not be conducted as there were an insufficient number of studies.

The vast majority of included studies analysed the association between sensation seeking and lack of premeditation with cigarette consumption, whereas far less studies examined the lack of perseverance and urgency traits. Although sensation seeking yielded the largest association with cigarette consumption, and positive urgency the smallest, all associations were in the small range, with little variation between them (r’s ranging from .17 to .20), indicating that each UPPS-P impulsive trait plays an important role in adolescent cigarette consumption. Unfortunately, only two studies fulfilled criteria in relation to the association between adolescent nicotine dependence and the UPPS-P impulsive traits and hence, meta-analyses could not be conducted. This is surprising given the large number of adult smoking studies which measure nicotine dependence. For instance, a recent meta-analysis of over 50 studies using adult samples found that positive and negative urgency yielded stronger associations with nicotine dependence compared to other UPPS-P impulsive traits (Kale et al., 2018). Findings from the present review highlight the need for future research to incorporate measures of nicotine dependence when examining the relationship between impulsivity and adolescent smoking. This will clarify the nature of the relationship between impulsivity and adolescent nicotine dependence, and also, highlight whether distinct impulsive traits contribute to the transition from casual cigarette consumption towards more problematic tobacco-use disorders. Lastly, moderator analyses were conducted to determine if any methodological characteristics moderated study level effect sizes. Consistent with previous meta-analyses that have examined the relationship between the UPPS-P impulsive traits and risky health behaviours (Kale et al., 2018; VanderVeen et al., 2016), age, gender, ethnicity or sample type were not found to moderate the association between impulsive traits and cigarette consumption.

4.1. Implications

Historically, impulsivity has been perceived as a stable trait characteristic not amenable to change; however, over the past decade, it has become increasingly clear that impulsive characteristics can be modified in treatment (Hershberger et al., 2017; Stai ger et al., 2007). As such, findings from the present meta-analysis highlight the need to focus research efforts on the development of novel prevention and intervention strategies that target the UPPS-P impulsive traits in adolescents. Indeed, several studies have demonstrated that interventions which specifically target sensation seeking have resulted in significant reductions in adolescent alcohol consumption and binge drinking (Conrod et al., 2011, 2006) and have even delayed the onset of alcohol consumption by up to six-months (Conrod et al., 2008). Such interventions are sorely needed for adolescent smokers given that nicotine dependence can develop rapidly and at low levels of cigarette consumption (Difranza et al., 2000; Rose et al., 2010) and we suggest that school-based intervention programs provide an ideal window of opportunity to implement and examine such strategies. Additionally, public media campaigns that have been tailored towards high sensation seeking individuals have been shown to be effective at reducing cannabis use (Palmgreen et al., 2001) and similar personality targeted communications that focus on adolescent cigarette use may be an effective public health strategy.

Importantly, this review proposes that prevention and intervention strategies should strive to incorporate all of the UPPS-P impulsive traits as they appear to share similar, positive associations with adolescent cigarette consumption. This multidimensional approach may result in enhanced treatment outcomes and reduce the economic and health burden related to adolescent cigarette consumption. For instance, the urgency traits, which are more affect driven, may benefit from interventions such as mindfulness (Robinson et al., 2014) or emotion regulation skills (Sloan et al., 2018), whereas lack of premeditation, which is more automatic, may benefit from computerised cognitive training tasks such as cognitive bias modification (see Wiers et al., 2013) and impulse control training. Indeed, in recent years, impulse control training has emerged as a potentially efficacious intervention to reduce unhealthy behaviours such as risky alcohol consumption (e.g., Hou ben et al., 2011; Jones and Field, 2013) and the consumption of unhealthy foods (e.g., Houben and Jansen, 2015; Lawrence et al., 2015). This computer-based training program involves repeatedly pairing target stimuli (i.e., alcohol or unhealthy food) with the requirement to exercise impulse control. At present, the efficacy of smoking-related impulse control training is being evaluated (Stager et al., 2019), and, if found to be effective, could be offered as a standalone treatment, or as an adjunct to existing treatments for impulsive adolescents. Such interventions could feasibility be incorporated into school substance misuse prevention programs and/or delivered to at-risk adolescents.

4.2. Limitations and Future Research

Although this is the first study to examine the association between the UPPS-P impulsive traits and adolescent cigarette consumption and nicotine dependence, it has several limitations that are typically experienced with meta-analyses. First, it is recognised that data that could not be obtained from authors could have produced different results than that reported; however, we also see this as a limitation of the literature in general. There is a trend towards the online publication of data (Costello, 2009; Lawrence et al., 2011) and, future research should aim to provide correlation matrices of all variables analysed. Second, there was substantial heterogeneity across studies, and, although a random effects model was used, and demographic and methodological variables were examined as potential moderators, it is likely that there are other sources of unexplained variance. Third, most of the included studies were from non-clinical populations which limits the generalisability of these findings to clinical populations. Additionally, all data pertaining to cigarette consumption was self-reported, and while generally considered reliable, a lack of biochemical verification may have limited the accuracy of data (Gorber et al., 2009). Lastly, only three studies were included in the meta-analysis for positive urgency which limits our ability to draw conclusions regarding this impulsive trait. Future research may consider utilising the UPPS-P model when assessing impulsivity and adolescent cigarette use.

4.3. Conclusion

This study was the first to synthesise existing research to examine
the relationship between the UPPS-P impulsive traits and both adolescent cigarette consumption and nicotine dependence. Results from a review of 51 studies demonstrated that each of the five UPPS-P impulsive traits are positively associated with adolescent cigarette consumption; however, additional research is needed to determine the association between the UPPS-P impulsive traits and adolescent nicotine dependence. Findings may help to inform novel prevention and intervention strategies that target these impulsive traits.

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Contributors
JB and PS conceptualised and designed the study. JB, MH and PS completed data acquisition and JK supervised data analysis. All authors contributed to and have approved the final manuscript. Contribution is indicated by order of authors except for the last author who was the senior author.

Conflicts of interest
No conflict declared.

Appendix A. Supplementary data
Supplementary material related to this article can be found, in the online version, at doi:10.1016/j.drugalcdep.2019.01.018.

References


2References marked with an asterisk (*) indicate studies included in the meta-analyses.


*Wills, T.A., Knight, R., Williams, R.J., Pagano, I., Sargent, J.D., 2015. Risk factors for exclusive e-cigarette use and dual e-cigarette use and tobacco use in adolescents.


