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The Acute Effects of Nicotine and Exercise on Working Memory in Smokers

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Abstract

Background: In a non-smoking population exercise and nicotine have been shown to improve cognition (Guirguis, 2016). In a non-deprived smoking model it is unknown if the exercise will provide the same benefit seen in non-smokers.

Hypothesis: Post-exercise treatment and post-nicotine treatment there will be an improvement in cognition but there will be no differences in cognition between treatment conditions.

Methods: Utilizing a randomized counterbalanced crossover study design smokers (N=26) completed three cognitive assessments. The primary outcome was working memory accuracy and reaction time (RT) measured by n-back assessments (i.e., 3-back).

Results: A repeated measure ANOVA revealed a significant treatment effect for accuracy on the 3-back [F (24) = 8.118, p=.002, n^2=.404]. Post-hoc paired sample t-tests uncovered a significant improvement in accuracy from baseline and the exercise condition [t (25) = 2.605, p=.015, d = .511] and an improvement in accuracy from baseline and the nicotine inhalation condition [t (25) = 3.447, p = .002, d = .676]. Non-significant differences were observed between the two treatments groups [t (25) = .892, p=.381, d=.175]. A repeated measures ANOVA revealed a non-significant treatment effect for RT on the 3-back [F (24) = .428, p=.772, n^2=0.021].

Conclusion: Exercise is pragmatically as effective as nicotine in improving acute working memory accuracy without a compromise in reaction time.

Keywords: Smoking, moderate intensity exercise, cognition, working memory.

Acknowledgements

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Chapter one: Background

Tobacco has numerous health consequences including but not limited to: cancer, heart disease, chronic lung diseases, pneumonia, and stroke (Stanhope et al., 1964). Tobacco continues to be the leading preventable cause of death to Canadians (Reid, Hammond, Rynard, & Burkhalter, 2015). Despite the deleterious health consequences, approximately 16 percent of Canadians continue to partake in smoking behaviours (Statistics Canada, 2016). Among these Canadians, Statistics Canada (2016) has found that males are more likely to be smokers than females; the highest rates of smoking in the country by province are in Nunavut, Northwest Territories, and the Yukon; and the lowest prevalence of smokers by province are British Columbia, Manitoba and Ontario. According to the Canadian Cancer Society (2017) tobacco smoking was responsible for over 20,000 deaths in Canada in 2016. In addition to the negative health outcomes posed to the smoker, smoking also harms the public through second- and third-hand smoke. Second-hand smoke can be defined as smoke that has been exhaled by the smoker or burned from the end of a cigarette, while third-hand smoke is defined as the smoke residue and gases that are left after a cigarette has been smoked, for example trapped within clothing and furniture (Protano & Vitali, 2011). Many of the health consequences associated with smoking (such as: ischaemic heart disease, lower respiratory infections, asthma, and lung cancer) are also associated with second-hand smoke (Öberg, Jaakkola, Woodward, Peruga, & Prüss-Ustün, 2011). Children of smokers are especially susceptible to the detrimental health effects as 40% of children worldwide are exposed to these passive cigarette smoking modalities (Ferrante et al., 2013; Öberg et al., 2011).

Smoking cessation can reduce the risk of the previously mentioned diseases for both the smoker and public. Smoker's feel the benefits of quitting within 12 hours, as they experience improved lung function, blood circulation, and removal of carbon monoxide from the blood (U.S. Department of Health and Human Services, 1990). The long-term effects from smoking cessation include; decreased risk of coronary heart disease and strokes (same risk as non-smoker) and risk of mortality reduced by 50% compared to current smokers (U.S. Department of Health and Human Services, 1990). Many smokers wish to quit smoker (approximately 75%), unfortunately most smokers who make a quit attempt relapse in the first eight days (Hughes, Keely, & Naud, 2004; Mullins & Borland, 1996). Furthermore, the success of unassisted quit attempt is very low, as the successfulness of the smoker remaining smoke free by the one-year mark is 3-5% (Centers for Disease Control and Prevention, 2011). Smoking has been known to be highly addictive due to its psychoactive ingredient nicotine (Benowitz, Ferrence, Slade, Room, & Pope, 2000).

1.1 Predisposition to nicotine dependence

There are known predisposing factors to nicotine dependence including; genetic, demographic, social, and psychological factors (Amos, Spitz, & Cinciripini, 2010; Hanson & Chen, 2007; Lasser et al., 2000; Malouff, Thorsteinsson, & Schutte, 2006). To maximize the effectiveness of new smoking interventions, these factors must be duly considered. These factors are explained further below.

1.1.1 Genetic factors

The genetic components involved in nicotine dependence should be acknowledged (Amos et al., 2010). For current smokers, there are certain genes that are associated with increased cigarettes smoked per day. The cholinergic receptor nicotinic alpha (CHRNA) genes (CHRNA3, CHRNA5

and CHRNB4) and cytochrome-P450 2A6 (CYP2A6), in particular, have been shown to play a significant role in the number of cigarettes smoked per day. The CHRNA genes encode for acetylcholine receptors (including nAChR) which are important sites of binding for acetylcholine—a neurotransmitter involved in processes such as arousal and attention. These receptors play a critical role in nicotine dependence, as nicotine acts as an agonist at nAChRs. The more receptors available, the stronger the effects felt from nicotine (Amos et al., 2010). CYP2A6 dictates an individual's ability to metabolize nicotine (Amos et al., 2010). The speed at which one metabolizes nicotine is related to the cigarettes smoked per day, such that the faster you metabolize the substance, the more cigarettes the individual would consume to ensure optimal nicotine levels in the blood would be achieved (Henningfield, London, & Pogun, 2009). Furthermore, Furberg and colleagues (2010), indicates that dopamine B-hydroxylase (DBH; catalyzes the conversion of dopamine to norepinephrine), plays a role in cessation success, but limited research to date has been focused in this area (Furberg et al., 2010). Thus, focusing on the genetic factors involved in nicotine metabolism, dependence, and cessation, may provide additional information for intervention development.

1.1.2 Demographic and social factors

Certain demographic factors are thought to play a role in cigarette consumption. Factors including having lower socioeconomic status, being male, having less education, engaging in high levels of alcohol consumption, and high levels of caffeine consumption, have all been identified as factors associated with greater tobacco usage (Hanson & Chen, 2007; Matarazoo & Saslow, 1960). Several social influences also play a role in the rates of an individual's smoking behaviour. For example, having a parent that smokes, being a member of social groups that engage in smoking, as well as social environments such as place of work (Ham et al., 2012).

Moreover, females tend to use cigarettes to control their weight more often than males (Pirie, Murray, & Luepker, 1991). Finally, low levels of brain-derived neurotrophic factor (BDNF) have been linked to smoking initiation (Amos et al., 2010). More specifically, BDNF plays a role in the neurobiological processes associated with socially stressful and anxiety-inducing situations; which is thought to be how the protein is implicated in smoking initiation. Due to these influences, demographic and social factors should be taken into consideration when developing an intervention for smoking cessation.

1.1.3 Psychological factors

Several psychological factors have been associated with increased smoking behaviours. Malouff and colleagues (2006) conducted a meta-analysis on personality traits (the five-factor model) that are linked to smoking behaviour. They found that smokers tend to have high openness, low conscientiousness, high extraversion, low agreeableness and high neuroticism. These results have since been replicated by a 2007 review examining the personality traits of extraversion, neuroticism, and smoking status (Munafò, Zetteler, & Clark, 2007). Individuals with these particular personality traits should be considered at risk for developing a smoking behaviour.

An array of psychological/mental disorders have also been linked to increases in smoking behaviour (Lasser et al., 2000). This population-based prevalence study concluded that individuals suffering from mental illness are about twice more likely to be smokers than individuals whom are not suffering (Lasser et al., 2000). Some of the most documented mental illnesses linked with smoking behaviour are substance use disorders (especially alcohol use disorder), depression, anxiety, and schizophrenia (Fergusson, Goodwin, & Horwood, 2003; Gehricke et al., 2007; Kalman, Morissette, & George, 2005; Kelly & McCreadie, 2000). A possible driving force behind this relationship is the concept of self-medication (Gehricke et al.,

2007). The concept of self-medication is when a morbidity arises, an individual will seek and use substances that are not recommended by their doctor but, rather, chosen by themselves. The added disorder on top of the nicotine use-disorder can be termed co-morbidity. These co-morbidities may increase the difficulty of attempting to quit and remaining abstinent.

1.2 Mechanisms behind nicotine administration

1.2.1 Mechanism of nicotine upon administration

The most effective way to administer nicotine is through the route of inhalation, with the potential benefits of the substance being achieved in under 10 seconds (Caldwell, Sumner, & Crane, 2012). The effects of nicotine in the body are related to the activation of cholinergic pathways. Once nicotine is administered into the body it mimics the binding of acetylcholine to the nicotinic acetylcholine receptors (nAChRs) throughout the brain and causes a release of many neurotransmitters (Benowitz, 2008). The neurotransmitter most commonly related to the euphoric and self-administration effects of nicotine is dopamine (Benowitz, 2008). The rewarding effects of nicotine is in part due to the binding of nicotine on the dopaminergic neurons (which have nAChRs on them) in the ventral tegmental area (VTA) which in turn releases the neurotransmitter dopamine in the VTA and nucleus accumbens (Clarke, Fu, Jakubovic, & Fibiger, 1988; Di Chiara, 2000). The release of dopamine in these areas of the brain have been shown to produce reinforcement effects for individuals to continue seeking the behaviour (Benowitz, 2008). Gamma-Aminobutyric acid (GABA) also plays a large role in the reuptake of dopamine, but when nicotine is administered, GABA's ability to down regulate dopamine is hindered. Hence, causing larger amounts of dopamine to be in the system for a longer period of time, producing longer euphoric effects (Mansvelder, Keath, & McGehee, 2002). Benowitz (2008) also indicates that many of the other neurotransmitters released have

acute benefits to an individual. For example, acetylcholine is responsible for increases in arousal and cognitive ability, norepinephrine is responsible for increases in arousal and suppression of appetite, glutamate is responsible for learning and memory enhancement, serotonin is responsible for decreases in appetite, and gamma-Aminobutyric acid (GABA) is responsible for reduction of anxiety and tension. Due to the rewarding effects felt from many of these neurotransmitters, individuals can become addicted to nicotine.

1.2.2 Self-administration, condition place preference, and positive reinforcement

Nicotine has repeatedly been identified as a drug that many animals and humans will self-administer (Corrigall & Coen, 1989; Slifer, 1983). Nicotine has also been shown to produce a conditioned place preference (rodent will prefer the location where administration of the psychostimulant took place) in the rodent model reinforcing the motivational effects of the substance (Le Foll & Goldberg, 2005; Vastola, Douglas, Varlinskaya, & Spear, 2002). Cigarette smoking has been related to positive reinforcement for behaviour initiation and continuation (Jarvik, 1991). The positive reinforcing effect of nicotine are related not only to the euphoric effects but also the cognitive enhancing effects of the drug through many of the neurotransmitters discussed previously (such as; acetylcholine, dopamine, and GABA; (Jarvik, 1991; Watkins, Koob, & Markou, 2000). The self-administration, the condition place preference, and positive reinforcement provides further evidence of the rewarding effects of nicotine.

1.2.3 Nicotine use disorder

Mild-Substance use disorder (which would include nicotine) is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) by two-three symptoms, moderate use as four-five symptoms and severe as six or more symptoms, out of a possible 12 symptoms in a 12 month period. These symptoms include; hazardous use, social/interpersonal problems related to

use, neglected major roles to use, legal problems, withdrawal, tolerance, use larger amounts/longer, repeated attempts to quit/control use, much time spent using, physical/psychological problems related to use, activities given up to use, and cravings (Hasin et al., 2013). As the disorder increases from mild to moderate to severe, it has been documented that it is harder to quit the behaviour (Hasin et al., 2013).

1.2.4 Withdrawal symptoms

During cessation of smoking, nicotine withdrawal symptoms in rats and humans have been documented (Hughes & Hatsukami, 1986; Malin et al., 1992). Within the rat model, a variety of symptoms consistently present themselves during nicotine withdrawal, including; behavioural signs (teeth-chattering, gasps, tremors, and ptosis), decreased activity counts, and weight gain (Malin et al., 1992). The human model provides further evidence of withdrawal symptoms from nicotine (Hughes, Higgins, & Bickel, 1994). In humans, these symptoms include anxiety, issues sleeping, depression, difficulty concentrating, impatience, irritability, restlessness, decreases in heart rate, and weight gain (Hughes et al., 1994; Hughes & Hatsukami, 1986). The mitigation of these withdrawal symptoms seems like a prospective way to increase the successfulness of quit attempts and should be taken into consideration during intervention development.

1.2.5 Acute effects of nicotine on cognition

The acute effects of nicotine on cognition in non-deprived (less than 2 hour abstinent) smokers and non-smokers has been studied in depth (Heishman, Kleykamp, & Singleton, 2010). Many different cognitive domains were examined, such as fine motor, alerting attention, orienting attention, short-term episodic memory, long-term episodic memory, and working memory. The effect sizes for these categories are as followed; fine motor tasks $g = 0.16$, alerting attention-accuracy and reaction time (RT) $g = 0.34$, orienting attention – accuracy $g = 0.13$, orienting

attention –RT g = 0.3, short-term episodic memory – accuracy g = 0.44, long-term episodic memory –accuracy g = 0.17, working memory-accuracy of g = -0.11, and working memory RT of g = 0.34. It is important to note that these effect sizes are pooled for both smokers and non-smokers, a variety of tests and different nicotine doses were used to examine the same category which could lead to differentiating results. The analysis examined the non-smokers and smokers separately when applicable, and the working memory effects of nicotine on a non-smoking population are as followed; for a non-smoking population the working memory-RT effect size was g = 0.31 whereas, the effect size for working memory-accuracy was g = -0.11 (Heishman et al., 2010). The negative effect found for accuracy may be attributed to a relatively large nicotine dose given to the non-smoking participants (Heishman & Henningfield, 2000). In comparison, the smokers produced a medium effect of g = 0.45 for working memory-RT. The lack of working memory-accuracy measures in the meta-analysis made it implausible to calculate an effect size for the smoking population. Currently the non-smoking, non-deprived literature provides evidence for a positive effect of nicotine on working memory (Ernst et al., 2001; Heishman et al., 2010; Houlihan, Pritchard, & Robinson, 2001). Finally in a nicotine-deprived paradigm, it has been shown that after a 12 hour abstinence, working memory deficits are seen (p < 0.01; Myers, Taylor, Moolchan, & Heishman, 2008), and administration of nicotine, once in a deprived state has significant decrease in errors rates on the 3-back task (t = 4.0, df = 5, p < 0.05; Xu et al., 2006). It is clear throughout the literature that nicotine plays a role in working memory tasks including an enhancing effect for non-smokers, non-deprived smokers, and nicotine-deprived smokers.

1.2.6 Mechanism behind nicotine effects on cognition

The ability of nicotine to improve cognition may be due to the interaction between nicotine and the presynaptic nAChR receptors in the brain which facilitates the release of acetylcholine (ACh), dopamine, serotonin, glutamate, and γ-aminobutryic acid (Wannacott, 1987). These neurotransmitters are associated with learning and memory (Martin & Aceto, 1981). Specifically in a rodent model, the α7 and α4β2 nicotinic receptors found in the hippocampus play an integral role in the cognitive effects from nicotine (Rezvani & Levin, 2001). Additionally, nicotine also exerts its effects on hippocampus by increasing hippocampal long-term potentiation (Hamid, Dawe, Gray, & Stephenson, 1997) and increasing hippocampal synaptic activity (Gray, Rajan, Radcliffe, Yakehiro, & Dani, 1996). These mechanistic pathways provide insight into the importance of the hippocampus for nicotine's effects on memory.

Several other areas of the brain are thought to be involved in nicotine's effects on attention and memory such as the prefrontal cortex, partietal cortex, and thalamus (Brody, 2006; Henningfield et al., 2009; Rezvani & Levin, 2001). This is thought to be due to the high density of nAChR found in these areas of the brain. Himmelheber, Sarter, and Bruno (2000) explored the neurotransmitters released during sustained attention in a rodent model and found that within the prefrontal cortex larger amounts of acetylcholine are released. The effects of nicotine produce similar neurotransmitters, hence may play a role in sustained attention.

Miniussi and Ruzzoli (2013) explain that cortical excitability is a possible biomarker for cognitive function. The administration of nicotine leads to higher cortical excitability which is a possible biomarker for cognitive enhancement in a non-smoking model (Grundey et al., 2015). Cortical excitability has been documented as a primary mechanism for the improvements seen on a working memory task post-nicotine administration (Grundey et al., 2015). In situations where

nicotine is administered over a chronic period, many of the cognitive performance systems (i.e., cortical excitability and acetylcholine release) are down-regulated as the body is used to the psychostimulant being administered (Li, Semenova, D'Souza, Stoker, & Markou, 2014). Hence, the down-regulation of these systems may be causing withdrawal symptoms including cognitive defects which can be eliminated by administration of nicotine (Lang, Hasan, Sueske, Paulus, & Nitsche, 2008).

1.2.7 Acute effects of exercise on cognition

Chang and colleagues (2012) completed a meta-analysis on the effects of exercise on cognition and concluded that exercise has a positive effect on cognition during (d = 0.101), immediately following (d = 0.108) and after a delay (d = 0.103). These effect sizes are pooled for the primary outcome but do not consider the intensity of exercise or duration of exercise) and therefore should be interpreted with caution. After further investigation, there seems to be a "sweet spot" of completing at least 11-20 minutes of exercise (d = 0.262) and that moderate intensity exercise produces the largest cognitive effects at all time points except after a delay (during d = 0.193, immediately following exercise d = 0.120, and after a delay following exercise d = 0.202) where high intensity exercise provided a larger effect (d = 0.465) only after a delay (Chang et al., 2012). More specifically, exercise has been studied in respects to working memory (Pontifex, Hillman, Fernhall, Thompson, & Valentini, 2009). It appears that aerobic exercise, provides decreased reaction times immediately following exercise and 30-minutes post exercise on a working memory task providing evidence for working memory enhancement (Pontifex et al., 2009). Currently, the effects of acute exercise on working memory in smokers is unknown.

1.2.8 Mechanism behind aerobic exercise effects on cognition

The mechanistic pathway for the cognitive enhancement seen by moderate intensity exercise is still in question. Mechanisms such as; increased cerebral blood flow, increased brain-derived neurotrophic factor (BDNF), general increases in arousal, and finally increases in neurotransmitter release in brain regions associated with cognitive functions have all been suggested (Chang et al., 2012; Colcombe & Kramer, 2003; Kamijo, Nishihira, Higashiura, & Kuroiwa, 2007). More specifically, the mechanistic pathways thought to play a role in working memory are; increases in BDNF to the hippocampus (Hillman, Erickson, & Kramer, 2008; Vaynman, Ying, & Gomez-Pinilla, 2004) and increased cerebral blood flow to areas including the hippocampus which would play a role in delivering oxygenated blood to optimize the structure (Delp et al., 2001). There is evidence to suggest aerobic exercise is unique in its ability to enhance and optimize cognitive functioning in such a way that it is a promising element to use in populations that face challenges to cognition (e.g. effects of withdrawal felt by smokers on working memory)

1.2.9 Exercise and nicotine on working memory in non-smokers

Previously, Guirguis (2016) examined the effects post-exercise and post-nicotine on a working memory task in a non-smoking young adult population (N = 23). Working memory is a component of cognition worth focusing on as it allows for complex decision making and goal-oriented behaviour which is important for sport and academic achievement (Alloway & Alloway, 2010; Baddeley, 1998; Bryan & Luszcz, 2010). Guirguis utilized a within-subject counterbalanced design with two experimental treatment groups; a moderate intensity exercise group and a nicotine administration group. The moderate intensity exercise group completed 20 minutes of moderate intensity exercise including a three minute warm-up and a two minute cool-

down. Moderate intensity exercise was calculated using 45-68% of maximum heart rate (MHR = 220-age). The participants in the nicotine group were given two pieces of nicotine polacrilex gum (2 mg per piece). The individuals where then instructed to chew the gum once every three seconds for standardization. The main outcome of working memory was the 3-back task, whereas the secondary outcomes included 0-back, 1-back, 2-back. The results from this work showed a significant improvement in 3-back accuracy (t (22) = 4.36, p < 0.001, η^2 = 0.46) and reaction time (t (22) = 3.20, p = 0.004, η^2 = 0.31) after exercise. The results also showed a non-significant improvement in 3-back accuracy (t (22) = .866, p = .396, η^2 = 0.03) and a significant improvement in reaction time (t (22) = 3.099, p = .005, η^2 = 0.30) post-nicotine administration. The treatment groups did significantly differ from one another in 3-back accuracy (t (22) = 2.57, p = 0.012, η^2 = 0.25), but did not significantly differ from one another in RT post condition (t (22) = 0.087, p = 0.931, η^2 = 0.00). The cognitive boost of exercise seen in this study provides non-smokers with a safe and healthy alternative to nicotine (smoking) for improving cognitive performance. Determining whether these findings can be replicated using smokers seems warranted.

1.3. Purpose and Hypothesis

1.3.1 Purpose

The purpose of the study was to examine the cognitive performance effects of a 20-minute bout of moderate intensity exercise compared to nicotine administration on non-deprived smokers.

1.3.2 Hypothesis 1

In comparison to a baseline working memory assessment, post-exercise and post-nicotine will show an enhancement in working memory performance.

1.3.3 Hypothesis 2

There will be no post treatment differences in working memory performance between nicotine inhalation group and the moderate intensity exercise group

1.3.5 Implications of this study

If the above hypotheses are supported this research will allow for further investigation into the possible effects different modalities of exercise (e.g., resistance training) have on cognitive performance in smokers. Furthermore, positive findings will provide a framework for the design and implementation of safe and effective (a) exercise strategies to boost cognition, and (b) exercise-aided smoking cessation programs.

1.4 Ethics Statement

The experimental procedure was approved by the Western University Health Science Research Ethics Board (HSREB) and met the standards of the Declaration of Helsinki. Each participant read the letter of information, which included the tasks involved with the study, and the risks associated with partaken in the interventions prior to providing written consent. (See Appendix A).

Chapter two: Methods

2.1 Participants

A sample of 26 adults was recruited for the study. The inclusion criteria consisted of: 1) being a smoker (at least five cigarettes a day self-reported, and verified with a carbon monoxide (CO) reading of >10 P.P.M. upon arrival), 2) aged 18-64 years, 3) having no contraindications to physical activity, 4) having no contraindications to nicotine, and 5) being right handed as it may be a moderating factor for reaction time (Kalyanshetti & Vastrad, 2013). Participants were

excluded for the following reasons: 1) self-reporting a mental illness, 2) being pregnant or breastfeeding, 3) self-reporting chronic obstructive pulmonary disease (COPD), 4) consumption of alcohol or drugs in the last 24 hours as it plays a role in the metabolism of nicotine, 5) consumption of caffeine (more than half a cup of coffee) as it plays a role in the metabolism of nicotine, and 6) self-reporting other major health complications (i.e., recent heart attack).

2.2 Design

The study utilized a randomized counterbalanced crossover design in which each participant was randomly assigned to the order of the treatment but completed both treatments (i.e., exercise and nicotine; see Figure 1).

2.3 Primary outcome

2.3.1 Working memory

Working memory was measured through the use of the n-back task (see figure 2). The n-back is an effective measure of working memory as it uses both short-term recognition of stimuli and an operation upon recognition of such stimuli (Baddeley, 1998). The n-back examination consisted of four different working memory cognitive loads; 0-back, 1-back, 2-back, and 3-back. The task was performed on a portable computer in the psychological assessment suite of the Exercise and Health Psychology Laboratory in isolation. The task was performed on the software Millisecond and the program INQUISIT 4.0.8.0. The individuals would complete a practice phase (scoring a minimum of 75% accuracy on each test) before completing the evaluation. Consistently achieving at least 75% accuracy was deemed appropriate for mitigating the practice effect in the n-back task in the non-smoking population (Guirguis, 2016). During the evaluation, the individuals would complete the 0-back, 1-back, 2-back, and 3-back, three times in random order. The evaluation took approximately 10-minutes. The version of the n-back used consisted of letter

stimuli that would appear on the portable computer screen. Each letter stimulus was presented upon the computer screen for 500 milliseconds (ms), followed by a 2000 ms interstimulus (blank screen). The number of stimuli changed depending upon the working memory load, for example; 0-back = 48 letters, 1-back = 48 letters, 2-back = 50 letters, 3-back = 54 letters. A correct response would be one that appeared "N" items back in the sequence in which a participant would press the letter A on the keyboard using their right hand as soon as a target appeared and was recognized as a correct response. In the 0-back working memory load, the target letter is given prior to the assessment, for example, the program will show a target letter "the target is W", and hence every time a "W" appears on the screen the individual should press "A". In the 1-back working memory load, a correct response would be if matching letters are consecutive, for example "F" "interstimulus" "F". In the 2-back working memory load, a correct response would be if a letter matched a previous letter that appear 2 back in the sequence, for example "T" "interstimulus" "X" "interstiumlus" "T". In the 3-back working memory load, a correct response would be if a letter matched a previous letter that appear 3 back in the sequences, for example "M" "interstimulus" "P" "interstimulus" "T" "interstimulus" "M" (see Figure 2). For each condition both accuracy (percent of errors) and reaction time (in ms) were collected. The 3-back letter condition was treated as the primary outcome measure as it is most sensitive to behaviour and medication effects (Loughead et al., 2009). Furthermore, the 3-back letter condition has been shown to be sensitive to exercise in a non-smoking population (Guirguis, 2016; Loughead et al., 2009). Finally, participants were told to answer as fast and accurate as possible.

2.4. Other outcomes

2.4.1 Fagerström test for cigarette dependence

Self-reported cigarette dependence was measured through the Fagerström Test for Cigarette

Dependence (Fagerström, 2012). The questionnaire is composed of six-items, cumulatively

scored from 0-10. Once summed, nicotine dependence is categorized as follows; very low = 0-2,

low = 3-4, medium = 5, high = 6-7 and very high = 8-10 (see Appendix B). The Fagerström Test

for Cigarette Dependence has been shown to be valid and reliable measure of cigarette

dependence (Etter, 2005) .

2.4.2 Physical-activity readiness questionnaire

The nine-item physical-activity readiness questionnaire was administered prior to participating in

exercise. The questionnaire is verified by the Canadian Society for Exercise Physiology (2017)

to ensure participants were eligible for the exercise treatment. Each item has only two possible

responses; yes or no. If any participant answered yes to any of the items, the participant was

excluded from the study for safety reasons (see Appendix B).

2.4.3 *Godin-leisure time exercise questionnaire*

The Godin-Leisure Time Exercise Questionnaire was administered to determine current levels of

physical activity (Godin & Shephard, 1985; Shephard, 1997). The questionnaire includes four-

items, regarding the number of times in the last seven days participation in exercise for at least

15 minutes of uninterrupted light, moderate, or strenuous exercise (see Appendix B). The Godin-

Leisure-Time Exercise Questionnaire has been shown to be valid and reliable measure of leisure

time physical activity (Eisenmann, Milburn, Jacobsen, & Moore, 2002).

2.4.4 Smoking history questionnaire

A four-item questionnaire created by the author was administered to assess smoking history (i.e.,

On an average day, how many cigarettes do you smoke?; see Appendix B).

2.4.5 Demographics

A three-item demographics questionnaire created by the author was administered to assess age

(to ensure proper heart rate for intensity of exercise), education, and sex (see Appendix B).

2.4.6 Pre-treatment questionnaire

A Pre-treatment questionnaire adapted from Guirguis (2016) was administered prior to

participation in any treatment. The questionnaire included questions regarding; consumption of

alcohol and drugs in the past 18 hours (to reduce cofounders), consumption of caffeine (to reduce

cofounders), and self-assessed ability to exercise (see Appendix B).

2.4.7 Vital signs

Vital signs (heart rate and blood pressure) were taken at multiple time points throughout the

entirety of the study. These were taken as a manipulation check to ensure the treatments were

received as intended. Heart rate was measured with the Polar RS100 heart rate device and blood

pressure was measured manually (see Appendix B).

2.5 Treatment

2.5.1 Moderate intensity exercise

Moderate intensity exercise was defined as 40-68% of heart rate maximum (heart rate maximum:

220-age). Moderate intensity exercise was utilized in this treatment, as it has been shown to be

the optimal intensity for cognitive enhancement and can be easily completed by untrained

individuals (Chang et al., 2011). The treatment consisted of 20 minutes of exercise including a 3-

minute warm up and a 2-minute cool down. The speed and incline was manipulated throughout the bout to ensure the participant was working at the proper intensity with the speed never surpassing 3 miles per hour (to ensure ability to walk) and if further manipulation was needed to ensure proper heart rate, the incline was adjusted. The treatment was completed on a Woodway PPS treadmill (Woodway, Waukesh, WI) with heart rate monitored through a Polar RS100 heart rate device.

2.5.2 Nicotine inhalation

The nicotine inhalation treatment was designed with an ecological approach. The treatment consisted of smoking a cigarette to completion. Participants were provided with Belmont Charcoal Filter cigarettes to smoke for free (every participants chose this option) or they could choose to smoke a cigarette of their preferred brand. This ecological approach was designed with the negative attitudes toward nicotine replacement treatments and the rate of delivery of the psychoactive substance (Etter & Perneger, 2001).

2.6 Procedures

2.6.1 Recruitment

Recruitment was done through an advertisement poster posted on social media, websites (such as kijiji.ca), and in print in many locations around London, Ontario (see Appendix A).

2.6.2 Screening

Upon contact from potential participants through email or telephone, initial screening by the student investigator took place. This included reinforcement of the inclusion criteria and informing them of the location of the Exercise and Health Psychology Laboratory.

2.6.3 Study procedures

An overview of study procedures is illustrated in Figure 1. Prior to arrival for study, participants were asked to keep consumption of coffee to half a cup the day of testing, abstain from alcohol and drugs for at least 18 hours prior to testing, and smoke a cigarette of choice 30 minutes prior to arrival (for standardization). Upon arrival to the Exercise and Health Psychology lab (located in room 408 of the Arthur and Sonia Labatt Health Science Building at Western University) participants were verified as smokers (based on the reading from the piCO+ Smokerlyzer being greater than 10 parts per million (P.P.M.)), given the letter of information and signed the informed consent form (see Appendix A). Participants then completed a demographic survey, smoking history questionnaire, PAR-Q readiness for exercise (Canadian Society for Exercise Physiology, 2017), Godin Leisure-Time Exercise Questionnaire (Godin & Shephard, 1985; Shephard, 1997), Fagerström Test for Cigarette Dependence (Fagerström, 2012), and pre-nicotine or pre-exercise questionnaire. After establishing familiarity with the cognitive task, baseline cognition performance was obtained through administration of the n-back task. Immediately following baseline, participants were randomized into either the exercise treatment condition or the nicotine treatment condition. Following the treatment a cognitive performance was obtained through administration of the n-back task. Upon completion of the first treatment (for example the exercise treatment) the participants would do the remaining treatment conditions (in this case the nicotine treatment). Finally, after completing the last treatment condition, a cognitive performance was obtained through the n-back task. Vitals (heart rate, carbon monoxide reading, and blood pressure) were assessed at baseline and post treatments (vitals were always taken in the seated position). After completion of the study, participants were compensated $15.00.

2.7 Statistical analyses

2.7.1 Sample size calculation

Due to the novelty of an exercise intervention in this population, an a priori power calculation was completed for a nicotine intervention in a non-deprived state. Using G*Power software with the power set at 0.8, the significance set at 0.05, and the effect size set at $g = 0.45$ (Faul, Erdfelder, Lang, & Buchner, 2007; Heishman et al., 2010), a sample size of 26 individuals was needed to detect this difference.

2.7.2 Manipulation check

To ensure the time (irrespective of treatment) did not play a role in the results, separate paired sample t-test were conducted from treatment performed first to treatment performed second. To ensure the order of the treatments did not play a role in the results separate repeated measures 2 conditions (exercise, nicotine) x 2 order (exercise treatment first or nicotine treatment first) ANOVAs were conducted.

2.7.3 Fidelity check

Paired sample t-tests were conducted on vitals (HR and BP) from baseline to post-treatment. This was to ensure that the treatments were received as planned.

2.7.5 Primary outcome

Two repeated measures one-way ANOVAs were conducted across the three treatment conditions (i.e., baseline, exercise and nicotine) for both n-back RT and accuracy. Bonferroni corrected paired sample post-hoc t-tests were conducted pending significant findings from the repeated measure ANOVAs (from baseline to exercise treatment, baseline to nicotine treatment, and exercise treatment to nicotine treatment). Alpha was set at 0.05.

Chapter three: Results

3.1 Data reduction

Individual data were excluded based upon the following criteria: a RT < 150 ms and/or a RT that was 2.5 standard deviation from the individuals mean (Miller & Low, 2000). Less than 3% of total trials were excluded from the study.

3.2 Demographics

Sample size, demographic and descriptive statistics for the participants involved in the study can be seen in Table 1.

3.3 Manipulation check

3.3.1 Accuracy

Four paired sample t-tests (from treatment completed first to treatment completed second) were computed to detect a time effect (did participants do better on second assessment compared to the first irrespective of treatment) for the 3- back (t (25) = .654, p = .519, d = .128), 2-back (t (25) = .794, p = .435, d = .156), 1-back (t (25) = 1.065, p = .296, d = .210), 0-back (t (25) = .490, p = 629, d = .096). Hence, no significant time effect was found. Four 2 conditions (exercise, nicotine) x 2 order (exercise treatment first or nicotine treatment first) repeated measure ANOVAs were conducted to examine the condition x order effect for the 3-back (F (24) = 1.103, p = .304, η^2 = .044), 2- back (F (24) = .346, p = .562, η^2 = .014), 1-back (F (24) = 1.191, p = .286, η^2 = .047), and 0-back (F (24) = .045, p = .835, η^2 = .002). Hence, no significant condition x order effect was found, see Figure 3.

3.3.2 RT

Four paired sample t-tests (from condition completed first to condition completed second) were computed to detect a time effect (did participants do better on second assessment compared to the first irrespective of treatment) for the 3-back (t (25) = 1.520, p = .141, d = .298), 2-back (t (25) = .530, p = .601, d = .104), 1-back (t (25) = -.096, p = .924, d = -.019), 0-back (t (25) = -.353, p = .727, d = -.069). Hence, no time effect was found. Four 2 conditions (exercise, nicotine) x 2 order (exercise treatment first or nicotine treatment first) repeated measure ANOVAs were conducted to examine the condition x order effect for the 3-back (F (24) = 6.309, p = .019, η^2 = .208), 2-back (F (24) = .681, p = .417, η^2 = .028), 1-back (F (24) = .065, p = .800, η^2 = .003), and 0-back (F (24) = .001, p = .971, η^2 = .000). Hence, a significant condition x order effect was found for the 3-back in favor of receiving the nicotine condition first, see Figure 4.

3.4 Fidelity check

3.4.1 Exercise

A paired-sample t-test was conducted from baseline to post exercise condition for heart rate (t (25) = -8.171, p< .0001, d= -1.6), systolic blood pressure (t (25) = -9.211, p < .0001, d = -1.81), diastolic blood pressure *(t (25) =.234, p = .817, d =.05)* and CO readings (t (25) =.443, p =.661 d = .09; see Figure 5). Significant change was found for heart rate and systolic blood pressure (all increasing post-exercise treatment).

3.4.2 Nicotine

A paired-sample t-test was conducted from baseline to post nicotine condition for heart rate (t (25) = -6.188, p <.0001, d = -1.21), systolic blood pressure (t (25) = -1.303, p =.205 d = -.26), diastolic blood pressure (t (25) =-5.516, p<.0001, d = -1.08) and CO readings (t (25) =-3.909, p

=.001, d = -0.77; see figure 5). Significant change was found for heart rate, diastolic blood, and pressure and CO readings (all increasing post-nicotine treatment).

3.4 Primary outcome

Means and standard deviations for 3-back accuracy and RT can be found in Table 2.

3.4.1 3-back accuracy

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise, and nicotine) was significant (F (24) = 8.118, p =.002, η^2 =.404). Paired sample post hoc t-tests uncovered significant differences between baseline and the exercise condition accuracy favoring the exercise condition (t (25) = 2.605, p =.015, d = .511). Significant differences were also found from baseline accuracy to nicotine condition accuracy favoring the nicotine condition (t (25) = 3.447, p =.002, d = 0.676). Non-significant differences were observed between the exercise condition accuracy and the nicotine condition accuracy *(t (25) =.892, p =.381, d = .175*; see Figure 6).

3.4.2 3-back RT

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise, and nicotine) was non-significant (F (24) = .428, p = .772 η^2 = .021; see Figure 7).

3.5 Secondary outcome

Means and standard deviations for 2, 1, 0-back accuracy and RT can be found in Table 2.

3.5.1 2-back accuracy

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise and nicotine) was non-significant (F (24) = .388, p = .682, η^2 =.031).

3.5.2 2-back RT

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise, and nicotine) was significant (F (24) = 5.985, p = .041, η^2 = .234). Paired sample post hoc t-test uncovered a non-significant difference between baseline RT and exercise condition RT (t (25) = .960, p = .346, d = .188). A significant difference was found from baseline accuracy to nicotine condition RT in favour of the nicotine condition (t (25) = 2.693, p = .012, d = .528). A non-significant difference was observed between the exercise condition RT and the nicotine condition RT (t (25) = 1.807, p = .083, d = .354).

3.5.3 1-back accuracy

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise, and nicotine) was non-significant (F (24) = .499, p = .613, η^2 = .040).

3.5.4 1-back RT

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise, and nicotine) was significant (F (24) = 5.902, p = .008, η^2 = .290). Paired sample post hoc t-test uncovered a non-significant difference between baseline RT and exercise condition RT (t (25) = 2.614, p =.015, d = .513). A significant difference was found from baseline RT to nicotine condition RT in favour of the nicotine condition *(t* (25) = 3.380, p= .002, d = .663). Non-significant differences were observed between the exercise condition RT and the nicotine condition RT (t (25) = .479, p= .636, d = .094).

3.5.5 0-back accuracy

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise, and nicotine) was non-significant (F (24) = .262, p = .772, η^2 = .021).

3.5.6 0-back RT

A repeated measure ANOVA across the three treatment conditions (i.e., baseline, exercise, and nicotine) was significant (F (24) = 4.677, p = .019, η^2 = .20). Paired sample post hoc t-test uncovered a non-significant difference between baseline RT and exercise condition RT (t (25) = -1.480, p = .151, d = .290). A non-significant difference was found from baseline RT to nicotine condition RT (t (25) = .781, p =.442, d = .153). Significant differences were observed between the exercise condition RT and the nicotine condition RT in favour of the nicotine condition (t (25) = 3.092, p = .005, d = .606).

Chapter four: Discussion

To the author's knowledge, this is the first study to investigate the effectiveness of an acute bout of moderate-intensity exercise versus smoking (nicotine) on cognitive performance (i.e., working memory) in a smoking population. Participants underwent both treatments in a randomized counterbalanced fashion. Our main finding showed significant improvement in accuracy from baseline after both treatments. Reaction times did not significantly improve from baseline to after treatments. Beyond theses general findings a number of specific issues warrant commentary.

4.1 Accuracy

In accordance with my hypothesis, following the moderate intensity exercise intervention a 15.72% increase in accuracy on the 3-back was observed. Similarly in the nicotine inhalation group a 23.36 % increase in accuracy was observed. The differences between the moderate intensity exercise group and the nicotine inhalation group were found to be non-significant and only a mean difference of 1.35 errors was observed. Using a non-smoking model, Guirguis

(2016) found 3-back accuracy in the exercise condition improved by 31.25% but only 6.5% in the nicotine condition. This 26.4% net difference suggested that exercise was superior to nicotine in enhancing cognitive performance (i.e., working memory). Taken together with the present findings, exercise has a more positive effect on accuracy in non-smoking models. In contrast, nicotine has a more positive effect on accuracy in smoking models. This raises the question why?

Participants' fitness may, in part, help answer this question. Fitness seems to play a role in exercises' effect on cognitive performance (Chang et al., 2012) as highly fit participants appear to benefit the most while less-fit participants might suffer adverse effects. This is because unfit participants are more likely to fatigue quicker, which is associated with impaired cognitive performance (Brown & Bray, 2015). Participants in the Guirguis study were self-selected opening the possibility they exercise regularly whereas participants in the current study were smokers who were likely less fit because they did not exercise regularly. This observation is reinforced by the Godin Leisure-Time Exercise questionnaire time data collected from both studies. In short, participants in the former study may have tolerated the 20 minutes of moderate intensity exercise (45-65% HR max) better than participants in the current study, which in turn led to less fatigue and superior cognitive performance.

An alternative reason for the differentiating results found between the current study and the Guirguis study in terms of accuracy on the 3-back task may be due to the novelty of nicotine administration in the non-smoking population of the Guirguis study. This may have contributed to feelings of dysphoria (profound state of unease or dissatisfaction). Past research has shown that nicotine-induced enhancement might be jeopardized as a consequence of dysphoria non-smokers experience (Heishman, Snyder, & Henningfield, 1993; Hindmarch, Kerr, & Sherwood, 1990). Additionally, the route of administration (inhalation) may have provided an added benefit

to the smoking population used the current study as it is the route of choice for smokers and provides the most effect way of administering nicotine into the blood (Caldwell et al., 2012). Finally, with both studies not collecting blood samples of cotinine (metabolized nicotine) it is unclear whether the nicotine dose were uniform between the non-smoking and smoking populations, which may also play a role in the cognitive effects.

Although past research has shown that the entire n-back protocol is sensitive to accuracy change by both acute exercise (Tomporowski, 2003) and nicotine (Heishman, Kleykamp, & Singleton, 2010), the primary outcome of the present study was the 3-back (the most difficult and challenging task). Only the 3-back has been shown to be sensitive to behaviour and medication effects (Loughead et al., 2009). When accuracy scores were examined on the 0, 1, and 2-back as secondary outcomes no significant difference was found from baseline to either treatment, or between treatments. These null findings confirm the poor sensitivity to detect cognitive enhancing effects of lower cognitive loads associated the n-back assessments (i.e., tasks are too easy). This is further illustrated by the uniformly high accuracy baseline scores which indicates a ceiling effect (see Table 2).

4.2 Reaction time (RT)

Opposite to my hypothesis, following moderate intensity exercise or nicotine inhalation RT was not significantly reduced from baseline for the 3-back condition. Reaction time increased from baseline after exercise by 7.16 ms whereas RT decreased from baseline after nicotine by 28.77 ms (see Table 2). This finding in not in line with previous literature. Past studies have reported significant decreases in RT for both exercise (Chang et al., 2012, Guirguis, 2016) and nicotine (Heishman et al., 2010; Guirguis, 2016). Both treatments in this study are known to

increase arousal (McMorris, Sproule, Turner, & Hale, 2011; Parrott, 1994; Perkins, Grobe, Epstein, Caggiula, & Stiller, 1993). Therefore, shorter RT is expected post-treatment.

The unexpected post-treatment results may be due to the condition x order interaction effect found in the manipulation check analysis. This interaction effect provided evidence the order that nicotine treatment was received played a role in RT (i.e., individuals receiving the nicotine treatment first performed significantly better on the exercise treatment received second). This suggests that the effect of nicotine carried over into the exercise treatment to decrease 3-back RT. Put another way, there may be a delay in nicotine treatment effects on 3-back RT. A plausible way to control for this would be to take cotinine (metabolized nicotine) samples throughout the procedures to ensure the amount of cotinine in the blood is consistent during the exercise treatment between groups. Additionally, expanding the length of the procedures to ensure the treatment conditions are on separate days would have provided a certain "wash-out" period long enough to ensure contamination from the treatment received first was not present. This may however, be difficult to accomplish as a smoking population adds additional recruitment/adherence issues that are not found in a general adult population(Sherman & Lynch, 2014).

With respect to the 2-back, those in the moderate intensity exercise condition had a 26.76 millisecond (ms) RT decrease from baseline that was found to be nonsignificant. Whereas, those in the nicotine inhalation intervention showed a 74.36 ms RT decrease from baseline that was found to be significant. No significant differences were found between the treatment groups. A similar finding was shown in the 1-back assessment. Specifically, a non-significant RT decrease was found from baseline after moderate intensity exercise (i.e., 71.47 ms); and significant RT decrease was found from baseline after nicotine inhalation (i.e., 83.47 ms). No significant

differences were found between treatment groups. For the 0-back, there was a non-significant increase in RT from baseline following the moderate intensity exercise intervention (i.e., 32.34 ms). In contrast, there was a non-significant decrease in RT from baseline after nicotine inhalation (i.e., 13.84 ms). A significant difference was found between conditions for the 0-back. Overall, there was consistent evidence that nicotine positively affected RT. These findings are more in line with past research which found significant decreases in working memory RT in non-smoking and non-deprived smokers administered nicotine (Heishman et al., 2010; Guirguis, 2016). Why exercise did not perform as well as nicotine in reducing RT using a smoking model remains unknown. It is possible that the nicotine treatment was producing a larger increase in arousal in comparison to the exercise treatment in the smoking population but more research is needed.

4.3 Speed-accuracy trade-off

Working memory tasks like the N-back provide accuracy and reaction time (RT) scores. Although there is a well-known speed-accuracy trade-off effect (performing a task faster jeopardizes its accuracy; Reed, 1973), this was not the case in either treatment as both showed improvements in 3-back accuracy without RT being compromised (i.e., slowed down). The author argues accuracy data are more important in these types of tasks. Performing a cognitive task faster has little implication if accuracy is jeopardized. For example, it is more important to get the correct answer on an exam than to finish quickly. With respect to the speed-accuracy findings seen in the 2, 1, 0-back, post nicotine treatment decreases in RT did not negatively affect accuracy scores.

4.4 Strengths and limitations

The within counterbalanced crossover design used in the present study can be seen as a strength. Utilizing participants as their own control eliminates the demographic variability between the groups. The randomization among condition order allows for an order and a condition x order effect to be detected, which aids in elucidating the stand-alone effects of each intervention. Additionally, the baseline being anchored with no possibility of receiving it second or third should be seen as both a strength and a weakness. As a strength, it allows a stable baseline measure to be established and comparisons to be made to the treatments. As a weakness, it does not provide a completely randomized paradigm that allows baseline to be free of contamination from either treatment.

Another strength was that fidelity checks were in place throughout the study to ensure the interventions were received as intended. For example HR, blood pressure, and CO readings were taken pre and post both treatments. This allowed for objective measures to be taken to ensure the exercise treatment was received as intended (as HR and systolic blood pressure increase with exercise and the CO readings would stay consistent; Shahraki, Mirshekari, Shahraki, Shahraki, & Naroi, 2012), as well as, providing an objective measures to ensure the nicotine inhalation treatment was received as intended (as HR, diastolic blood pressure and CO readings increase with nicotine; Ernst et al., 2001; Foulds et al., 1997).

A further strength was that an ecological approach to nicotine administration was used to mimic the acute cognitive effects received by a smoker from a cigarette. The protocol allowed individuals to smoke a cigarette of their choice (a premium cigarette Belmont Charcoal Filter Regular was provided free of charge if preferred). As this increases the ecological validity of the nicotine administration, the exact nicotine content in the blood would be varied as smoking

topography plays a large role in nicotine uptake, which should be considered a limitation. Further limitations include the generalizability of the study. These findings cannot be generalized to all smoking population as the sample was taken only from London, Ontario and the surrounding area. The cognitive assessment also only included the n-back assessment which has be validated for a working memory assessment (Jonides et al., 1997) but does not include other cognitive assessments such as; fast-counting, stroop task, or the go-no-go which should be examined. Finally, more sensitive cognitive measures such as the anti-saccade task may provide a more accurate comparison between an exercise treatment and a nicotine treatment in the smoking population (Samani & Heath, 2018).

4.5 Future directions

The next logical step in this line of research would be to examine the cognitive deficits faced by smokers who are nicotine deprived (i.e., abstain from smoking); and the possibility to replenish these cognitive deficits with an exercise treatment. Beyond the first logical next step, alternative future directions from this work include; separating treatment conditions to take place on different days, implementing the protocol in a real life setting as oppose to a laboratory setting for "real world" validity, examining the possibility of a cumulative cognitive benefit from exercise and nicotine, examining the effects of exercise after a time delay, examining more of the cognitive domains (as only working memory was examined), examining the possibility of different modalities of exercise such as resistance training or yoga, and finally examining the possibility of using other modalities of exercise as a means to tackle many co-morbidities faced by smokers (i.e., depression, anxiety, schizophrenia, and additional addictions).

Utilizing a research design that would disentangle the effects felt from exercise alone and nicotine alone on the 3-back assessment RT (places the treatment conditions on separate days)

would further clarify the effects of the treatments on working memory. This is not without its complications with recruitment and adherence in the smoking population that would have to be addressed prior to conducting the experiment.

The next step of implementing this protocol into the "real world" (treatment facility) would provide the needed validity for exercise to be used as a stand-alone/and or an adjunct to traditional treatment for nicotine addiction. This could include group walking sessions or exercise classes, as well as individual tailored sessions and the effectiveness of both should be examined. The possibility of a cumulative cognitive benefit from exercise and nicotine should be examined in a nicotine-deprived model with the use of NRT. This could provide insight into how exercise may lengthen or attenuate the cognitive benefits seen from using NRT during a quit attempt.

It is important to examine the timing effects that are produced from exercise in the smoking population. This would be important to determine the longevity of the cognitive effects felt from exercise. For example, if exercise provides a cognitive benefit 30-minutes post exercise it may provide added incentive for an individual to utilize exercise as an adjunct for smoking cessation.

Comparisons between the effects from nicotine administration and moderate intensity exercise through examination of other cognitive domains (fine motor abilities, alerting attention, orienting attention, and episodic memory) should be examined, as this study only focused on working memory through the n-back task. Nicotine has been shown to have positive effects on five other cognitive domains (fine motor abilities; $d = 0.16$, alerting attention-accuracy; $d = 0.34$, alerting attention-RT; $d = 0.34$, orienting attention-RT; $d = 0.3$, and short-term episodic memory-accuracy; $d = 0.44$; Heishman et al., 2010). If exercise could enhance these cognitive domains to

the same extent as nicotine administration, it would provide added evidence of the utility of exercise in the domain of smoking cessation.

The possibility of different modalities of exercise providing cognitive benefits in the smoking population should also be examined. For example, if strength training and yoga are deemed effective for cognitive replenishment it may provide a smoker attempting to quit alternative avenues and variability to stay motivated to keep exercising.

Finally, examining the possibility of using exercise for populations with co-morbidities that are associated with smoking such as; mental health (i.e., depression, anxiety and schizophrenia), groups susceptible to higher rates of smoking (such as the indigenous people of Canada), and individuals struggling with multiple addictions, is important. Smoking cigarettes is often in conjunction with other mental health issues (Lasser et al., 2000) and if a harm reduction approach was taken it is possible that exercise could help with many psychological and physiological symptoms (Stathopoulou, Powers, Berry, Smits, & Otto, 2006), while decreasing the number of cigarette smoked simultaneously. For example, certain populations such as the indigenous people of Canada, smoke at higher rates than the rest of the Canadian population (Statistics Canada, 2015). Additionally, the average body mass index (BMI) for the indigenous people of Canada is also above national average (Statistics Canada, 2015). Thus, a moderate intensity exercise intervention for smoking cessation may provide a spillover effect on obesity in this at risk populations.

4.6 Conclusion

Exercise is pragmatically as effective as nicotine in improving acute working memory accuracy without a compromise in reaction time. Exercise is recommended over nicotine inhalation as a safer, healthy alternative for acute cognitive enhancement in smokers.

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Tables and figures

Table 1: Demographic and smoking behaviour variables

Variable	n	%	M (SD)
Age	26	-	34.8(12.1)
Male	14	54.8	
Fagerström Test of nicotine dependence	26	-	4.9(2.4)
Cigarettes/Day	26	-	16(7.5)
Years smoking	26	-	16.3(11.1)
Approximate time of last cigarettes (minutes)	26	-	38.7(19.9)
Physical activity (weekly frequencies)	26	-	-
Strenuous	26	-	2.3(2.5)
Moderate	26	-	3.8(2.6)
Mild	26	-	5.1(2.4)
Total weekly leisure activity (METs)[1]	26	-	55.5(35.7)
Education	26	-	-
Post-secondary achievement	12	46.1	-
High school diploma	8	30.8	-
None	6	23.8	-

Note. METs= metabolic equivalents units.

Table 2: Means, standard deviations and 95% confidence intervals for n-back assessment

Trial	M	SD	95% CI
Baseline			
3-back Error %	17.62	6.12	[15.26, 19.97]
3-back RT	782.24	162.24	[719.88, 844.60]
2-back Error %	8.12	6.99	[5.43, 10.80]
2-back RT	651.95	117.55	[606.77, 697.14]
1-back Error %	5.30	6.32	[2.87, 7.73]
1-back RT	591.92	127.65	[542.85, 640.99]
0-back Error %	3.21	6.43	[0.74, 5.68]
0-back RT	479.29	75.59	[450.23, 508.34]
Exercise			
3-back Error %	14.85	6.92	[12.19, 17.51]
3-back RT	789.40	266.88	[639.04, 844.21]
2-back Error %	7.12	6.11	[4.77, 9.46]
2-back RT	625.20	136.38	[572.77, 627.90]
1-back Error %	4.05	4.79	[2.21, 5.89]
1-back RT	520.45	118.18	[475.02, 565.88]
0-back Error %	3.63	5.32	[1.58, 5.67]
0-back RT	511.53	106.80	[450.23, 508.34]
Nicotine			
3-back Error %	13.50	6.95	[10.83, 16.72]

3-back RT	753.47	195.78	[678.21, 828.72]
2-back Error %	8.00	7.55	[5.10, 10.90]
2-back RT	577.59	130.87	[527.29, 627.90]
1-back Error %	3.81	4.41	[2.11, 5.50]
1-back RT	508.46	108.29	[466.83, 550.08]
0-back Error %	4.19	6.27	[1.78, 6.60]
0-back RT	465.45	81.02	[434.31, 496.59]
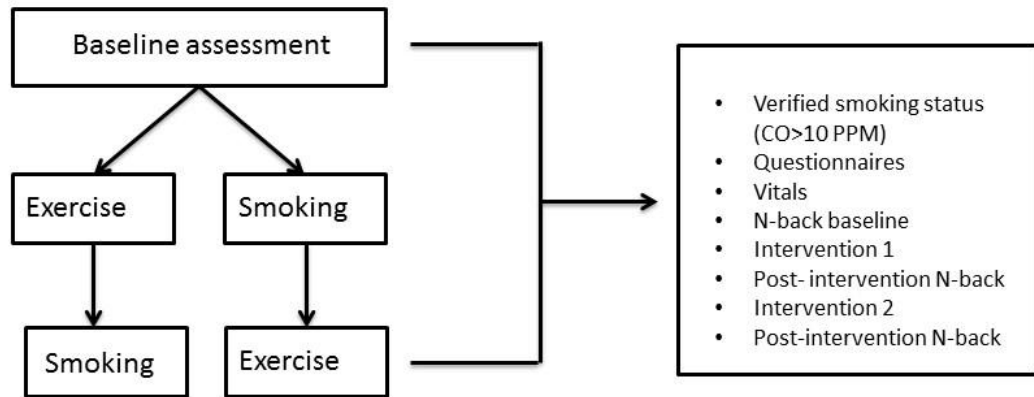
Figure 1: An overview of the study procedures.
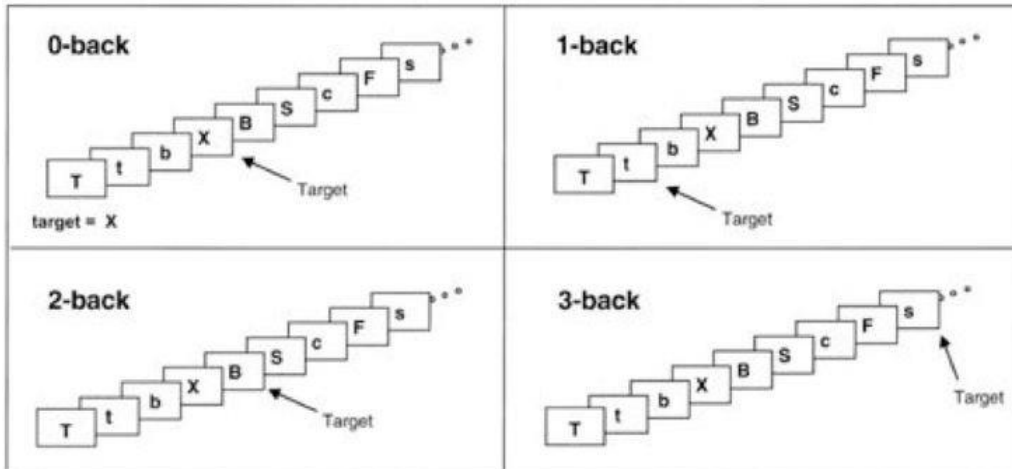
Figure 2: A visual representation of the different cognitive loads of the n-back task. Figure taken from Braver, Cohen, Nystrom, Jonides, Smith and Noll (1997).
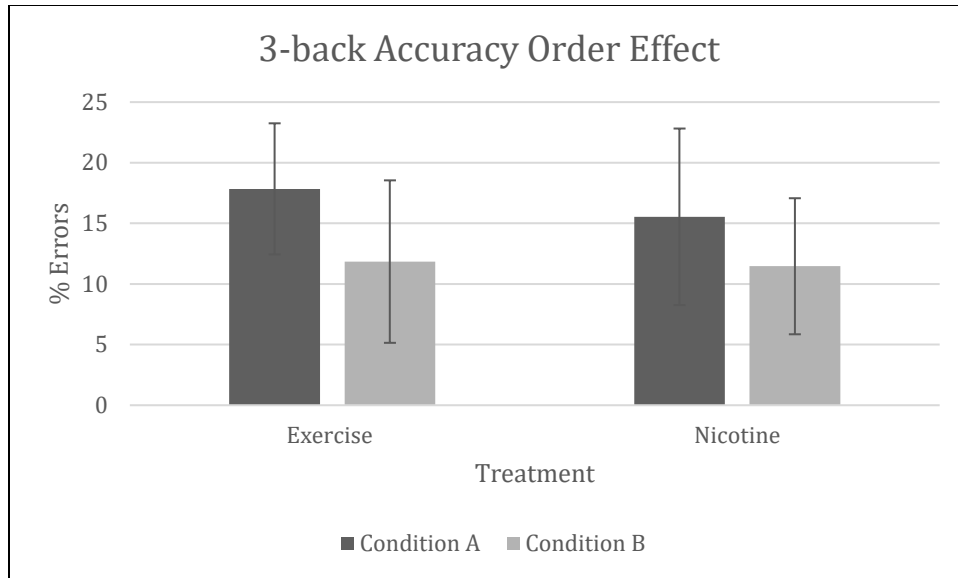
Figure 3: Comparison of the 3-back accuracy order effect. Condition A = Received exercise treatment followed by nicotine treatment. Condition B = Received nicotine treatment followed by exercise treatment. Error bars represent standard deviation.
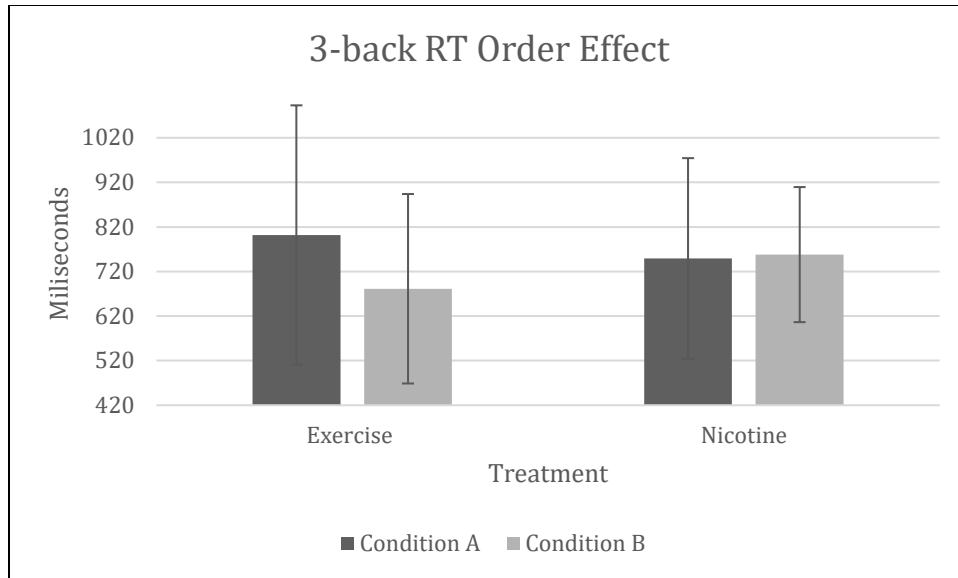
Figure 4: Comparison of the 3-back RT order effect. Condition A = Received exercise treatment followed by nicotine treatment. Condition B = Received nicotine treatment followed by exercise treatment. Error bars represent standard deviation.
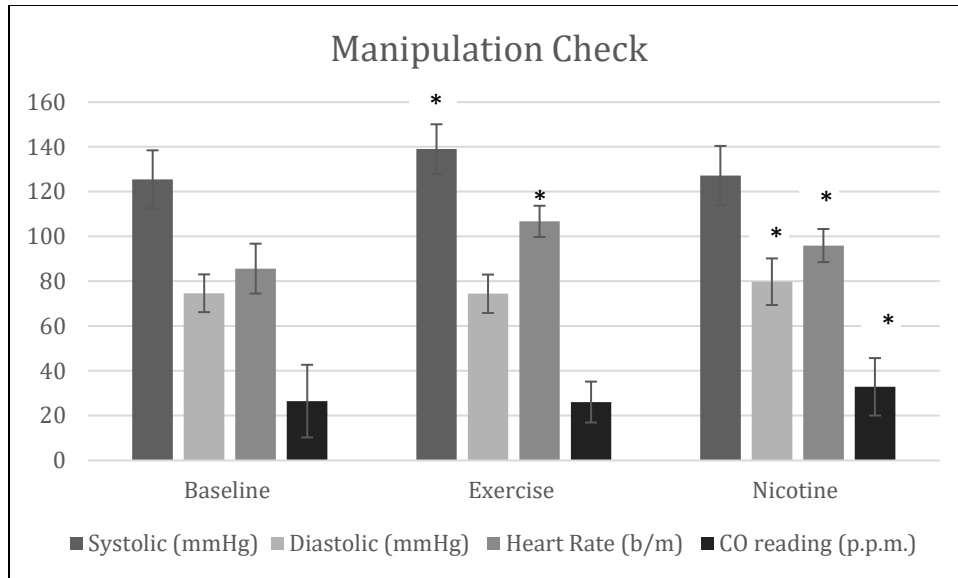
Figure 5: Vitals between baseline, exercise and nicotine treatment conditions. Error bars represent standard deviation. * = p < 0.05, all comparison for significance are from baseline to post-treatment.
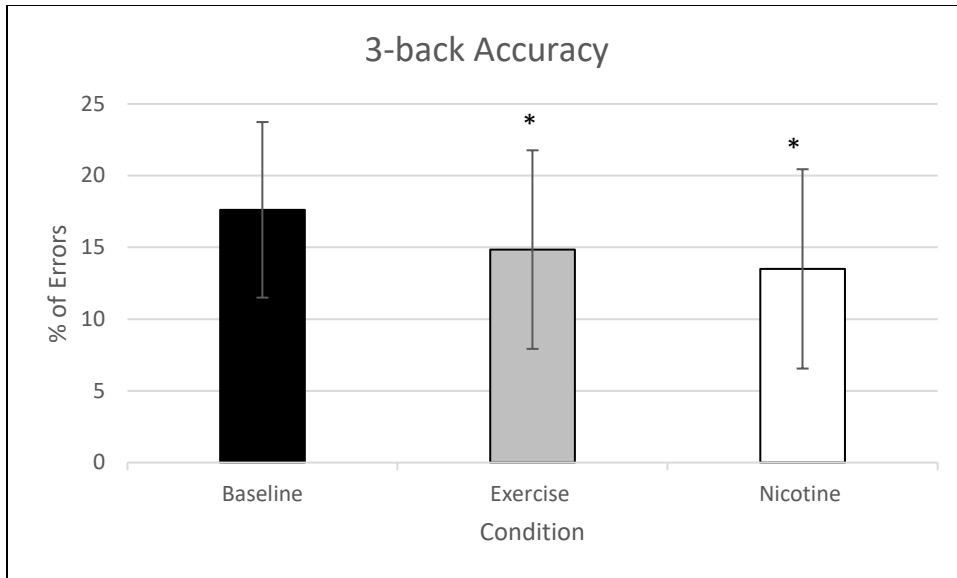
Figure 6: Comparison of accuracy on the 3-back task at baseline, immediately following exercise and immediately following nicotine administration. *= p <0.05, all comparisons for significance are from baseline to post-treatment.
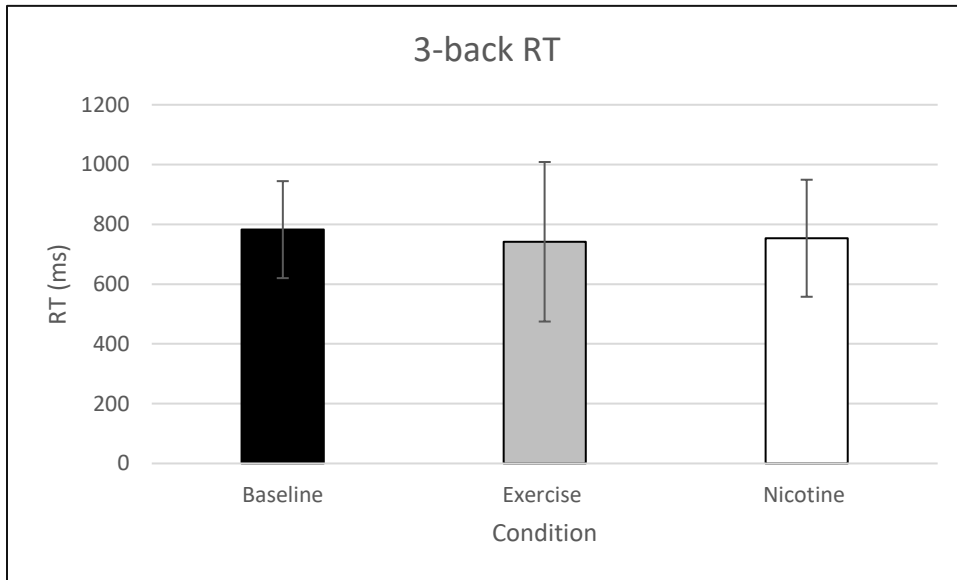
Figure 7: Comparison of RT on the 3-back task at baseline, immediately following exercise and immediately following nicotine administration.

Appendix A

Ethics Approval Notice

Western Research

Western University Health Science Research Ethics Board
HSREB Full Board Initial Approval Notice

Principal Investigator: Prof. Harry Prapavessis
Department & Institution: Health Sciences\Kinesiology, Western University

Review Type: Full Board
HSREB File Number: 109011
Study Title: The Acute Effects of Exercise and Nicotine on Cognition in Smokers

HSREB Initial Approval Date: April 07, 2017
HSREB Expiry Date: April 07, 2018

Documents Approved and/or Received for Information:

| Document Name	Comments	Version Date
Instruments	Questionnaires v2 clean	2017/04/04
Western University Protocol	Received Mar 27, 2017	
Revised Letter of Information & Consent	Letter of Information clean	2017/03/23
Advertisement	Advertisement (with version date)	2017/03/23

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.
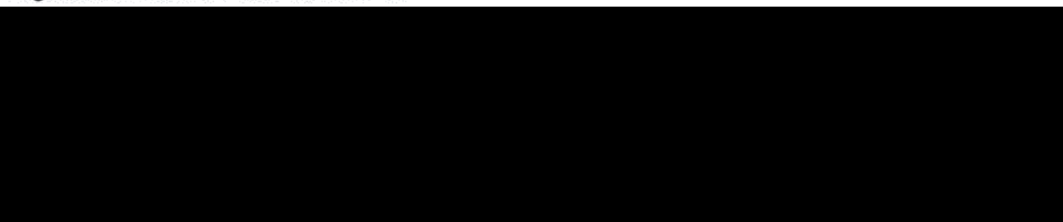
Letter of Information and Consent Form

Project Title: The Acute Effects of Exercise and Nicotine on Cognition in Smokers

Principal Investigator
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Co-investigators
Matthew Fagan, M.A. (School of Kinesiology, Western University)
Siobhan Smith, M.A. (School of Kinesiology, Western University)
Wuyou Sui, Ph.D. (school of Kinesiology, Western University)

Letter of Information

Invitation to Participate

You are being invited to participate in a research study examining the acute effects that moderate intensity exercise (a brisk walk) and nicotine inhalation (smoking) have on working memory in the smoking population. Working memory can be thought of as a type of short-term memory that allows one to make quick and accurate decisions about any information that has been presented previously. You are being invited to attend three sessions at the Exercise and Health Psychology Lab at Western University. The study has two phases embedded within it. The first phase involves a baseline assessment of working memory as well as post intervention assessment of working memory. The first phase is designed with a counter-balanced (each participant is given both interventions) while the second phase is designed with a randomized trial (each participant is only receives one of the two interventions) and will be done in a nicotine-deprived state (not smoking for 12 hours). It is important to understand that randomization happens by chance and is much like flipping a coin. The purpose of this letter is to provide you with the information needed to make an informed decision about participating in this research. Please take your time to read this letter and please do not hesitate to ask questions throughout. Please take note that this is a student project. We hope to recruit 34 participants that are over the age of 18 years.

Purpose of this Study

The primary objective of this study is to examine the short-term effects of exercise and nicotine on working memory of non-deprived and nicotine-deprived smokers.

Invitation to Participate in Research and Eligibility Criteria

You are being invited to take part in this research study because

- Are over the age of 18 years
- Smoke 5 cigarettes or more per day
- Do not have Chronic Obstructive Pulmonary Disease
- Are not an individual who is inhaler dependent
- Do not have any cognitive problems
- Are not pregnant
- Do not have a medical condition that prevents you to exercise

- Do not have an orthopaedic limitation
- Can read and write in English

Study Procedures

If you choose to participate in this study you will be asked to attend three sessions located at the **Arthur and Sonia Labatt Health Sciences Building (HSB 408)** at Western University. The sessions will be scheduled to your best convenience. The total time commitment of this study 155 minutes over a three day period. Below is a detailed description of the tasks you will be asked to complete.

During this study you will be asked to complete

During your first session at the laboratory you will be asked to complete:
Time involvement = 70 minutes
- Surveys (Item-1)
    - Demographic questionnaire (Item-a)
    - Smoking history questionnaire (Item –b)
    - Godin Leisure-Time Exercise Questionnaire (Item –c)
    - Pre-exercise or pre-nicotine (Item-d)
    - Fagerstrom Test for Nicotine Dependence (Item-e)
- A cognitive computer task – N-back (Item- 2)
- An intervention condition either: (Item-3)
      i) Moderate Intensity Aerobic Exercise or
      ii) Nicotine Inhalation

During your second session at the laboratory you will be asked to complete:
Time involvement = 35 minutes
- Surveys (Item-1)
    - Pre-exercise or pre-nicotine (Item-d)
- An intervention condition, either: (Item -3)
      i) Moderate Intensity Aerobic Exercise or
      ii) Nicotine Inhalation group
- A cognitive computer task-N-back (Item-2)

Item-4: You are asked to abstain from alcohol for at least 18 hours prior to your laboratory meetings and restricted to ½ cup of coffee

During your third session at the laboratory you will be asked to complete:
Time involvement= 50 minutes
- Surveys: (Item-1)
    - Pre-exercise or pre-nicotine (Item-d)
- An intervention condition, either: (Item-3)
      i) Moderate Intensity Aerobic Exercise or
      ii) Cigarette smoking
-A cognitive computer task-N-Back (Item-2)

Item-5: You are asked to abstain from alcohol for at least 18 hours prior to your laboratory meetings and restricted to ½ cup of coffee. You are also ask to abstain from smoking cigarettes or the use of any tobacco products for 12 hours prior to your laboratory visit.

Task descriptions

1) Provide demographic and smoking and exercise information
The surveys will include:
   a. Demographic questionnaire (which asks you identifiable information concerning, your age, email telephone number, and education)
   b. Smoking history questionnaire ("What is the approximate date and time of the last cigarette you have smoked?")
   c. Exercise behaviour in the last 7-days questionnaire ("In the last 7 days, how many times have you completed mild intensity exercise for 15 minutes or more?")
   d. Pre-exercise/nicotine questionnaire will be filled out before completing either task
   e. Fagerstorm Test for Nicotine Dependence (Information about your smoking behaviour)

2) Participate in a cognitive computer task
A number of tasks have been used to measure aspects of cognitive functions (intellectual processes by which one becomes aware of, perceives, or comprehends ideas). In our study, we will be using an N-back computer task to measure working memory. The N-back task is a 5 minute task that displays a letter on a computer screen for an interval of 500ms, followed by a 1000ms blank screen interstimulus. You will have to click the left button of a computer mouse as soon as a target appears. In the 1-back condition, the target is defined as a letter flashing that is the same as the one preceding it. For example, "x, interstimulus, x" would be the target.

3) Take part in an intervention condition: i) Moderate Intensity Exercise or ii) Cigarette Smoking

   i) Moderate Intensity Exercise (You will complete a single, 20-minute bout of moderate intensity aerobic exercise. Exercise consisted of a 2-minute warm-up, followed by 15 min of walking at a rate, which will allow you to reach 2/3 of your max heart rate, and then a 3-minute cool down on a treadmill)
      a. Vital signs (heart rate and blood pressure) will be recorded just prior to, and just after the exercise is complete.
   ii) Nicotine inhalation (You will smoke a cigarette of your choice in the 20 minute time period allocated, at this time you will refrain from conversation)
      a. Vital signs (heart rate and blood pressure) will be recorded just prior to, and just after nicotine administration.

Note that you will perform both procedures (exercise, and nicotine inhalation) by being randomized to one procedure first and then required to perform the other procedure on a separate day.

4) Abstain from drinking alcohol/coffee for at least 18 hours

We ask that prior to your laboratory visit you abstain from drinking alcohol and restrict to ½ a cup of coffee for at least 18 hours.

5) Abstain from drinking alcohol/coffee for at least 18 hours

We ask that prior to your laboratory visit you abstain from drinking alcohol and restrict to ½ a cup of coffee for at least 18 hours. We also ask if you could refrain from smoking cigarettes or using any tobacco related products for at least 12 hours.

Diagram of the study overview
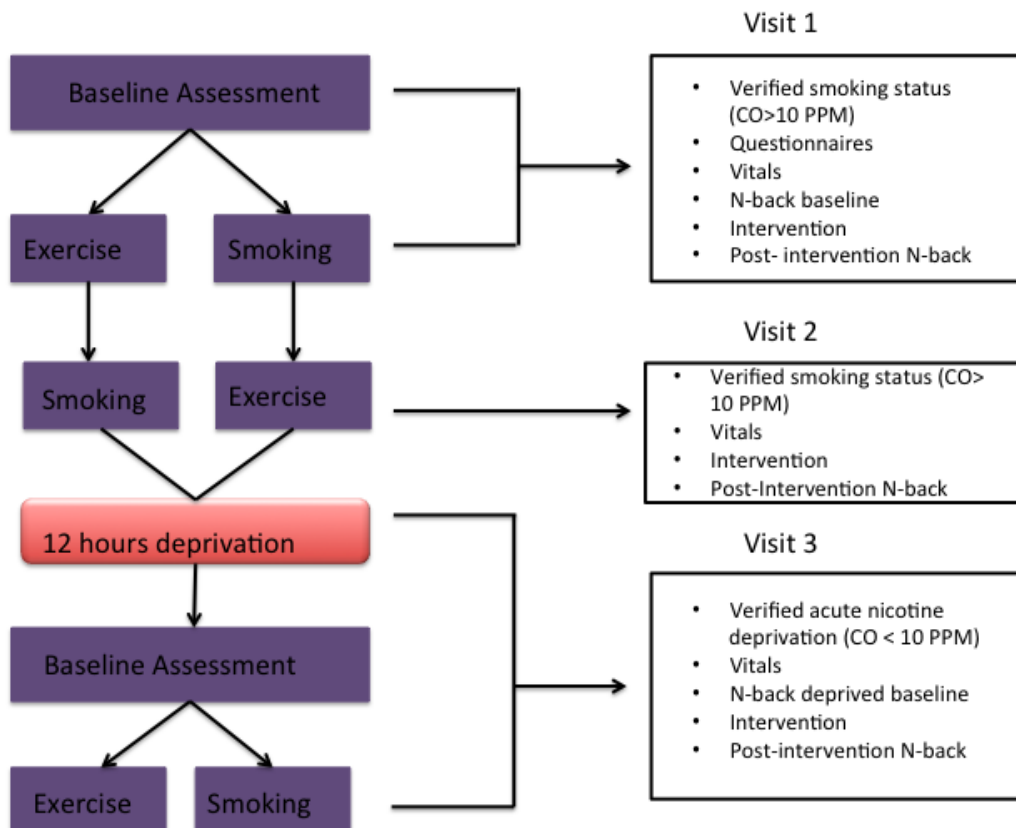
Possible Risks and Harms

Below are the documented side effects that are possible to experience while taking part in this study. It is important to note it is possible, however unlikely that other not known side effects may take place.

Exercise: There are some inherent risks of injury associated with exercise participation, particularly among people who are not used to exercising. You may, for example, feel mild muscle "tightness" or soreness that lasts for a couple of days, possible chest tightness when exercising, or even death. To minimize the physical risks of exercise, proper warm-up/cool-down

and stretching protocols will be performed by a trained exercise counsellor. Additionally, the exercise program delivered will be tailored to your individual fitness level, and modified according to your comfort level. Furthermore, you will only be allowed to participate in this exercise program if you complete the PAR-Q (Physical Activity Readiness Questionnaire) forms to ensure that it is safe for you to begin an exercise program. The exercise facilitator will be both CPR and First Aid trained, and experienced in working with previously inactive populations. If any physical or mental risks arise during the intervention, the Student Emergency Response Team (SERT) will be available to provide immediate assistance. SERT will assist the exercise supervisor until the 911 emergency services arrive. Should you have a minor injury while exercising you will receive medical treatment onsite as necessary. A first aid kit and ice packs will be available for minor injuries.

Smoking: There are some inherent risks of cigarette smoking that should be acknowledged. Smoking can cause many types of cancers, heart disease, stroke, chronic obstructive pulmonary disease, diabetes, as well as many others. Smoking has been shown to cause fertile issues for women attempting to become pregnant. The acute effects of a cigarette include an increase in heart rate, an increase in blood pressure, and an increase in the aoritic stiffness index.

Acute smoking denervation (12 hours): There are known withdrawal symptoms of cigarettes including; nervousness, headache, increased appetite, dizziness, constipation, fatigue, irritability and tobacco craving which all can be unpleasant.

Compensation

You will be compensated for your time. If you complete all three visits you will receive a 15 dollar gift card. Parking will also be free at the EHPL if you wish to drive to your sessions.

Do I have to take part?

Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your future care. If you decide to take part you will be given this Letter of Information to keep and be asked to sign the consent form. If you withdraw from the study, you maintain the right to request that any data collected from you not be used in the study. If you make such a request, all of the data collected from you will be destroyed. Please contact the study co-investigators, Matthew Fagan, Siobhan Smith, or Wuyou Sui if you wish to withdraw from the study.

Participation in other studies
If you are participating in another study at this time, please inform the study researchers right away to determine if it is appropriate for you to participate in this study.

New findings
If, during the course of this study, new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the investigator.

Are there any costs associated with participation?

This study is covered by an insurance policy and if during the course of the study any injury should occur which is not due to your fault or negligence, all medical expenses necessary to treat such injury will be paid provided: a) you comply at all times with the study researcher's instructions b) you promptly report any such injury to the study researchers conducting the study, and c) the expenses are not otherwise covered by your provincial health care. Financial compensation for such things as lost wages, disability or discomfort due to this type of injury is not routinely available. You do not waive any legal rights by signing the consent form.

Will information obtained in the study be confidential?
All the information you provide to the researcher will be kept in the strictest confidence. You will be assigned an identification number and all data collected from you will be recorded and stored on the Exercise and Health Psychology lab's research (R') drive, under this number only. Study researchers will not have any way of connecting your data to you. All data will be stored in coded form on computers accessible only to research staff in a secure office. You will not be identified in any documents relating to the research. No information obtained during the study will be discussed with anyone outside of the research team. If the results of the study are published, your name will not be used.

Representatives of the University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research. If we find information we are required by law to disclose, we cannot guarantee confidentiality. We will strive to ensure the confidentiality of your research-related records. Absolute confidentiality cannot be guaranteed, as we may have to disclose certain information under certain laws.

Questions?
If you have any questions about your rights as a research participant or the conduct of the study you may contact the Office of Research Ethics.
If you have any questions about the study, please contact the study co-investigators, Matthew Fagan, Siobhan Smith or Wuyou Sui.

This letter is for you to keep. You will be given a copy of this letter of information and consent form once it has been signed. If you have any concerns, please feel free to contact one of the researchers below. You may request the general findings of this research study from the researchers after the study is complete.

Informed Consent

Study Title: The Acute Effects of Exercise and Nicotine on Cognition in Smokers

I have read the Letter of Information, had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction. I will be given a copy of the Letter of Information and consent form once it has been signed.

<u>Consenting Signature:</u>

Participant: _____
                                         Please Print Name

Participant: _____
                                         Please Sign Name

Date: _____

Please send me my overall conclusions from this research: Yes □ No □

Researcher Signature: _____
                                                       Please Sign Name

Person obtaining informed consent: _____
                                                             Please Print Name

Recruitment Poster

Smoker volunteers needed for a cognitive performance research study

We are examining the acute effect of exercise and nicotine on cognitive performance.
Participants must be:
Smokers (at least 5 cigarettes a day)
Over the age of 18
No mental illness or pregnancy
Able to perform moderate intensity aerobic exercise (a quick walk)

Participants will receive compensation for their time and continued participation. Contact us if you would like to learn more about our study.

Version date: 23/03/2017

Exercise & Health
Psychology Laboratory
EHPL

Western
UNIVERSITY·CANADA

Appendix B

Sociodemographic Questionnaire

Date of Birth: _____/_____

                    MM   YYYY

Sex: Male or Female

Section A – Education

1. What is the highest degree you earned?

    (*Please check one*)   ☐ High school diploma
                            ☐ College certificate

                            ☐ Bachelor's degree

                            ☐ Master's degree

                            ☐ Doctorate

                            ☐ Professional (MD, LLB, DDS)

                            ☐ Other (specify:_____)

                            ☐ None of the above

Smoking History Questionnaire

1. On an average day, how many cigarettes do you smoke?

2. What is your preferred brand of cigarettes?

3. When was the approximate time of your last cigarette?

4. How many years have you been smoking?

Physical Activity Readiness Questionnaire (PARQ)

1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?

a.   [ ]Yes

b.   [ ]No

2. Do you feel pain in your chest when you do physical activity?

a.   [ ]Yes

b.   [ ]No

3. In the past month, have you had chest pain when you were not doing physical activity?

a.   [ ]Yes

b.   [ ]No

4. Do you lose your balance because of dizziness or do you ever lose consciousness?

a.   [ ]Yes

b.   [ ]No

5. Do you have a bone or joint problem that could be made worse by a change in your physical activity?

a.   [ ]Yes

b.   [ ]No

6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart?

a.   [ ]Yes

b.   [ ]No

7. Do you know of any other reason why you should not do physical activity?

   a. [ ]Yes

   b. [ ]No

Fagerström Test for Cigarette Dependence
Please circle one of the provided answers for each question

1) How soon after waking do you smoke your first cigarette?
   a) Within 5 minutes
   b) 5-30 minutes
   c) 31-60 minutes
2) Do you find it difficult to refrain from smoking in places where it is forbidden? e.g. Church, Library, etc.
   a) Yes
   b) No
3) Which cigarette would you hate to give up?
   a) The first in the morning
   b) Any other
4) How many cigarettes a day do you smoke?
   a) 10 or less
   b) 11-20
   c) 21-30
   d) 31 or more
5) Do you smoke more frequently in the morning?
   a) Yes
   b) No
6) Do you smoke even if you are sick in bed most of the day?
   a) Yes
   b) No

Godin Leisure-Time Exercise Questionnaire

1. During the last 7 days, how many times did you do the following kinds of exercise for more than 15 minutes during your free time (write on each line the appropriate number)?

a) STRENUOUS EXERCISE (heart beats rapidly)

(e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling).

b) MODERATE EXERCISE (not exhausting)

(e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing).

c) MILD EXERCISE (minimal effort)

(e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking).

Times Per Week

_____ times

_____ times

_____ times

2. During the last 7-Day period (week), in your leisure time, how often did you engage in any regular activity long enough that your heart would beat rapidly (work up a sweat)?

1. Often _____ 2. Sometimes _____ 3. Rarely/Never _____

ID: ——————————————. Date: ——————————————

Pre-study eligibility form

<u>Please circle one of the following answers to the questions.</u>

1) Have you abstained from alcohol and drugs in the past 18 hours? YES or NO

2) Have you limited your consumption to 1⁄2 cup of caffeine today? YES or NO or N/A

3) Are you physically well enough to be able to perform 20 minutes of moderate intensity exercise today? YES or NO

Vital Sign Form

Baseline

BP:

HR:

CO reading:

Immediately follow nicotine treatment

BP after:

HR after:

CO reading:

Immediately following exercise treatment

BP:

HR:

CO reading:

Curriculum Vitae for Matthew Fagan

<u>EDUCATION</u>

Degrees

- Masters of Art (Thesis) in Kinesiology, Psychological Basis, Western University, 2016-Present
- Bachelors of Arts Honors in Kinesiology, Western University, 2012-2016

<u>TEACHING</u>

Teaching Assistant

- Kinesiology 3330, Lab in Exercise Physiology (2016)
- Kinesiology 4433, Physiology of Exercise Training (2017)

<u>FUNDING</u>

- Ontario Graduate Scholarship (OGS), 2017-2018

<u>COMMUNITY AND VOLUNTEER ACTIVITES</u>

- VP Research; Canadian Cancer Society Research Bureau, Canadian Cancer Society Research Institute.
- Research discovery leader, SHAD.
- Financial Committee; Canadian Obesity Network Student Meeting.

<u>PRESENTATIONS</u>

- The possibility of exercise in an acute smoking model: cravings and withdrawal symptoms. Spoken Science Series, London, Canada (2018). Oral.
- The acute effects of exercise and nicotine on cognition in smokers. Society for Research on Nicotine and Tobacco, Baltimore, United States (2018). Poster.
- The Effects of Exercise on Cravings in Temporarily Abstinent Pregnant Smokers. Canadian Cancer Society Blitz, London, Canada (2017). Oral.
- The role of nicotine and exercise in cognition. Exercise is Medicine Canada, London, Canada. (2017). Oral.
- Acute Effects of Exercise and Nicotine on Cognition in Smokers. Eastern Canada Sport and Exercise Psychology Symposium, Kingston, Canada. (2017). Oral.

<u>BROADCAST INTERVIEWS</u>

- Alternative methods to increase cognition in smokers. GradCast, 94.9 CHRW. (2018).

PUBLICTIONS

- Fitzgeorge, L., Tritter, A., Fagan, M. J., Nagpal, T. S., & Prapavessis, H. (2018). Informing population-specific smoking policy development for college campuses: An observational study. Tobacco Prevention and Cessation. Submitted.
- Siobhan Smith, Matthew James Fagan, Jordan Lesarge, Harry Prapavessis. (2018). Standing and Dynamic Sitting in the University Classroom: A Real Possibility. Learning Environments Research. Submitted.
- Sui, Y., Smith, S., Fagan, M. J., Rollo, S., Prapavessis, H. (2018). The effects of sedentary behaviour interventions on work-related productivity and performance outcomes in real and simulated office work: A systematic review for consideration to. Applied Ergonomics. Submitted.
- Nagpal T. S., Fagan M. J., Prapavessis H, PhD. (2017). Treatment options for smoking cessation in pregnant women: A narrative review. Medical Research Archives. 5(7). Published.