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Reactive and Proactive Mechanisms of Response Inhibition in Gambling Disorder

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Reactive and Proactive Mechanisms of Response Inhibition in Gambling Disorder

by

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Abstract

Response inhibition, one component of cognitive control, refers to the ability to inhibit automatic responses and has been found to be impaired in gambling disorder. Recent models of cognitive control distinguish between two mechanisms: reactive (ability to stop in response to a stop-stimulus) and proactive control (ability to anticipate and prepare for a stop). Previous studies have focused on reactive modes of control in gambling disorder. Thus, the primary aim of this study was to assess the mechanisms of response inhibition in individuals with gambling disorder (n=27) and community controls (n=21) using a variant of the traditional stop-signal task. Second, the relationship between trait impulsivity, and reactive and proactive control was examined. No group differences in reactive or proactive control were found. However, one domain of trait impulsivity (premeditation) was associated with worse proactive control in the gambling group. Implications for impulsivity-focused approaches to treatment and future directions are discussed.

Keywords: response inhibition, cognitive control, gambling disorder, proactive control, reactive control

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List of Abbreviations

Abbreviation	Definition
ADHD	Attention Deficit/Hyperactivity Disorder
ANOVA	Analysis of Variance
BIS	Baratt Impulsivity Scale
CIDI	Composite International Diagnostic Interview
FTND	Fagerstrom Test of Nicotine Dependence
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
HAM-D	Hamilton Depression Rating Scale
MDMA	3,4-Methylenedioxy-Methamphetamine
SCID-5	Structured Clinical Interview for DSM-5 Disorders
SSRT	Stop Signal Reaction Time
SSAT	Stop Signal Anticipation Task
UPPS	UPPS Impulsive Behavior Scale

Chapter 1: Introduction

1.1 Gambling Disorder

Gambling disorder affects 1-3% of the general population and is characterized by persistent and recurrent maladaptive gambling behaviours leading to social, occupational, financial, and health impairments (APA, 2013; Okuda et al., 2009). Core features of gambling disorder include preoccupation with gambling, prolonged tolerance, craving, withdrawal, unsuccessful efforts to quit, and concealment of gambling-related problems (APA, 2013). Further, although casual gamblers may sometimes "chase" their losses in hopes of financial reconciliation, individuals with gambling disorder chase their losses continuously and over longer periods of time (Xian et al., 2008). Individuals with gambling disorder also frequently struggle with multiple comorbid mental health conditions. The rate of co-occurrence of nicotine dependence, substance use disorders, mood disorders, and anxiety disorders with gambling disorder ranges from 37-60% (Lorains et al., 2011).

In 2013, pathological gambling was renamed gambling disorder and re-categorized from the "Impulse Control Disorder" section to the "Substance-Related and Addictive Disorders" section of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (APA, 2013). The change was based on the premise that gambling disorder resembles substance-related disorders with respects to neurotransmission, brain circuitry, comorbidity, and response to treatment (Rash et al., 2016). Moreover, akin to substance use disorders, impulsivity is one of the central features implicated in the development and maintenance of gambling disorder (Wareham & Potenza, 2010; Hodgins & Holub, 2015).

1.2 Components of Impulsivity

The extant literature suggests impulsivity is one of the most robust characteristics associated with gambling disorder (MacKillop et al., 2014). Broadly defined, impulsivity is the tendency to act rashly without adequate consideration of adverse consequences (Hodgins & Holub, 2015). Cross-sectional studies have revealed higher scores on self-report and cognitive measures of impulsivity in persons with gambling disorder compared to control groups (Ledgerwood et al., 2009; Michalczuk et al., 2011). Significant positive relationships between various facets of impulsivity and problem gambling severity have also been established in adolescents and adults (Steel & Blaszczynski, 1998; Alessi & Petry, 2003; Cyders & Smith, 2008; Secades-Villa et al., 2016). In addition, longitudinal studies indicate a strong etiological role of impulsivity in gambling disorder (MacKillop et al., 2014). For instance, Vitaro, Arseneault and Tremblay (1999) found that high impulsivity in 12-14 year olds predicted problem gambling in late adolescence even more so than aggression and anxiety. These findings were corroborated by a more recent 30-year prospective community based study wherein children exhibiting impulsivity at age 7 were three times more likely to develop gambling problems in adulthood (Shenassa et al., 2012). To date, however, a significant amount of contention remains in the current gambling literature concerning the various conceptualizations, definitions, and components of impulsivity.

The various conceptualizations of impulsivity can be seen in the wide range of assessment modalities used to index different components of impulsivity. Personality models define impulsivity as a stable enduring trait (trait impulsivity) measured through self-report questionnaires such as the Baratt Impulsivity Scale (BIS) (Patton et al., 1995) and the UPPS Impulsive Behavior Scale (UPPS) (Whiteside & Lynam, 2001). At a cognitive level, impulsivity

is manifested via two behavioural expressions: impulsive choice and impulsive action (Brevers et al., 2012). Impulsive choice refers to the tendency to select higher-risk immediate rewards over delayed and less risky rewards with greater benefit, and is measured using delayed discounting tasks (see Matta et al., 2012). Impulsive action is characterized as a deficit in response inhibition/inhibitory control (Lawrence et al., 2009a; Conversano et al., 2012), and is predominately assessed using laboratory-based behavioural tasks such as the stop-signal and go/no-go task.

Despite a fair number of studies that have found impaired response inhibition in gamblers, no study to date has examined the underlying processes associated with poor performance. One likely process that has been suggested in the literature but has not been investigated in gambling disorder, is the inability to anticipate stop signals or cues (Heimburg et al., 1999; Vink et al., 2006). This process has been referred to as 'proactive control' (Zandbelt & Vink, 2010; Braver, 2012). Aron (2011) advocates for the inclusion of proactive control in current models of response inhibition as many everyday situations (1) require selectivity, (2) involve more than solely a rapid punctate stopping process, and (3) require goal-driven control, which is monitored for short to long periods of time. In addition, the relationship between self-reported impulsivity and proactive control has yet to be established (MacKillop et al., 2014; Leppink et al., 2016). As such, further study of proactive control and its relationship to self-reported traits of impulsivity is warranted.

1.3 A Measure of Response Inhibition Using the Stop-Signal Task

Response inhibition refers to the ability to suppress actions that are no longer relevant or inappropriate in certain situations (Mostofsky & Simmonds, 2008). Deficits in response inhibition lead to interference in goal-directed behaviour and may result in detrimental impulsive actions (Bari & Robbins, 2013; Verbruggen & Logan, 2008). The stop-signal task is a widely used cognitive task that provides a measure of response inhibition, basic psychomotor speed, and the ability to monitor and adjust response strategies (e.g., slowing responses proceeding unsuccessful inhibition) (Lawrence et al., 2009a; Verbruggen & Logan, 2008). During the "go" trials of the task, participants are instructed to respond as quickly as possible to a visual stimulus. However, on a minority of trials, participants are required to inhibit an already initiated pre-potent motor response upon presentation of an auditory or visual "stop-signal". As described comprehensively by Logan and colleagues (1984), the stop-signal paradigm is based on the horse-race model of stopping. In short, this model postulates that the "go" process required when a go stimulus is presented and the "stop" process required upon presentation of a stop-signal, are in competition. If the "stop" process is executed before the "go" process, an individual's response is inhibited successfully on the task. On the other hand, the response will not be inhibited successfully if the "go" process "outraces" the "stop" process. The latency of this stop process, referred to as the stop-signal reaction time (SSRT), is the chief measure used to determine response inhibition deficits in various patient groups.

Individuals with neuropsychiatric (e.g., obsessive compulsive disorder, Tourette's) and substance use disorders display slower SSRTs (Verbruggen & Logan, 2008; Lei et al., 2015). In the context of a gambling addiction, impaired response inhibition may lead to greater engagement in gambling activities and numerous failed quit attempts. Indeed, higher

disinhibition, as measured by the stop-signal task, has been linked to more severe forms of gambling disorder (Brevers & Noel, 2013) and is associated with higher rates of relapse (Goudriaan et al., 2008).

Studies using the stop-signal task to assess response inhibition in individuals with gambling disorder have produced mixed results. For example, Leppink and colleagues (2016) recently examined SSRT in a sample of 80 individuals with gambling disorder, parsed into low versus high impulsivity groups based on mean scores on the BIS and Eysenck impulsiveness questionnaire (EIQ), and found no significant differences in performance. Likewise, past studies that have compared SSRT in individuals with gambling disorder to control groups have produced similar results (no differences in SSRTs) (Lorains et al., 2014; de Ruiter et al., 2012). Contrastingly, a majority of studies using the stop-signal task have identified significant impairments in response inhibition among gamblers (Goudriaan et al., 2005; Goudriaan et al., 2006; Brevers et al., 2012; Odlaug et al., 2011; Brevers & Noel, 2013). A recent meta-analysis revealed response inhibition deficits were apparent in individuals with gambling disorder, as well as heavily dependent cocaine, MDMA, tobacco, methamphetamine and alcohol users (Smith et al., 2014). Of note, studies controlling for comorbidities have found mixed results in regards to response inhibition. For example, gamblers with a diagnosis of attention deficit/hyperactivity disorder (ADHD) have been found to exhibit worse response inhibition than those without (Rodriquez-Jimenez et al., 2006). In contrast, comorbid conditions such as antisocial personality disorder and nicotine dependence have not been linked to increased deficits in performance on the stop-signal task (Goudriaan et al., 2006; Kraplin et al., 2015). To date, there is a lack of research controlling for the effects of comorbid conditions on performance in individuals with gambling disorder (Grant et al., 2010; Billieux et al., 2012; Kraplin et al., 2015). Thus, further

research should directly assess the potential impact of comorbidities on performance on the stop-signal task.

Although ample evidence points to impaired response inhibition in gambling disorder, less is known about the specific processes constituting poor performance. More specifically, earlier studies in gambling disorder have not employed stop signal tasks in which the anticipation of a stop can be accurately estimated. Thus, an important next step in research is to explore whether the anticipatory or proactive processes preceding the presentation of stop-signals influences successful suppression of inappropriate responses.

1.4 Proactive and Reactive Processes in Response Inhibition

Response inhibition is considered a complex sub-process of cognitive control and cannot be considered a unitary construct (Brydges et al., 2012; Roberts et al., 2011). According to the recently developed 'dual mechanisms of control' framework, cognitive control constitutes two distinct yet complimentary modes– reactive and proactive control (Braver, 2012). Reactive control is thought of as a "late correction" mechanism involved in conflict resolution after an interfering stimulus (e.g., stop signal) has been presented (Khng & Lee, 2014). The SSRT in the traditional stop-signal task is considered a measure of reactive control (Smittenaar et al., 2015). Conversely, proactive control is considered an "early selection" mechanism involved in the anticipation and prevention of an interfering or cognitively demanding stimulus before it occurs. Further, proactive control entails the sustained maintenance of goal-relevant information that is lacking in reactive control. While overlapping brain regions such as the right inferior frontal gyrus, supplementary motor area, and striatum have been implicated in both forms of control, activations in the dorsolateral prefrontal cortex have been uniquely implicated in proactive control (Smittenaar et al., 2015).

The traditional stop signal task is largely a measure of reactive control, and thus, has been argued to be a limited model of response inhibition in psychiatric patients (Smittenaar et al., 2015). In response, researchers have implemented modified versions of the stop signal task to appropriately model proactive control. The stop signal anticipation task (SSAT) is one such variant of the stop signal task, which provides a measure of both reactive and proactive control (Zandbelt & Vink, 2010). In this paradigm, visual cues are used to indicate stop-signal probability as a way to manipulate the anticipation of stopping. To this end, as stop signal likelihood increases, participants are expected to utilize these cues to proactively prepare an inhibitory response.

Studies using the SSAT and other tasks with similar parameters, have observed increasing reaction times as a function of higher stop-signal probability in healthy populations (Vink et al., 2005; Zandbelt & Vink, 2010; Zandbelt et al., 2013a; Zandbelt et al., 2013b). In clinical populations, however, proactive control has been shown to be impaired. Zandbelt et al. (2011) found that in comparison to controls, patients with schizophrenia and their first-degree siblings exhibited reduced proactive control on the SSAT while reactive control was not affected. Other studies that have employed similar tasks of proactive and reactive control have also replicated these findings in schizophrenia patients (Vink et al., 2006; Lesh et al., 2013).

By dissociating reactive and proactive control, a more precise understanding of the cognitive and neural mechanisms underlying impaired response inhibition in gambling disorder can be gained. Furthermore, the above-mentioned studies demonstrate that proactive control may represent a more robust marker of disease pathology; the results show that proactive but not reactive control was impaired. Moreover, studies have suggested proactive control primes the same inhibitory network for reactive control, such that increases in proactive control (greater

level of preparation) lead to improved reactive control/SSRT (faster reactive stopping) (e.g., Chikazoe et al., 2009).

Given that the ability to stop a planned response (i.e., reactive control) seems to correspond to the degree to which stopping is anticipated (i.e., proactive control), it is surprising that previous research in gambling disorder has only focused on the late-acting/reactive inhibition of pre-potent motor responses. Consequently, there is less knowledge regarding the early-acting/proactive purposeful inhibitory control mechanisms underlying impaired performance. The study of proactive control may also have treatment implications. Response inhibition training has demonstrated efficacy in altering impulsive and compulsive behaviours (Stevens et al., 2015). For instance, Verbruggen and colleagues (2012) found that a brief period of training on a variant of the stop-signal task, which included a proactive component, led to 10-15% less monetary risk taking in a non-clinical sample. Currently, no studies have focused on the proactive processes involved in response inhibition in clinically diagnosed gamblers. Thus, both proactive and reactive processes should be given more attention in current models of response inhibition for a better understanding of two potentially differential mechanisms of control in gambling disorder.

1.5 Relationship between Self-Report Trait Measures of Impulsivity and Proactive Control

There is widespread consensus that compared to healthy controls, individuals with gambling disorder endorse higher levels of trait impulsivity (Fuentes et al., 2006; Sáez-Abad & Bertolín-Guillén, 2008; Ledgerwood et al., 2009; Michalczuk et al., 2011; Lai et al., 2011; Grecucci et al., 2014; Choi et al., 2014). Elevated traits of impulsivity are related to greater gambling involvement (Hodgins & Holub, 2015), more severe symptomatology (Steel &

Blaszczynski, 1998), and poor psychosocial outcomes (Ledgerwood & Petry, 2010). Previous studies have examined impulsivity as a trait using a wide range of self-report measures.

Whiteside and Lynam (2001) developed the UPPS Impulsive Behavior Scale (UPPS) to reconcile some of the ambiguity in the current literature on impulsivity The UPPS is predicated on the Five Factor Model of personality and is a byproduct of an extensive exploratory factor analysis. The most current version is the UPPS-P (Cyders & Smith, 2008), which separates five distinct personality dimensions that were previously subsumed under the term impulsivity. The first factor, negative urgency, refers to an individual's tendency to act impulsively under conditions of negative affect. The second factor, positive urgency, assesses an individual's tendency to act impulsively in response to heightened positive mood. The third factor, lack of perseverance measures a person's impulsive behaviours as a result of difficulties coping with boredom, stress, or fatigue. The fourth factor, lack of premeditation, evaluates an individual's tendency to engage in risky behaviour without consideration of potential negative consequences. Last, sensation seeking encompasses two components: an openness to pursue novel activities that may or may not be hazardous and a tendency to enjoy exciting and novel pursuits. Each scale reflects discrete personality traits that lead to engagement in impulsive-type behaviour without planning or sufficient foresight about negative consequences.

The UPPS-P can be used in research to better understand, for example, why two individuals may gamble excessively for completely different reasons. While one gambler may engage in harmful behaviours to escape depressive feelings (negative urgency), another gambler may partake in the same activities as a way to sustain their excitement or "high" (positive urgency). As such, this new approach may permit researchers to ascertain the specific impulsivity-related personality traits that are uniquely related to gambling behaviour. Another

advantage of the UPPS-P scale is the inclusion of a recently identified emotional component of impulsivity named urgency. Urgency is described as the tendency to engage in impulsive acts in the presence of intense mood states (Whiteside & Lynam, 2001; Dick et al., 2010). Cross-sectional relationships between urgency and other maladaptive behaviours such as excessive reassurance seeking, drinking to cope, early marijuana use, and bulimic symptoms have been reported in the literature (Anestis et al., 2007). Furthermore, recent studies indicate that higher levels of negative urgency are associated with higher gambling severity and worse outcomes (Albein-Urios et al., 2014; Torres et al., 2013). Thus, urgency is a strongly relevant construct in gambling research, since engagement in excessive gambling activities is often used as a route to either assuage feelings of distress, boredom, anxiety, and depression, or to maintain positive mood states (Dick et al., 2010).

As the UPPS-P is a relatively novel self-report instrument of impulsivity, more case-controlled studies are required to distinguish specific pathways to problematic gambling behaviour. In addition, there is a need to disentangle the relationship between impulsive-related traits and response inhibition, as problem gamblers who obtain high scores on self-report measures of impulsivity may not necessarily display impaired control over motor responses. Evidence suggests reactive control, as measured by the stop signal task, is associated with self-reported trait impulsivity in healthy controls (Logan et al., 1997; Enticott et al., 2006). In gamblers however, self-reported trait impulsivity has not been found to be related to reactive control (Lorains et al., 2014; Lawrence et al., 2009a).

The UPPS represents an emerging personality approach to impulsivity, which warrants further investigation in persons with gambling disorder. In addition, the association between

different facets of the UPPS and mechanisms of response inhibition requires further examination in the present research.

1.6 Objectives and Hypotheses of Present Study

The present study had three main objectives. First, to replicate past findings of reactive control in gambling disorder, overall SSRT was examined. The effect of block on SSRT was also examined in each group to assess differential learning as the task progressed. Consistent with previous studies, we expected gamblers would have slower SSRTs, indicating higher impulsive responding (hypothesis 1). Second, the proactive processes underlying response inhibition were investigated. We hypothesized gamblers relative to controls, would have more difficulty anticipating the occurrence of stop signals (hypothesis 2). The third objective of the study was exploratory. The relationship between different mechanisms of response inhibition (proactive and reactive processes) and self-reported trait impulsivity, as measured by the UPPS-P, was examined.

Chapter 2: Methodology

2.1 Participants and Recruitment

Twenty-seven individuals with a lifetime gambling disorder diagnosis and 21 controls were recruited from the community through media announcements (e.g., newspaper ads, posters), notices at local treatment agencies, and an existing registry of individuals interested in research participation. The Composite International Diagnostic Interview (CIDI***)*** was used to identify a gambling disorder diagnosis. All participants in the gambling group endorsed a minimum of 4 symptoms (maximum = 9 symptoms) for at least 6 months at some point during their lifetime. For the purposes of this study, the term "gambler" will be used to refer to the individuals with gambling disorder who participated in the present study. All participants completed a pre-screening phone interview and an in-person screening visit to determine eligibility for the study.

To be eligible, all participants had be over the age of 18 to sign consent for the study. The exclusion criteria for all participants included: (1) an intelligence quotient (IQ) less than 80 on the Wechsler Test of Adult Reading (2) diagnosis of a past or current psychotic disorder, (3) a current or past neurological condition known to significantly influence neurocognitive function (e.g. multiple sclerosis, epilepsy), (4) uncorrectable visual problems that could interfere with study procedures, (5) colour blindness, (6) history of stroke, and (7) a diagnosis of dementia, delirium, or another cognitive disorder. Community controls with a personal or family history of gambling disorder were further excluded.

2.2 Procedure

The study was approved by the University of Calgary Research Ethics Board. All research participants who met inclusion criteria provided written informed consent prior to any research procedures. Depending on the participant, the study took approximately 2-5 hours to complete. More specifically, some participants' sessions were abbreviated, as their clinical data was already collected from a larger scale study in the laboratory, and was simply updated for the purposes of the current study. Of importance, the cognitive component of the study was administered within the first hour of the study when participants were assumed to be the most alert and to maintain consistency.

The Structured Clinical Interview for DSM-5 Disorders (SCID-5) was administered to each participant by a trained graduate student or postdoctoral fellow. Participants were evaluated for mood disorders, schizophrenia spectrum and other psychotic disorders, substance use disorders, anxiety disorders, feeding and eating disorders, obsessive-compulsive and related disorders, trauma and stressor-related disorders, and adult attention-deficit/hyperactivity disorder. Additional questions about tobacco use, as well as the Fagerstrom Test for Nicotine Dependence (FTND), were administered to supplement the substance use disorders module of the SCID-5. Diagnoses for all participants were assigned at case consensus meetings, which were attended by all interviewers and at least one principal investigator. Other clinical interviews and self-report measures were also collected to obtain information regarding diagnoses, medical history, past brain injury, gambling severity, impulsivity, and substance use.

The stop signal anticipation task (SSAT) was administered amongst a larger cognitive battery by a trained research assistant or graduate student in a quiet testing room. All tasks in this extensive battery were preordered in a way to facilitate optimal attention and alternate between

tasks measuring different cognitive domains. Participants were reimbursed for their time in the form of gift cards.

2.3 Measures

2.3.1 Clinical Measures

Composite International Diagnostic Interview (CIDI)

The gambling module of the CIDI was used to assess frequency of gambling, gambling history, and whether participants met criteria for lifetime gambling disorder. The CIDI is a structured clinical interview based on the diagnostic criteria outlined by the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (Kessler et al., 2008; Hodgins et al., 2012). To remain relevant to the most recent conceptualization of gambling disorder, the information from the CIDI was used to determine diagnosis based on the DSM-5 criteria.

Hamilton Depression Scale (HAM-D)

Each participant also completed the Hamilton Depression Scale (HAM-D), as mood has been found to alter cognitive performance (Porter et al., 2008). The HAM-D, a 17-item questionnaire, was administered before cognitive testing to evaluate depressive symptoms experienced in the past week. Participants were asked about depressive symptoms related to mood, feelings of guilt, agitation, daily activities, somatic symptoms, suicide, insomnia, motor retardation, weight loss, and anxiety. The severity of each symptom was scored on a 3 to 5 point scale. The following severity ranges of depressive symptoms were considered: 0-7 (no depression), 8-16 (mild depression), 17-23 (moderate depression), and 24-52 (severe depression) (Zimmerman et al., 2013).

Brain Injury Screening Questionnaire (BISQ)

Though not an exclusion criterion, information about past acquired brain injuries was collected using the BISQ to account for the potential impact of brain injury on cognition. For the purposes of the study, only Part One was utilized to assess brain injuries and hospitalizations. More specifically, participants were asked to indicate if they have ever experienced a blow to the head in various situations (e.g., motor vehicle accidents, falls, sports injuries, alcohol blackouts, physical abuse etc.) and whether the injury resulted in a loss of consciousness or a period of being dazed or confused. If unconsciousness or periods of daze and confusion were reported, participants were asked to specify the year of occurrence and duration of each event.

Problem Gambling Severity Index (PGSI; Ferris & Wynn, 2001)

The PGSI is a 9-item questionnaire used to assess problem gambling severity in the past 12 months. Subjects answer questions on a 4-point alternative scale (0 = never, 1 = sometimes, 2 = most of the time, 3 = almost always). A score of 0 indicates a non-problem gambler. A score between 1 and 4 indicates low levels of problem gambling with few, if any, negative consequences. A score between 5 and 7 indicates moderate levels of problem gambling which lead to some negative consequences. A score of 8 or more indicates severe problem gambling with several negative consequences and possible loss of control (Currie et al., 2013). The PGSI was used to supplement the SCID data by specifically providing additional information about gambling habits in the past year.

2.3.2 Impulsivity Measures

UPPS Impulsive Behavior Scale (UPPS-P)

The UPPS-P is a 59-item questionnaire designed to measure five distinct facets of personality associated with impulsive behaviour: negative urgency, positive urgency, (lack of) perseverance, (lack of) premeditation, and sensation seeking (Whiteside & Lynam, 2001). Participants responded to each item of the UPPS-P on a 4-point Likert scale ranging from 1 (strongly agree) to 4 (strongly disagree).

Stop Signal Anticipation Task (SSAT)

The SSAT was developed by Zandbelt and Vink (2010) and is based on the original stop-signal paradigm (see Logan & Cowan, 1984). This modified version allows a measure of stop signal reaction time (reactive control) and whether inhibition improves as the anticipation of a stop signal increases (proactive control). The task was administered using Presentation® (NeuroBehavioral Systems, Albany, CA, USA), a stimulus delivery and experiment control program, on a Dell laptop with a 14’ by 7.5’ screen. The task took approximately 25 minutes to complete. Three horizontal lines displayed one above the other formed the background, which was presented to the participants throughout the task. Stimuli were presented in 3 blocks separated by two 24 second rest periods. All blocks consisted of STOP trials, which were pseudorandomly interspersed between GO trials. On every trial, a rising bar would rise towards the middle line at a constant speed (800 milliseconds). On a majority of trials (GO trials), participants were required to stop the bar as closely as possible to the middle line by pressing the spacebar. On a minority of trials (STOP trials), the rising bar would stop automatically before reaching the middle line. This spontaneous halt is the stop signal and indicates that a response must be suppressed. Stop signal likelihood was manipulated across trials and could be

anticipated based on the colour of the middle line (green, 0%; yellow, 17%; amber, 20%; orange, 25%; red, 33%). See Figure 2. 1 for a detailed overview of the task by each block.

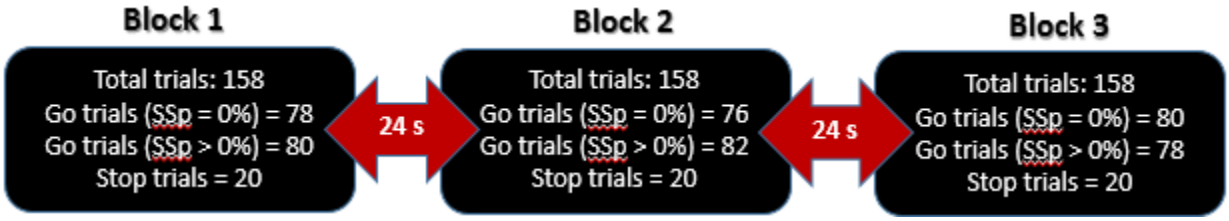

Figure 2.1. Stop Signal Anticipation Task by Block. There are a total of 234 GO ONLY trials and 180 GO/STOP trials (60 of which are stop trials). SSp = stop signal probability.

The initial stop signal onset time was set to 550 milliseconds (250 milliseconds before 800 millisecond target response time) for all stop-signal probability levels and was adjusted in real time for each participant to ensure an overall target accuracy level of 50%. If actual performance surpassed target performance on one of the trials, the stop signal onset time was shifted 25 milliseconds towards the target response time to increase difficulty. Twenty-five milliseconds were subtracted from the stop signal onset time if actual performance was lower than target performance. Thus, level of difficulty was kept constant to minimize differences in task performance across gamblers and controls. Prior to task initiation, participants completed several practice blocks to familiarize themselves with the stimuli and eliminate practice effects.

2.4 Statistical Analysis

SPSS for Windows, version 24.0, was used to conduct all statistical analyses. All tests were two-tailed with statistical significance set at $p < 0.05$. Descriptive statistics (mean, standard deviations, and ranges) were presented for all relevant variables. Differences in demographic characteristics were determined by independent sample *t*-tests for continuous variables (e.g., age, IQ), and chi-square tests for categorical variables (e.g., marital status, sex). Demographic

variables were included in statistical models where warranted. Variables that did not meet the assumption of normality were retained given ANOVA is fairly robust to this violation (Maxwell & Delaney, 2004). The Welch-Satterthwaite method was applied to adjust degrees of freedom for continuous clinical variables that violated the assumption of homogeneity. An independent t-test was conducted to compare the average response time for GO trials in the GO ONLY and the GO/STOP blocks to ensure participants exerted more control on responses to the latter GO trials.

To test *hypothesis 1*, the average SSRT for each individual was calculated using the integration method (Verbruggen & Logan, 2008), which entailed subtracting the mean delay time from the approximate overall median reaction time on GO ONLY trials (value at 50^{th} percentile on GO ONLY distribution). Outliers were removed based on the method used in Zandbelt and Vink (2010). Specifically, reaction times on all GO trials throughout the task that exceeded 1.5 times the interquartile range away from the 25^{th} and 75^{th} percentiles of the reaction time distribution of each task condition (i.e. 4 stop-signal probability levels) were deemed as outliers. The overall mean SSRT obtained by gamblers and controls was compared using a one-way ANOVA. Furthermore, the SSRT was calculated individually for each block to determine whether there was a learning effect over time. A repeated measures ANOVA with block (3 levels) as the within-subjects factor and diagnostic group (2 levels) as the between-subjects factor was conducted to examine learning effects across time in the respective groups.

To test *hypothesis 2*, a repeated measures ANOVA with GO trial condition (4 levels) as the within-subjects factor and diagnostic group (2 levels) as the between-subjects factor was conducted to test for differences in GO reaction time modulation as a function of stop signal likelihood. The trial X group interaction was examined to determine between-group differences on proactive control performance.

To address the *third objective* of the study (whether specific UPPS-P personality domains predict reactive and proactive performance on the SSAT), a multiple regression analysis was conducted in each group, with reactive (SSRT) and proactive performance ([reaction time in response to red cue] – [reaction time in response to yellow cue]) on the SSAT as the dependent variables and the UPPS-P subscales as the predictor variables. Only one outlier on the perseverance domain of the UPPS-P was deemed an influential case (control participant, value = 2.90), and was removed from the analysis (see Table A.1 in Appendix for regression statistics).

Given the high co-occurrence of head injuries and psychiatric comorbidities in gambling disorder, participants were not excluded for these factors. No significant group differences on the BISQ were identified, and thus, no secondary analyses were conducted. In addition, the final sample did not permit separating groups by comorbidities. Finally, correlational analyses were conducted to examine the relationship between the HAM-D, PGSI, reactive control, and proactive control in both groups. No significant relationships were found (refer to Tables A.2 and A.3 in Appendix)

Chapter 3: Results

3.1 Participant Characteristics

The sample consisted of individuals with gambling disorder (*n*=27) and community controls (*n*=21). In the gambling group, 6 participants were identified as past gamblers (no gambling activity in the last 12 months). The severity of gambling disorder was relatively similar in both past gamblers (2 mild, 2 moderate, 2 severe) and current gamblers (9 mild, 5 moderate, 7 severe). Demographic and clinical data, as well as statistical tests of mean differences between groups are reported in Table 3.1. Gambling characteristics for gamblers are presented in Tables 3.3 and 3.4. The Welch-Satterthwaite method was applied to the following variables: HAM-D, PGSI, and UPPS-P perseverance and sensation seeking. There were no significant differences between groups in sex, age, work status, number of children, annual income, IQ, and head injuries. However, there were significant differences in mean years of education and marital status, such that controls had higher years of mean education than gamblers, and more controls than gamblers were married. Further, there was a trend towards a higher frequency of smoking in the gambling group ($p = 0.06$). Moreover, as expected, individuals with gambling disorder scored significantly higher than controls on the HAM-D and PGSI, indicating both greater symptoms of depression in the previous week and more severe gambling problems, respectively. Of note, there was significant variability in the PGSI means in the gambling group (9.67 ± 7.32; score range: 0-25) and the overall mean severity level in past gamblers (n = 6) was low (M = 3.00). On the UPPS-P, there was a significant between-group difference on each subscale except sensation seeking (refer to Table 3.1). More specifically, individuals with gambling disorder displayed elevated scores on all subscales except negative urgency. No gender differences in either group was found, with the exception of higher scores on sensation seeking in male (M =

2.89 ± 0.47) versus female (M = 2.13 ± 0.47) gamblers ($t(25) = 4.01$, $p < .001$). Furthermore, comorbidities did not account for group differences on the UPPS-P. Finally, there were significantly higher rates of major depressive disorder ($X^2(2) = 7.63$, $p = 0.02$) and alcohol use disorder ($X^2(2) = 8.74$, $p = 0.01$) in individuals with gambling disorder than in controls (refer to Table 3.2). In the gambling group, no individuals endorsed current major depressive disorder, 41% met crtieria for past major depressive disorder, 18% met criteria for current alcohol use disorder, and 30% met criteria for past alcohol use disorder. In the control group, 10% met criteria for both current and past major depressive disorder (20% total), and 10% met criteria for past alcohol use disorder.

Table 3.1
Demographic and Selected Clinical Variables for Controls and Gamblers.

	CON (n=21)	GD (n=27)	Tests of group differences
Sex (% female)	48	36	$X^2(1) = 0.54$, $p = 0.46$
Mean age	46.19 ± 13.33	45.00 ± 15.31	$t(46) = 0.28$, $p = 0.78$
Mean years of education	16.05 ± 2.01	14.44 ± 2.12	$t(46) = 2.67$, $p = 0.01$*
Marital Status	Single (19%) Married (57%) Divorced (24%) Widowed (0%)	Single (48%) Married (19%) Divorced (26%) Widowed (7%)	$X^2(3) = 9.37$, $p = 0.03$*
Mean number of children	1.14 ± 1.11	0.85 ± 1.20	$t(46) = 0.86$, $p = 0.39$
Work status	Employed (62%) Unemployed (14%) Retired (14%) Student (10%)	Employed (52%) Unemployed (15%) Retired (22%) Student (11%)	$X^2(3) = 0.64$, $p = 0.89$
Mean estimated annual salary ($)	62190.48 ± 32472.48	48335.41 ± 35526.11	$t(46) = 1.39$, $p = 0.17$
Smoking status	Current smoker (5%) Past smoker (14%) Non-smoker (81%)	Current smoker (22%) Past smoker (30%) Non-smoker (48%)	$X^2(2) = 5.72$, $p = 0.06$

Mean WTAR	103.24 ± 11.26	103.19 ± 12.01	$t(46) = 0.16$, $p = 0.98$
Mean HAM-D	1.19 ± 1.78	3.81 ± 5.39	$t(33) = -2.37$, $p = 0.04$*
Mean PGSI	0.14 ± 0.48	9.67 ± 7.32	$t(26) = -6.74$, $p < 0.001$**
BISQ			
Lifetime blow to head	Yes (67%) No (33%)	Yes (67%) No (33%)	-
Mean number of blows	2.14 ± 2.11	3.33 ± 2.35	$t(30) = -1.49$, $p = 0.15$
Lifetime loss of consciousness	Yes (33%) No (67%)	Yes (33%) No (67%)	-
Mean number of times unconscious	1.29 ± 0.76	2.22 ± 2.11	$t(14) = -1.11$, $p = 0.28$
Amount of time unconscious (most severe case)	*"Don't know"* (43%) *"< 1 minute"* (0%) *"1-10 mins."* (14%) *"11-20 mins."* (0%) *"21-30 mins."* (29%) *"1-23 hours"* (14%)	*"Don't know"* (11%) *"< 1 minute"* (22%) *"1-10 mins."* (44%) *"11-20 mins."* (11%) *"21-30 mins."* (0%) *"1-23 hours"* (11%)	$X^2(5) = 7.67$, $p = 0.18$
Mean UPPS-P scores			
Negative urgency	3.10 ± 0.49	2.46 ± 0.61	$t(46) = 3.92$, $p < 0.001$**
(lack of) premeditation	1.90 ± 0.31	2.26 ± 0.46	$t(46) = -3.06$, $p = 0.004$**
(lack of) perseverance	1.69 ± 0.32	2.04 ± 0.58	$t(42) = -2.66$, $p = 0.01$*
Sensation seeking	2.48 ± 0.82	2.61 ± 0.59	$t(36) = -0.61$, $p = 0.55$
Positive urgency	1.77 ± 0.37	2.16 ± 0.51	$t(46) = -3.02$, $p = 0.004$**

Note. *. Significant at $p = 0.05$ (2-tailed); **. Significant at $p = 0.01$ (2-tailed). CON, community controls; GD, individuals with gambling disorder; WTAR, Weschler Test of Adult Reading; HAMD, Hamilton Depression Scale; PGSI, Problem Gambling Severity Index; BISQ, Brain Injury Screening Questionnaire.

Table 3.2
Comorbid Mental Health Disorders for Controls and Gamblers.

Mental Health Condition	CON (n=21)	GD (n=27)	Test statistic
Mood disorders, % total (n) [1]	29% (6)	56% (15)	$X^2(1) = 3.50$, $p = 0.062$
Substance use disorders, % total (n) [2]	19% (4)	52% (14)	$X^2(1) = 5.42$, $p = 0.020$*
Anxiety disorders, % total (n) [3]	10% (2)	11% (3)	$X^2(1) = 0.32$, $p = 0.858$
Eating disorders, % total (n) [4]	5% (1)	4% (1)	$X^2(1) = 0.33$, $p = 0.856$
ADHD, % total (n)	0% (0)	7% (2)	$X^2(1) = 1.62$, $p = 0.203$
PTSD, % total (n)	0% (0)	11% (3)	$X^2(2) = 2.49$, $p = 0.288$

Note. *. Significant at $p = 0.05$ (2-tailed). [1]. Mood disorders in the sample included major depressive disorder, persistent depressive disorder, substance induced depression, and premenstrual dysphoric disorder. [2]. Individuals with substance use disorder in the sample abused alcohol, cannabis, and cocaine; one person abused hallucinogens. [3]. Anxiety disorders in the sample consisted of specific phobias, panic disorder, social anxiety disorder, and agoraphobia. [4]. Eating disorders in the sample consisted of anorexia and bulimia nervosa. CON, community controls; GD, individuals with gambling disorder; ADHD, Attention Deficit/Hyperactivity Disorder; PTSD, Posttraumatic Stress Disorder. The values in the chart represent the percentage of individuals in each respective group who met diagnostic criteria for the listed disorder. Values were rounded up to the nearest whole percent.

Table 3.3
Continuous Variables on the CIDI for Participants with Gambling Disorder

CIDI variable	Mean (SD)	Confidence Interval (95%)	
		Lower bound	Upper bound
Age at first bet (years)	18.27 (9.93)	13.87	22.68
Greatest monetary loss in a single year ($)	46090.91 (41123.40)	27857.81	64324.00
Greatest amount of gambling in any given year (days)	205.59 (118.91)	152.87	258.31
Amount of gambling in the last year (days)	126.64 (117.23)	74.66	178.62
Longest time period without gambling (months)	7.20 (8.56)	3.41	11.00
Age of GD onset	30.14 (13.50)	24.15	36.12

Table 3.4
Categorical Variables on the CIDI for Participants with Gambling Disorder

CIDI variable	Outcome
Lifetime frequency: n (%)	
51-100	1 (4%)
101-500	2 (7%)
501-1000	5 (19%)
1000+	19 (70%)
Last occurrence of gambling symptom/problem: n (%)	
Past month	13 (48%)
2-6 months	6 (22%)
7-12 months	2 (7%)
12+ months	6 (22%)
Prefer gambling alone or with friends: n (%)	
Alone	23 (85%)
With friends	4 (15%)
Symptoms of dissociation (% yes)	27 (100%)
Lifetime treatment: n (%)	
Yes	12 (44%)
No	15 (56%)

3.2 Stop Signal Anticipation Task (SSAT)

Descriptive statistics for the SSAT are provided in Table 3.5. Two tests were conducted on the SSAT data to ensure participants understood the task and exerted more cognitive control during the GO ONLY trials. First, response times on GO ONLY trials (stop signal probability of 0%) in both controls (M = 807 ms, SD = 14.67) and gamblers (M = 810 ms, SD = 12.65) were similar to the target response time of 800 ms, confirming participants understood the task and were able to perform the response task accurately. Second, response times on the GO/STOP trials in both controls (M = 825 ms, SD = 23.28) and gamblers (M = 824 ms, SD = 16.90) were significantly slower than their respective response times on GO ONLY trials (control group: $t(20) = -6.63$, $p < 0.001$; gambling group: $t(26) = -6.82$, $p < 0.001$).

A one-way ANOVA was conducted to test whether gamblers exhibited a slower SSRT on the SSAT, indicating impaired reactive control (hypothesis 1). However, contrary to the hypothesized outcome, no significant difference in SSRT between groups ($F(1, 46) = -0.96$, $p = 0.33$) was found. Furthermore, a block (3 levels) X group (2 levels) repeated measures ANOVA was conducted to determine whether there was a learning effect between groups as the task progressed. There was no significant main effect of group on SSRT ($F(1, 46) = 0.74$, $p = 0.39$). However, a significant main effect of block on SSRT was found ($F(2, 92) = 5.35$, $p = 0.006$). Finally, no significant interaction ($F(2, 92) = 0.95$, $p = 0.39$) was observed. Therefore, although there were no between-group differences in learning effects, these findings suggest SSRT improved in both groups as the task progressed.

A trial (4 levels) X group (2 levels) repeated measures ANOVA was conducted to examine proactive control (hypothesis 2). There was a significant main effect of trial on reaction time ($F(3, 138) = 17.71$, $p = 0.001$) but no significant main effect of group ($F(1, 46) = 0.08$, $p = 0.85$) The trial X group interaction effect was not significant, suggesting no difference in proactive control performance between groups; Mauchly's Test of Sphericity was violated ($p<.05$), and thus, the Huynh-Feldt correction was applied to the F-statistic ($F(3.54, 162.59) = 0.84$, $p = 0.46$, $\varepsilon = 0.88$). Nonetheless, participants slowed responding in accordance to the degree to which they anticipated stop-signals in both the control (linear contrast, $F(1, 20) = 74.49$, $p < 0.001$) and gambling group (linear contrast, $F(1, 26) = 58.92$, $p < 0.001$). Specifically, the average response time increased linearly as a function of stop-signal probability in both groups.

Given, the difference in years of education between groups, the above-mentioned ANOVAs were also conducted with education added as a covariate; no changes in significance

were observed on any of the findings. Therefore, the analyses are presented without inclusion of education as a covariate.

Table 3.5
Descriptive Statistics for SSAT Task

Measure	CON (n=21)	GD (n=27)	Test Statistic
GO ONLY RT (mean % ± SD)	807 ± 14.67	811 ± 12.65	$t(46) = -0.88$, $p = 0.38$
GO/STOP RT			
SSP 17%	821 ± 26.29	820 ± 19.73	$t(46) = 0.18$, $p = 0.86$
SSP 20%	822 ± 25.95	822 ± 16.52	$t(46) = 0.04$, $p = 0.97$
SSP 25%	827 ± 22.38	825 ± 16.12	$t(46) = 0.31$, $p = 0.76$
SSP 33%	831 ± 21.00	829 ± 19.96	$t(46) = 0.22$, $p = 0.82$
Overall	825 ± 23.28	824 ± 16.90	$t(46) = 0.20$, $p = 0.84$
SSD average (ms)	568 ± 29.63	566 ± 24.98	$t(46) = 0.25$, $p = 0.81$
SSRT (mean % ± SD)			
Block 1	250 ± 20.32	256 ± 20.81	$t(46) = -1.02$, $p = 0.31$
Block 2	246 ± 22.74	247 ± 23.63	$t(46) = -0.06$, $p = 0.95$
Block 3	240 ± 22.88	248 ± 23.79	$t(46) = -1.18$, $p = 0.25$
Overall	245 ± 19.63	251 ± 19.88	$t(46) = -0.98$, $p = 0.33$
Accuracy: (mean % ± SD)			
SSP 17%	44 ± 13.48	51 ± 14.34	$t(46) = -1.71$, $p = 0.10$
SSP 20%	50 ± 8.39	50 ± 7.93	$t(46) = 0.15$, $p = 0.89$
SSP 25%	51 ± 4.78	51 ± 5.25	$t(46) = 0.13$, $p = 0.90$
SSP 33%	51 ± 3.71	50 ± 4.59	$t(46) = 0.23$, $p = 0.82$
Overall	49 ± 4.21	51 ± 5.87	$t(46) = -1.03$, $p = 0.31$
Stop Failure RT (ms)	799 ± 26.42	801 ± 25.73	$t(46) = -0.31$, $p = 0.76$

Note. *. CON, community controls; GD, individuals with gambling disorder; SSAT, stop signal anticipation task; SD, standard deviation; SSD, stop signal delay; SSRT, stop signal reaction time; SSP, stop signal probability; RT, reaction time.

3.3 Association between Trait and Cognitive Impulsivity

Given the modest sample size, two preliminary multiple regression analyses were conducted to identify whether trait impulsivity (UPPS-P domains) significantly predicted participants' reactive (SSRT) and proactive performance on the SSAT (refer to Table A.1 in Appendix). The overall regression models for reactive ($R^2 = 0.45$, $F(5, 19) = 2.27$, $p = 0.11$) and proactive control ($R^2 = 0.25$, $F(5, 19) = 0.91$, $p = 0.50$) were nonsignificant in controls. Similarly, the overall regression models conducted in the gambling group were nonsignificant for reactive

(R^2 = 0.06, F(5, 26) = 0.27, p = 0.93) and proactive control (R^2 = 0.23, F(5, 26) = 1.25, p = 0.32). Thus, in controls and gamblers, trait impulsivity was unrelated to both reactive and proactive control. Interestingly, however, closer examination of beta weights showed premeditation was a significant predictor of performance in the gambling group (b= -12.48, SE= 4.02, r(27)= -0.39, p = .03), such that lower premeditation on the UPPS-P predicted worse proactive control.

Chapter 4: Discussion

Previous studies of response inhibition in gambling disorder have solely focused on reactive mechanisms of control. To further the literature, the current study sought to examine both reactive and proactive mechanisms of control using a variant of the traditional stop-signal task. More specifically, the SSAT was utilized to allow measure of proactive control by manipulating stop-signal probability across trials. Furthermore, as an exploratory objective, the relationship between these mechanisms of response inhibition and trait impulsivity were evaluated.

4.1. Reactive and Proactive Control

The first aim of the present study was to add to the literature on reactive control. Current studies on reactive control in gambling disorder are both sparse and have produced mixed findings. Some studies have found impaired reactive control in gamblers, indicated by slower SSRTs, while others have identified no significant differences. The findings from the present study were in accordance to past studies that have failed to find impaired reactive control in gambling disorder (Lawrence et al., 2009b; de Ruiter et al., 2012; Lorains et al., 2014; Leppink et al., 2016). SSRT values reported in studies of healthy controls on the standard stop-signal paradigm are usually between 200 and 250 milliseconds (Zandbelt & Vink, 2010); all participants' SSRTs in the current study fell within this normal range.

One implication of this finding may be that poor reactive control is not a core deficit in gambling disorder. In fact, some studies have suggested impaired pre-potent motor inhibition may not be a central aspect of impulsivity in gambling disorder (e.g., Leppink et al., 2016). Nonetheless, these findings should be interpreted with caution, given the modest sample size of the study. For instance, the sample size did not allow separate analyses of gamblers with and without alcohol use disorder. Lawrence et al. (2009b) found SSRT was slower in alcohol-

dependent individuals compared to controls, whereas no differences were observed between controls and problem gamblers. Therefore, one plausible explanation for intact stop-signal performance in some groups of gamblers could be the absence of the neurotoxic effects of alcohol and drug use on brain structure and chemistry, particularly in the prefrontal cortex (Potenza, 2006; Clark, 2014). Indeed, approximately half of the gamblers in the present study did not meet diagnostic criteria for any substance use disorder, and in turn, may have attenuated the SSAT outcomes. On a similar note, only two individuals in the gambling group had an ADHD diagnosis, which has consistently been shown to impair performance on the stop signal task in children (Senderecka et al., 2012) and in adults (Lijffijt et al., 2005; Verbruggen & Logan 2008). In a study by Rodriguez-Jimenez and colleagues (2006), SSRT was compared in controls and individuals with gambling disorder with and without a comorbid ADHD diagnosis; impairment in performance was only reported in the gamblers with a history of ADHD. Taken together, it is conceivable that reactive and/or proactive control are only impaired in a selection of gamblers (e.g., gamblers with co-occurring ADHD and substance use disorders). This notion is in line with the pathways model (see Blaszczynski, A. & Nower, 2002), which suggests some subsets of gamblers (i.e. “the behaviorally conditioned gambler”) endorse low levels of impulsivity. The current finding emphasizes that individuals with gambling disorder do not constitute a homogenous population and may require different targets of intervention for successful treatment outcomes.

The second aim of this study was to compare proactive control in individuals with gambling disorder and controls. Contrary to our hypothesis that gamblers would display impaired proactive control, we found no significant differences between the two groups. This finding is in contrast to other studies that have reported impaired proactive control in other clinical disorders, such as

schizophrenia (Vink et al., 2006; Zandbelt et al., 2011; Lesh et al., 2013). Further, it is important to note that although gamblers in the current study exhibited sound reactive and proactive control, they were significantly elevated on most domains of trait impulsivity, providing support for the idea that (1) high scores on self-report measures of impulsivity are not directly indicative of impaired motor control and (2) self-report and cognitive measures of impulsivity could be measuring different aspects of this behaviour (Moeller et al., 2001).

Furthermore, both gamblers and controls were able to use contextual cues in the task to guide their stopping behaviour, such that response time increased linearly as a function of higher stop signal probability. This finding suggests a flexible cognitive control system in both groups that is capable of applying proactive strategy adjustments based on changing task conditions, and that can attain a balance between competing goals (Verbruggen & Logan, 2008). Additionally, although these results should be considered preliminary, we hope this study will serve as a stepping stone for future research on subprocesses of response inhibition in other samples of gamblers, especially given the recent promise of response inhibition training in subclinical populations of gamblers, the elderly, and schizophrenia patients (Lesh et al., 2013, Stevens et al., 2015). Overall, however, the aforementioned findings should be interpreted with caution given the lack of comparative research on proactive control in the gambling literature. Given the emerging research in support of the dual mechanisms of control framework (Braver, 2012), additional studies are warranted to replicate these findings.

In sum, the pattern of findings suggest response inhibition may not be (1) central to the neuropsychological profile of gambling disorder, and (2) the main cause of detrimental impulsive or risky behaviour in gambling disorder. Alternatively, it may be that the SSAT is a sub-optimal assessment for detecting clinical differences of response inhibition in gambling

disorder. Nevertheless, these findings provide a more nuanced understanding of response inhibition in gambling disorder.

4.2 The Association between Trait impulsivity and Response Inhibition

The third aim of this study was to determine the predictive capacity of the five impulsivity facets of the UPPS-P on reactive and proactive control. Group differences were observed on all domains of the UPPS-P, except sensation seeking. Consistent with previous research, gamblers in the current study scored higher on the premeditation, perseverance, and positive urgency subscales (Savvidou et al., 2017). Contrastingly, controls displayed higher levels of negative urgency than gamblers. This latter finding is paradoxical, as studies have consistently reported heightened levels of negative urgency in gambling disorder (see meta-analysis by MacLaren et al., 2011). The sample characteristics of the current study (e.g., comorbidities in control sample, past gamblers in gambling group) may, in part, explain this result. Other possibilities for this finding may include response bias and/or the unusual lack of current depressive symptoms observed in the gambling sample.

To explore the relationship between trait impulsivity and response inhibition in community controls and individuals with gambling disorder, two separate regression analyses were conducted. In line with past studies, no relationship between reactive control and trait impulsivity was observed in the gambling group (Lorains et al., 2014; Lawrence et al., 2009b). Regarding proactive control, although neither of the overall regressions indicated a relationship with trait impulsivity, a significant association between premeditation and proactive control was found in the gambling group. This finding suggests proactive control is worse in gamblers who lack the ability to reflect on the consequences of an act prior to engagement.

Lack of premeditation has been strongly linked to gambling behaviour (Whiteside et al., 2001; Michalczuk et al., 2011; Blain et al., 2014), higher gambling severity (Haw, 2015), co-occurring mood disorders (Lister et al., 2015), and illicit substance use (Mitchell & Potenza, 2014). Based on the data from the current study, it seems that lack of premeditation is also significantly associated with lower levels of proactive control in gambling disorder. That is, gamblers who self-report difficulty planning out actions and anticipating consequences show a lower capacity to use informative contextual cues to prepare for inhibition (i.e. slowing responses for greater likelihood of a successful stop). As such, impairments in proactive control may be uniquely related to certain impulsive traits in individuals with gambling disorder. This finding not only adds to the understanding of the cognitive correlates of trait impulsivity, but also has practical relevance for treatment development. For example, the UPPS-P may possess utility as a screener used in clinical settings to develop more accurate profiles of treatment seeking gamblers. From the current findings, one might speculate that a gambler elevated on the premeditation subscale of the UPPS-P may benefit from cognitive remediation as part of their care (e.g., response inhibition training; see Verbruggen et al., 2012). More generally, clinicians may be able to distinguish between various subgroups of gamblers (e.g., high versus low premeditation) using measures of trait impulsivity, and then use this information to tailor the course of intervention accordingly.

Lastly, the unique association found between premeditation and proactive control fits well with the conceptual overlap of these two constructs, as both require some level of anticipation (either of a consequence or an interfering stimulus in the environment, respectively). Future studies are warranted to confirm this relationship. Nonetheless, despite an apparent association

between premeditation and proactive control, directionality and causation cannot be assumed from correlational analyses, and thus, this finding should be interpreted with caution.

4.3 Limitations and Future Directions

A number of limitations are acknowledged in this study. First, the sample size of the current study was modest, reducing the power of the statistical analyses. Therefore, the findings from this research should be considered preliminary and subject to replication. Future studies using larger sample sizes are required to elucidate the precise mechanisms of response inhibition in gambling disorder, especially given the general scarcity of cognitive studies of impulsivity in this population. Second, the sample size of the gambling group did not permit examination of the outcome variables with gamblers parsed based on preferred mode of gambling (e.g., strategic versus non-strategic), current gambling status, or comorbid conditions. Considering the heterogeneity of the gambling disorder population, it is recommended that future studies account for these within-group differences. This effort is important, as it may be the case that only some subgroups of gamblers are impaired on reactive and/or proactive control (e.g., strategy based gamblers may be less likely to demonstrate impulsive deficits sought in the current study), and as a result, may benefit from treatment targeting different areas of weakness. Third, the current study included controls with various comorbidities and brain injuries to preserve external validity. However, this may have attenuated effect sizes and convoluted interpretation of the results, which can be addressed by more stringent exclusion criteria for control groups in future studies. Fourth, the SSAT may be argued to lack a sufficient level of reward/punishment saliency to appropriately map onto gambling behaviour. Thus, prospective studies using stop-signal tasks with greater ecological validity may be superior in capturing the true essence of response inhibition deficits in gambling disorder.

Future studies should also explore whether the explicitness of the pre-cues that inform participants of stop-signal probability affect proactive control outcomes. Although no group differences in proactive control were detected through the SSAT, it is conceivable that differences may emerge with the presentation of more implicit pre-cues. Future research might also consider employing neuroimaging techniques to elucidate the neural correlates of reactive and proactive control, as differences in neural processes do not always manifest in the form of behavioural differences (Li et al., 2008).

4.4 Conclusion

The present study provides new information regarding the mechanisms of response inhibition in individuals diagnosed with gambling disorder. No group differences in reactive and proactive control were detected in this study, suggesting impaired response inhibition may not be a central feature of all individuals with gambling disorder. Interestingly, both controls and gamblers were able to successfully use the task cues to guide their stopping behaviour, such that reaction time slowed significantly as a function of higher stop signal probability. The modest sample size, as well as the sample characteristics of this study should be considered in interpretation of these results. Furthermore, there was exploratory evidence to suggest low levels of premeditation are associated with worse proactive control in gamblers, which supports a large body of studies that have reported unique relationships between self-reported and behavioural measures of impulsivity.

Despite a wide array of treatment options available for gambling disorder, including cognitive behavioural therapy, self-help groups (e.g. Gambler's Anonymous), and motivational interviewing, relapse rates in this population remain at a staggering 50-90% (Petry et al., 2006; Collier, 2008). In response, researchers have begun to recommend impulsivity-focused

approaches to treatment (e.g., MacKillop et al., 2014), given its relevance to gambling behaviours and outcomes. In order to determine which aspects of impulse control should be targeted in treatment, studies should continue to decompose impulsivity into lower-order components. To the authors' best knowledge, this study was the first to investigate proactive control in individuals with gambling disorder. Thus, there is a particular need for future studies to use variants of the stop-signal paradigm, which allow measurement of proactive control to determine whether this aspect of response inhibition is impaired in gambling disorder.

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Appendix

Table A.1

Unstandardized and Standardized Item Statistics for Regression Models

	Controls								Gamblers							
	Reactive Control				Proactive Control				Reactive Control				Proactive Control			
UPPS-P Scale	Unstd.	SE	Std.	*p*	Unstd.	SE	Std.	*p*	Unstd.	SE	Std.	*p*	Unstd.	SE	Std.	*p*
Negative Urg.	-7.93	14.92	-0.20	0.60	11.73	9.68	0.53	0.25	7.34	8.22	0.23	0.38	1.24	4.02	0.31	0.76
Premeditation	-16.66	15.10	-0.26	0.29	-6.35	9.80	-0.18	0.53	0.70	11.14	0.02	0.95	-12.48	5.44	-2.29	0.03
Perseverance	-25.37	15.59	-0.41	0.13	6.38	10.12	0.19	0.54	-2.32	8.62	-0.07	0.79	4.30	4.21	1.02	0.32
Sensation Seek.	-5.71	6.26	-0.22	0.38	4.12	4.06	0.29	0.33	-5.90	8.46	-0.18	0.49	0.69	4.14	0.17	0.87
Positive Urg.	-16.23	18.12	-0.30	0.39	17.79	11.76	0.60	0.15	10.68	11.32	0.27	0.36	3.73	5.53	0.67	0.51

Note. Unstd. = unstandardized regression weights; SE = standard error; Std. = standardized regression weights; Negative Urg. = Negative Urgency; Positive Urg. = Positive Urgency.

Table A.2
Correlations between HAM-D, PGSI, Proactive Control, and Reactive Control in Gamblers (n=27)

Variable	HAM-D	PGSI	Reactive Control	Proactive Control
HAM-D	-	0.10	0.01	-0.12
PGSI		-	0.05	-0.01
Reactive Control			-	0.11
Proactive Control				-

Note. HAM-D = Hamilton Depression Rating Scale; PGSI = Problem Gambling Severity Index.

Table A.3
Correlations between HAM-D, PGSI, Proactive Control, and Reactive Control in Controls (n=21)

Variable	HAM-D	PGSI	Reactive Control	Proactive Control
HAM-D	-	0.03	0.18	0.25
PGSI		-	0.08	0.17
Reactive Control			-	-0.03
Proactive Control				-

Note. HAM-D = Hamilton Depression Rating Scale; PGSI = Problem Gambling Severity Index.