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Short communication

# Cigarette smoking status in pathological gamblers: Association with impulsivity and cognitive flexibility

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ABSTRACT

*Background:* While the majority of pathological gamblers are current cigarette smokers (CS), some have quit smoking (former smokers, FS) while others never smoked (never smokers, NS). The reasons for elevated smoking rates in pathological gambling are not known, but gamblers may use nicotine as a putative cognitive enhancer. This study evaluated impulsivity and cognitive flexibility in a sample of pathological gamblers with differing smoking status.

*Methods:* Fifty-five subjects with pathological gambling (CS, $n = 34$; FS, $n = 10$; NS, $n = 11$) underwent cognitive assessments using the Stop-Signal (SST) and Intradimensional/Extra-dimensional (ID/ED) set-shift tasks.

*Results:* CS reported less severe gambling problems than either FS or NS on the Yale Brown Obsessive Compulsive Scale modified for Pathological Gambling, and CS was associated with significantly fewer directional errors on the SST task, compared to NS. In addition, in CS, higher daily cigarette consumption was associated with fewer total errors on the ID/ED task.

*Conclusions:* The potential role of nicotine as a cognitive enhancer was supported by objective tests of impulsivity and cognitive flexibility. Human laboratory studies using nicotine challenges in pathological gambling will shed further light on this relationship.



## 1. Introduction

Only recently has the comorbidity between cigarette smoking and pathological gambling been recognized, with as many as 60% of pathological gamblers (PG) also smoking (McGrath and Barrett, 2009). The reasons for this covariation are likely manifold. Nicotine causes increased expression of dopamine in brain reward centers, and may add to or even multiply the pleasurable effects of gambling. At the same time, gambling may enhance the enjoyment of cigarette smoking. Additionally, there are some 4000 chemical constituents in tobacco smoke, including inhibitors of the catabolic enzyme, monamine oxidaze (MAO) (Fowler et al., 2003; Hoffmann and Wynder, 1986). Inhibition of MAO, whose function is to decompose monoamine neurotransmitters (MN; e.g., dopamine), results in greater longevity and activity of MNs in the synapse. Blanco et al. (1996) found deficient MAO activity in individuals with pathological gambling. The possibility that PG use smoking to ameliorate MAO deficiencies remains to be confirmed.

Nicotine, the primary chemical responsible for smoking, has a diverse set of psychological effects, including on executive functioning. The role of nicotine as a cognitive enhancer has been controversial, but a recent review suggests that nicotine indeed yields improvements in mental functioning (e.g., attention and some forms of memory) that transcends mere withdrawal relief (Heishman et al., 2010). Yet the beneficial effects of nicotine are perhaps most apparent in those whose brains are not functioning optimally. For instance, nicotine has proven therapeutic in those with attention – deficit/hyperactivity disorder, schizophrenia, and Alzheimer's type dementia (Newhouse et al., 2004). Several studies have found that PG exhibit impaired performance on neurocognitive measures of response inhibition, including the domains of motor inhibition and delay discounting (van Holst et al., 2010). While a high proportion of PG currently smoke, a large percentage have either quit smoking or never smoked. In this report, we evaluate the association between cigarette smoking and two computerized tests of executive functioning; the Stop-Signal task (SST) and the Intradimensional/Extra-dimensional (ID/ED) set-shift task. Based on cognitive enhancing effects of nicotine, we hypothesized that PG who were current smokers would perform better than former- and non-smokers on tests of impulsivity and cognitive flexibility.

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## 2. Method

### 2.1. Participants

Data for the current analyses were pooled from one pharmacological trial previously completed ($n = 28$) (Grant et al., 2010), and two ongoing clinical trials using cognitive behavioral therapy ($n = 23$) and pharmacotherapy ($n = 4$) for the treatment of PG. The institutional review board for the University of Minnesota approved procedures. After review of the study procedures and having had the opportunity to ask questions, all subjects provided voluntary written informed consent. All studies were carried out with the standards of Good Clinical Practice and in accordance with the Declaration of Helsinki.

Men and women aged 18–75 with a primary diagnosis of DSM-IV PG were recruited by newspaper advertisements. All subjects met the DSM-IV criteria for PG with the clinician-administered Structured Clinical Interview for PG (SCI-PG, Grant et al., 2004). All subjects were required to have gambled within one week prior to enrollment. Eligible subjects were required to have a score of 15 or greater on the Yale Brown Obsessive Compulsive Scale Modified for PG (YBOCS-PG, Pallanti et al., 2005).

### 2.2. Procedures and measures

All observations were collected at baseline prior to any clinical intervention or experimental manipulation. CS were instructed to smoke according to their usual schedule, and were not abstinent or tobacco-deprived prior to or during testing. Under constant and controlled conditions, cognitive testing was conducted using two previously validated tests taken from CANTABeclipse software (Cambridge Cognition Limited, 2006). The Stop-Signal task was used to assess motor inhibition (i.e., impulsivity, Aron et al., 2004; Logan et al., 1984). On this test, subjects were instructed to respond to a left- or right-facing arrow which appeared on a computer screen in a rapid fashion. Corresponding motor responses were measured as were the subjects' ability to inhibit responses when an auditory "beep" (Stop-Signal) sound occurred on a subset of trials. Through an algorithm, the time taken to internally suppress prepotent motor responses was measured, i.e., Stop-Signal Reaction Times (SSRT). Key outcome variables were SSRT, mean reaction time on 'go' trials, and the total number of directional errors made. This task has been shown to be dependent on distributed neural circuitry including the right inferior frontal gyrus (Aron et al., 2004).

Aspects of cognitive flexibility relating to set-shifting were measured using the Intra-dimensional/Extra-dimensional Shift Task (ID/ED task), developed from the Wisconsin Card Sorting Test assessing frontal lobe integrity (Lezak et al., 2004). This test involved nine stages using multidimensional stimuli presented as a visual discrimination task. On the task, subjects were presented with two stimuli on-screen for each trial, and attempted to learn an underlying 'rule' about which stimulus was correct. After each choice, the task provided the subject with feedback (right/wrong). After meeting learning criterion (6 consecutive correct choices), the rule was changed by the computer, and the subject attempted to learn the new rule in order to maintain success. Key outcome variables were the number of errors made on the Intra-dimensional (ID) and Extradimensional (ED) stages of the task.

Smoking status and cigarettes smoked/day were determined based on self-report. General psychological function were assessed using the Clinical Global Impression-Improvement and Severity scales (CGI, Guy, 1976), the Perceived Stress Scale (PSS, Cohen et al., 1983), the Hamilton Anxiety Rating Scale (HAM-A, Hamilton, 1959), and the Hamilton Depression Rating Scale (HAM-D, Hamilton, 1960). Gambling urges and behavior were assayed with the Gambling Symptom Assessment Scale (G-SAS, Kim et al., 2009) and the PG-YBOCS (Pallanti et al., 2005).

### 2.3. Analyses

All analyses were conducted with the Statistical Analysis System Version 9.1.3. Values of $p < .05$ were considered statistically significant, based on two-tailed tests. The primary classification variable was smoking status (0 = never smoker [NS]; 1 = former smoker [FS]; and 2 = current smoker [CS]). Comparisons across smoking status were made using one-way ANOVAs and chi-square tests of independence. The relationship of smoking status and daily cigarette consumption to cognitive flexibility was tested with one-way ANOVAs and Pearson product-moment correlations.

## 3. Results

### 3.1. Sample characteristics

No differences in demographic variables were observed across smoking status. Of the 55 subjects (56.4% female), the mean age was $49.9 \pm 11.5$. The distribution of subjects in each group was NS ($n = 11$), FS ($n = 10$), and CS ($n = 34$). The majority of the sample was white (76.4%), unmarried (78.2%), and lacking at least a college education (61.8%). Current smokers smoked a mean $18.1 \pm 7.8$ cigarettes/day (56% smoked 1 pack/day or more). With respect to psychiatric history and symptoms, the sample was largely homogenous: psychiatric history (family, 94.4%, personal 72.7%); history of alcohol or drug dependence (38.2%); HAM-D, $7.2 \pm 4.6$; HAM-A, $6.6 \pm 4.0$; and PSS, $21.6 \pm 7.0$. The one exception was the CGI where CS gamblers rated themselves to be significantly less impaired ($4.4 \pm 0.6$) than either NS gamblers ($5.0 \pm 1.0$) or FS gamblers ($5.2 \pm 0.8$), $F(2, 52) = 6.91$, $p = 0.0022$. Concerning gambling history, the mean age of onset of pathological gambling was $38.5 \pm 11.2$ and did not differ significantly between groups. While all groups had equivalent G-SAS scores ($32.0 \pm 6.4$), CS gamblers rated the severity of their gambling problems to be significantly less ($23.0 \pm 7.1$) than either NS gamblers ($28.2 \pm 2.2$) or FS gamblers ($28.5 \pm 6.8$), $F(2, 52) = 3.48$, $p = 0.0381$.

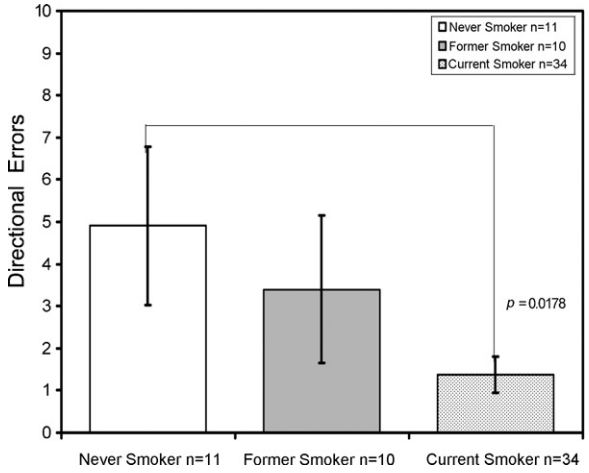


**Fig. 1.** Relationship between directional errors on the Stop-Signal Task and smoking status in pathological gamblers. Current smokers tended to make fewer error that either non-smoking group.

### 3.2. Cognitive testing

*3.2.1. Stop-Signal task.* Smoking status was significantly associated with performance on the SST, $F(2, 50) = 3.30$, $p = 0.0449$ (see Fig. 1). CS gamblers made fewer directional errors than NS gamblers, $t(44) = 2.45$, $p = 0.0178$. Among CS gamblers, no associations were observed between cigarettes smoked each day and directional errors.

*3.2.2. ID/ED task.* Smoking status was not related to any ID/ED parameter. Total errors, however, were inversely related to cigarettes smoked each day, $r(31) = -0.49$, $p = .0048$ (see Fig. 2)

## 4. Discussion

This is the first study to assess the association between smoking and cognitive function in PG. The key finding was that smoking was associated with greater inhibitory control and while smokers did not differ from non-smokers on a measure of cognitive flexibility, among smokers, greater tobacco consumption was associated with greater cognitive flexibility.

Stop-Signal performance is dependent on a right lateralized fronto-striatal neural network including the right inferior frontal and bilateral anterior cingulate cortices (Aron et al., 2004). Multiple neuroimaging studies indicate that inhibitory control activates these regions (Hampshire et al., 2010). One interpretation of these findings suggests that because nicotine self-administration improves Stop-Signal inhibitory control, gamblers may smoke to deal with their impulsivity. At the same time, improved execu-