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Inhibitory control dysfunction in nicotine dependence and the influence of short-term abstinence

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ABSTRACT

Background: Although the majority of substance use disorders depict reliable deficits in inhibitory control (IC), similar deficits are not consistently found in nicotine dependence. The mixed results of past research may have been due to confounding variables known to independently influence IC function, including age, concurrent drug use and particularly, length of nicotine abstinence.
Methods: A stop signal task was used to examine stop signal reaction time (SSRT), a typical measure of IC, in nicotine dependence across two studies that attempted to closely control for IC confounds. Study 1 compared the SSRT of 37 dependent cigarette smokers (11 females) to 36 non-smokers (13 females), following 3-h of nicotine abstinence. Study 2 compared 22 dependent cigarette smokers' (11 females) SSRT scores when satiated on nicotine to their performance following 10-h of nicotine abstinence.
Results: Nicotine dependent individuals did not differ from controls in SSRT performance following 3-h abstinence, but showed a significant decline in performance following 10-h abstinence, when compared to nicotine satiation.
Conclusions: During shorter abstinence periods, the acute benefits of nicotine satiation appear to facilitate inhibitory control; however, IC was poorer during extended periods of nicotine abstinence. In turn, this suggests that the reliability of IC dysfunction in nicotine dependence varies according to abstinence length and needs to be carefully considered for future behavioural and neuroimaging examination of IC within this population.

1. Introduction

Current models of substance dependence suggest that deficits in executive control are critical to ongoing drug use (Jentsch and Taylor, 1999). In particular, inhibitory control (IC), which is the ability to inhibit a pre-potent response, may be especially involved in maintaining drug dependence (Goldstein and Volkow, 2002; Lubman et al., 2004). IC impairment is prevalent within varying forms of drug-dependence, including alcohol, methamphetamine and cocaine dependence (Fillmore and Rush, 2002; Li et al., 2009; Lubman et al., 2004; Monterosso et al., 2005). The reliability of IC dysfunction in individuals dependent on substances with widely differing neurochemical profiles suggests IC dysfunction is a common feature of addiction and would therefore feature similarly in nicotine dependence.

Research examining IC performance in nicotine dependence has to date yielded a varied set of findings. Nicotine dependent individuals demonstrate impaired performance on measures of impulsivity, such as delay discounting tasks, in which smaller immediate monetary rewards are favoured over larger but delayed rewards (Bickel et al., 1999; Mitchell, 1999; Reynolds et al., 2004); and risky financial decision making, in which potentially higher pay-offs are chosen while accepting the increased risk of losing everything (Lejuez et al., 2003). For example, Yakir et al. (2007) reported a selective deficit in impulsivity within both current and past smokers when compared to controls. However, studies measuring IC over a pre-potent motor response using the Go/No-go and stop signal tasks (Dinn et al., 2004; Spinella, 2002; Yakir et al., 2007) have not reliably demonstrated IC impairment in comparison to control populations. For example, Spinella (2002) found that IC performance on a Go/No-go task was negatively correlated with smoking behaviour, where levels of IC deficit were proportional to smoking severity. In contrast, Dinn et al. (2004) also administered the Go/No-go task and found no difference in performance between smokers and non-smokers.

The mixed findings of past research may be due to factors that independently affect IC function. Demographic variables that influence IC, such as age (Kramer et al., 1994) have not always been

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controlled. For example, Spinella's (2002) sample varied in cigarette use (levels not reported in the paper) and age (range = 19–70 years, mean = 31.1 SD = 16.7), with the latter variable not used as a covariate in the correlation between nicotine use and IC performance. Similarly, because most of these studies have recruited college or community samples, they have not always screened for IC confounds such as history of traumatic brain injury (Dimoska-Di Marco et al., 2011) or other types of drug abuse (Fillmore and Rush, 2002; Li et al., 2009; Monterosso et al., 2005).

IC performance also appears sensitive to variation in the duration of nicotine abstinence prior to cognitive testing. In other dependent populations, administration of a drug of dependence (e.g., cocaine or heroin) reduces levels of IC deficit otherwise present in dependent individuals, with short-term abstinence inducing the opposite effect (Goldstein and Volkow, 2011). In parallel to these findings, acute nicotine administration reverses otherwise prevalent IC deficits in ADHD (Potter and Newhouse, 2004) and abstinence from cigarettes in an otherwise healthy population has been associated with decreased IC performance (Harrison et al., 2009). As such, satiated smokers may have acutely elevated IC performance that masks underlying IC deficits (Dawkins et al., 2007). However the influence of nicotine abstinence on the presence/absence of IC deficits in past studies remains unclear, as few have approached abstinence as an independent factor interacting with IC ability.

Given the small number of studies and mixed findings, the aim of the present study was to examine IC function in nicotine dependence whilst controlling for demographic and drug use confounds. To examine the influence of nicotine abstinence on IC dysfunction we also conducted a within-subject comparison between nicotine satiation and short-term, 10-h abstinence.

Study 1 compared a group of dependent smokers to a control group of non-smokers on IC performance using a stop signal task (Logan et al., 1997). To limit acute effects of nicotine, dependent smokers completed the SST following 3-h of nicotine abstinence. It was hypothesised that after controlling for variables that had confounded previous studies (demographics, other drug use, brain injury), nicotine dependence would be associated with poorer IC in comparison to controls, indicated by higher stop signal reaction time (SSRT). Study 2 examined the influence of nicotine abstinence on IC performance by comparing dependent nicotine smokers' SSRT after a 10-h period of abstinence to performance at nicotine satiation. It was hypothesised that in dependent smokers inhibitory performance would be significantly poorer following prolonged nicotine abstinence than at satiation.

2. Methods

2.1. Study 1

Participants: 37 dependent cigarette smokers (11 females; mean age 23.70; SD = 4.32) and 36 non-smokers (13 females; mean age 23.14; SD = 4.85) were recruited for the study. Inclusion in the smokers group required smoking 15 or more cigarettes a day for a minimum of two years. Non-smoking participants had each consumed less than 10 cigarettes in their lifetime. Exclusion criteria for both groups included a history of neurological or psychiatric disorders, current use of psychotropic medication or any medication known to affect heart rate or respiration, and current substance abuse or dependence (other than nicotine for the smoking group). The groups did not significantly differ on the variables of age, education or gender (see Table 1). Participants were recruited via advertisements at the University of Melbourne. All provided written informed consent prior to participation, approved by the human ethics committee at the University of Melbourne.

Table 1
Mean demographic and questionnaire data for smoking and non-smoking groups.

Questionnaire variables	Smokers	Non smokers
Age	23.70	23.14
Gender (male/female)	26/11	23/13
Years of education	14.81	15.25
No. of Cigarettes (per day)	16.86**	0
CO levels (ppm)	7.59	–
AUDIT	12.84**	4.67
DAST	2.46**	.39
FTND	3.73**	0

Note: CO levels = carbon monoxide levels measures in parts per million (ppm).
** $p < 001$, refers to corresponding independent samples *t*-test.

To limit both acute and withdrawal effects of nicotine, maximum time since participants' last cigarette at task completion was limited to 3-h by instructing participants to consume their last cigarette 2-h prior to testing. All participants were also asked to abstain from illicit drug use for 48-h prior to testing and not consume alcohol or caffeine for 10 or 1 h, respectively, prior to participation.

Measures: Non-nicotine drug use behaviour was measured using the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993) and the Drug Abuse Screening Test (DAST; Skinner, 1982). Smokers' breath carbon monoxide (CO) concentrations were monitored using a calibrated Micro + Smokerlyzer (Bedfont Scientific Ltd., Rochester, UK). In addition, smokers completed the Fagerström test for nicotine dependence (FTND; Heatherton et al., 1991) to measure nicotine dependence. Mean values for each measure are displayed in Table 1.

Stop signal task: Participants performed 300 trials of the stop-signal paradigm, in which the go-stimuli were the letters O and X mapped to corresponding button press responses, respectively. The stop-signal was a red box that surrounded the go-stimulus on 25% of trials. The delay between the onset of the go-stimulus and the onset of the stop-signal (stop-signal delay, SSD) was initially set to 250 ms and was thereafter adjusted dynamically in increments of 50 ms contingent upon the performance of the participant. Successful inhibitions resulted in an increase of the SSD, making inhibition more challenging on the following trial, whereas failed inhibitions resulted in a reduction of the SSD, thereby facilitating inhibitory success. This procedure ensured that on average each participant in each session had a probability of successful inhibition approaching 50%. Stop-signal reaction time (SSRT) was derived as the mean reaction time to go-stimuli (MRT) minus the SSD for the 50% inhibition threshold (SSRT = MRT − SSD) (Logan et al., 1997). This measure corresponds to inhibition latency, whereby higher SSRTs indicate poorer inhibition abilities. Participants with stop accuracy below 40% or above 60% were removed from the analysis, in accordance with the conservative criteria of Congdon et al. (2012).

Upon arrival, all participants completed the questionnaires and their expired CO levels were measured to confirm patterns of cigarette use. Following this, they undertook the SST.

Results: Smokers and non-smokers differed on measures of dependence and cigarette consumption, with smokers scoring significantly higher than non-smokers on number of cigarette's consumed per day ($t(36) = -34.94$, $p < .01$) and level of nicotine dependence ($t(36) = -10.92$, $p < .01$), following adjustment for unequal variance. Descriptive statistics for both groups are provided in Table 1.

SST performance did not differ between groups for SSRT ($t(71) = .40$, $p = .69$, $d = .08$) go trial RT ($t(71) = .06$, $p = .96$, $d = .02$) or stop trial accuracy ($t(71) = -.11$, $p = .92$, $d = .03$). The descriptive statistics for SST performance for both groups are reported in Table 2. There was no significant effect of gender on SSRT in either group $F(1) = .13$, $p = .72$.