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Comparison of the Effectiveness of Conners' CPT and the CPT-Identical Pairs at Distinguishing Between Smokers and Nonsmokers with Schizophrenia

Michelle Roth^a, L. Elliot Hong^b, Robert P. McMahon^c, and Rebecca L. Fuller^d

^aDepartment of Psychology, The Catholic University of America, 620 Michigan Avenue, NE, Washington, DC, 20064 USA, rothmica@gmail.com ^bMaryland Psychiatric Research Center, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland, 21228 USA, ehong@mprc.umaryland.edu ^cMaryland Psychiatric Research Center, Department of Psychiatry, University of Maryland School of Medicine, PO Box 21247, Baltimore, Maryland, 21228 USA, rmcmahon@mprc.umaryland.edu ^dDepartment of Psychology, The Catholic University of America, 620 Michigan Avenue, NE, Washington, DC, 20064 USA, fuller@cua.edu

Abstract

Sustained attention deficits and high rates of smoking are often observed in patients with schizophrenia. This has led to the hypothesis that patients may smoke as an attempt to ameliorate cognitive deficits related to abnormal nicotinic structure and function. Continuous performance tasks (CPT) are often used to index sustained attention deficits in patients with schizophrenia, however, there are important differences between tasks that may impact performance in smokers and nonsmokers with schizophrenia differently. The Conners' CPT (CCPT) has a high signal-to-noise ratio and is commonly used to assess impulsivity. The CPT-Identical Pairs (CPT-IP) has a low signal-to-noise ratio and is commonly used to assess negative symptoms in patients with schizophrenia. We sought to determine whether there were differences of sustained attention between patient smokers vs. nonsmokers, and if one CPT would provide a better separation of sustained attention between groups. Results revealed that both instruments detect more impaired sustained attention deficits in patient smokers compared to nonsmokers. Patient smokers performed significantly worse on the majority of the CPT-IP composite scores compared to the C-CPT composite scores. These results do not support the self-medication theory, as patient smokers performed worse than patient nonsmokers. Researchers studying sustained attention in schizophrenia may wish to consider the CPT-IP over the C-CPT, as well as control for smoking status.

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Corresponding author: Michelle Roth, 252 O'Boyle Hall, The Catholic University of America, 620 Michigan Avenue, NE, Washington, DC, 20064. Phone: 1-202-355-4410. rothmica@gmail.com.

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Conflict of Interest

There are no conflicts of interest to report for any of the authors.

Contributors

Michelle Roth conducted statistical analysis, interpreted results, and wrote the manuscript. L. Elliott Hong designed the study, wrote the protocol, and assisted with manuscript preparation. Robert P. McMahon provided oversight for statistical analyses and assisted in manuscript preparation. Rebecca L. Fuller assisted with methodology, interpreting the results and manuscript preparation. All authors contributed to and have approved the final manuscript.

Keywords

schizophrenia; nicotine; sustained attention; Continuous Performance Tasks

1. Introduction

People with schizophrenia (herein referred to as patients) have among the highest rates of smoking in the general population (D'Souza & Markou, 2012; Smith et al., 2006). This observation has led to the widely-discussed hypothesis that the high rates of smoking in patients indicate an attempt at self-medication to correct or transiently improve several of the cognitive deficits related to abnormal nicotinic structure and function (Segarra et al., 2011). This hypothesis would imply that there may be differences in the mechanisms responsible for cognitive functioning between patient smokers and nonsmokers that could provide information about this aspect of the heterogeneity of the schizophrenia syndrome. Demonstration of differences between these two groups, however, would depend upon a number of factors including the pre-smoking degree of impairment, down-regulation of receptors that mediate nicotine effects, and the type of cognitive functions involved.

Among the cognitive functions impaired in schizophrenia, sustained attention is one of the most robust and commonly replicated (Cornblatt et al., 1988; Hong et al., 2011, 2009), and is also closely related to the nicotinic acetylcholine receptors (nAChR) in the central nervous system (Dyer et al., 2008). To measure deficits in a particular type of cognitive operation such as sustained attention, it is obviously important to employ tasks that are optimally sensitive. However, few such evaluations have been performed in the schizophrenia-smoking literature. In this study, we compare two commonly used paradigms that have been used to index sustained attention in patients with psychotic disorders and other mental illness.

1.1. Measurement of Sustained Attention: Continuous Performance Tasks

Sustained attention is an instrumental assessment. The Conner's CPT (C-CPT; Conners, 2002) and CPT-Identical Pairs (CPT-IP; Cornblatt et al., 1988) are two sustained attention tasks that have commonly been used to examine nicotine or smoking effects. In the C-CPT, the participant must press the space bar key as quickly as possible when a target stimulus (any letter except "X") is presented on the screen (a "hit"), and refrain from responding when the non-target stimulus (the letter "X") is presented. The C-CPT has a high signal-to-noise ratio (d'); the target stimulus (signal) occurs 90% of the time, and a non-target stimulus (noise) occurs 10% of the time. Thus, the participant must inhibit the tendency to press a key when the non-target stimulus is displayed. This feature allows C-CPT to be efficacious for identifying and assessing impulsivity and is sensitive to errors of commission. The C-CPT has been found to be effective at distinguishing attention disorders in children and adults (Barkley et al., 1996; Levin et al., 1998).

In comparison, the CPT-IP instructs the participant to respond by pressing a key when two identical stimuli are presented in sequence (the target), and refrain from responding when the 2nd stimulus does not match the preceding stimulus. Thus, the participant must process and hold in working memory the first stimulus long enough to compare it to the next stimulus. As such, the CPT-IP carries a working memory load and is considered more demanding than the C-CPT. The three blocks of 150 trials are presented with increasing cognitive load, in which the first block contains two-digit targets, the second block three-digit targets, and the third block four-digit targets. In contrast to the C-CPT, the CPT-IP has a *lower* signal-to noise ratio (d'); target stimulus-pairs (signal) occur 20% of the time, and the non-target stimulus-pairs (noise) occur 80% of the time.

1.2. Previous Findings of Sustained Attention and Nicotine Effects in the Patient Population

The nuances between the C-CPT and CPT-IP may lead researchers to different conclusions about sustained attention deficits and the effects of nicotine on components of sustained attention in the patient population. Previous studies have looked at different combinations of smokers, nonsmokers, patients, and healthy controls when examining the effects of nicotine on sustained attention in schizophrenia. Smith et al. (2006) found that a nicotine nasal spray significantly decreased C-CPT hit reaction time in 12-hour nicotine-deprived patient smokers. Sacco et al., (2005) found nicotine reversed the effects of overnight smoking abstinence on C-CPT hit rate impairments but not reaction time in patient smokers and healthy control smokers; Levin et al., (1996) found nicotine administration significantly improved C-CPT hit reaction time standard error in 8/hr nicotine-deprived patient smokers. Hahn et al. (2012), found no differences between non-deprived patient smokers and patient nonsmokers on the CPT-IP. Wing et al., (2010), found patient nonsmokers had significantly lower hit rates on C-CPT, compared to non-deprived patient smokers and patient former-smokers. Employing the CPT-IP, Barr et al. (2008) found that nicotine administration significantly decreased hit reaction time, hit reaction time standard deviation, and errors of commission, but not hit rate in patient and control nonsmokers. Depatie et al. (2002) compared 9.5/hour nicotine deprived patient smokers to healthy control smokers and found nicotine significantly improved CPT-IP hit rate and d' .

Both Connor's CPT and CPT-IP are sensitive to nicotine or smoking, but may be different considering psychopathology. Researchers have examined the effects of nicotine on sustained attention in patients by comparing patient smokers to healthy control smokers (Depatie et al. 2002; Sacco et al., 2005) or patient nonsmokers to healthy control nonsmokers (Barr et al., 2008). Other studies have looked at only patient smokers (Smith et al., 2006; Levin et al., 1996), or patient nonsmokers (Dyer et al., 2008). Only two studies to date (to our knowledge) has looked at both patient smokers and patient nonsmokers on measures of sustained attention (Hahn et al., 2012; Wing et al., 2011). Additionally, there is no standard instrument for measuring sustained attention, with some studies employing the C-CPT (Smith et al., 2006; Sacco et al., 2005; Levin et al., 1996), and others employing the CPT-IP (Barr et al., 2008; Depatie et al., 2002; Dyer et al., 2008). To our knowledge, no studies to date have directly compared Connor's CPT vs. CPT-IP between patient smokers and patient nonsmokers.

1.3. The Present Study

The purpose of the present study was to test whether there were overall differences between patient smokers and nonsmokers on sustained attention, and if one task, the C-CPT or CPT-IP, might better capture sustained attention deficits in patient smokers and patient nonsmokers. We hypothesized that if the self-medication theory holds true, patient smokers may perform better on sustained attention tasks compared to nonsmokers. We also reasoned that the CPT-IP, which was created for measuring sustained attention with a working memory demand specifically for differentiating schizophrenia and healthy controls (Cornblatt et al., 1988), would be more sensitive and therefore more effective in distinguishing sustained attention differences compared to the C-CPT, which was developed to be sensitive to impulsivity. Because the C-CPT and CPT-IP have comparable composite measures (i.e., d' , hit rate, hit rate response time, hit rate response time standard deviation, and errors of commission) we hypothesized that the composite scores of the CPT-IP, when compared to the C-CPT, would be significantly better at distinguishing patient smokers from patient nonsmokers.

2. Material and methods

2.1. Participants

All participants (N= 53, mean age 40.58, range 19–55) were outpatients identified as having schizophrenia or schizoaffective disorder, received antipsychotic medication, and were clinically stable for 4 weeks or longer. Two patients received first generation antipsychotics; the remainder received second generation antipsychotics. Participants were either current smokers (n=31), defined as smoking any amount of cigarettes every day for a year, or nonsmokers (n= 22) who had never smoked (< than 100 cigarettes smoked in lifetime) or had not smoked within the past year. Patients undergoing smoking cessation therapy were excluded, as were patients with major medical conditions, atrioventricular block identified on an electrocardiogram, and/or renal insufficiency.

2.2. Procedure

All participants gave informed consent which was approved by the University of Maryland institutional review board. Following consent, each participant completed a semi-structured interview and answered clinical and demographic information, and CO measurement was collected (not timed to the last cigarette). Participants then completed the C-CPT and CPT-IP. Patient smokers were allowed to smoke ad libitum no less than 30 minutes before each CPT testing to avoid peak nicotine level from last cigarette, but also to avoid early withdrawal symptoms from prolonged abstinence. Study duration was approximately 2-hours.

2.3. Assessments

2.3.1. Clinical—The Brief Psychiatric Rating Scale, BPRS, (Overall & Gorham, 1962) was the primary measure used to assess diagnosis related symptoms. Negative symptoms were assessed with the Schedule for Negative Symptoms, (SANS; Andreasen, 1984); patients' overall level of functioning was assessed with the Global Assessment of Functioning Scale, (GAF; Endicott et al., 1976). The Hamilton Scale for Depression, (HAMD; Hamilton, 1960), was used to assess patients for depression.

2.3.2. Smoking Status—The number of cigarettes smoked per day (CPD) was the primary measure to establish smoking status. Smokers were considered those who indicated smoking any amount of cigarettes a day for the last year or longer. The end-expired carbon monoxide level (COLevel) was collected from smokers only as a means to approximate validation of the CPD measure. Patient smokers were allowed to smoke if desired no less than 30 minutes before each CPT testing. The 1 hr to 30 minute smoking window was to avoid peak nicotine level from last cigarette, but also to avoid early withdrawal sx from prolonged abstinence

2.3.3. Neuropsychological—Sustained attention was assessed with both the C-CPT and CPT-IP. Composite measures included: discriminative power (d'): the difference between the signal and noise distributions, a higher number indicates a better ability to detect the signal from noise; hit rate: the amount of correct signal detections; hit reaction time: milliseconds to have correct response; hit reaction time standard deviation; the average variation in hit reaction time; commission errors: errors made to non-targets, a measure of impulsivity; and omission errors: individual's response tendency to avoid errors of commission

2.4. Statistical Analysis

One-way analysis of variance (ANOVA) was used to assess the differences between smokers and nonsmokers. Alpha was established at 0.05. The CPT-IP was analyzed in two ways: 1) as a composite of the three blocks of 150 trials; and 2) using only the third, and most difficult block (CPT-IP-3). Cohen's effect size (d) were computed for all t-tests and evaluated with suggested norms for effect size: small = 0.20; medium = 0.50; large = 0.80. The Spearman rank correlation was limited to composite scores that showed significant smoking status effects.

3. Results

3.1. Demographic and Clinical Variables

The two groups were similar in terms of sex and age ($p = .770$) (Table 1). There were no differences in BPRS total symptom score ($p = .968$) negative symptoms ($p = .205$), nor depression ($p = .363$) between the schizophrenia smokers and schizophrenia nonsmokers. Smoking related measures are shown in Table 1. The average number of cigarettes smoked per day (CPD) of the smokers was 17 (SD=13.11; Range= 1–40), and their average end-expired carbon monoxide level (COLevel) was 17.58 (SD= 10.70; Range= 0–37).

3.2. Neuropsychological Performance

Neuropsychological task performance was compared between schizophrenic smokers ($n=31$) and schizophrenic nonsmokers ($n= 22$), (Table 2). The data were analyzed using one-way ANOVAs for smoking status. Inspection of Table 2 indicates that patients perform similarly on the CPT-IP as averaged across blocks and on the third block only. As such, the third block of the CPT-IP is considered as the primary measure of sustained attention on the CPT-IP.

Performance was significantly impaired in schizophrenia smokers on the majority of the CPT-IP-3 composite scores compared to schizophrenia nonsmokers. Of the six composite measures, four were significant with large or medium effect sizes: d' ($F(1,52)= 7.63, p < .01, \eta^2 = .14$), Hit Rate ($F(1,52)= 7.71, p < .01, \eta^2 = .19$), Hit Rate Reaction Time Standard Deviation ($F(1,52)= 8.35, p < .01, \eta^2 = .09$) and Random Errors ($F(1,52)= 6.20, p < .05, \eta^2 = .09$). CPT-IP composite scores that failed to reach significance included: False Alarms ($F(1,52)= .032, p > .05$), and Response Time ($F(1,52)= .21, p > .05$).

For C-CPT, only one of the six composite scores was significantly different between the two groups. Commission errors, the tendency for a participant to respond incorrectly, was significantly more common in schizophrenia smokers compared to schizophrenia nonsmokers, and showed a medium effect size ($F(1, 52)= 4.96, p = .030, \eta^2 = .09$). The remaining C-CPT composite measures failed to reach significance: d' ($F(1, 52)= 2.54, p = .117$), Hit Rate ($F(1, 52)= .84, p = .364$), Hit Response Time ($F(1, 52)= .72, p = .40$), and Response Time SD ($F(1, 52)= 1.29, p = .261$).

4. Discussion

Our comparative study of two sustained attention assessment instruments, the C-CPT and the CPT-IP, revealed that both tasks detect more impaired sustained attention in patient smokers compared to nonsmokers, although the CPT-IP was more sensitive for detecting group differences in sustained attention in this context. The CPT-IP features a progressive cognitive load across blocks which taxes working memory, where the C-CPT maintains the same difficulty level throughout blocks and does not tax working memory. However, these between task nuances do not explain the underlying mechanisms contributing to group

differences between patient smokers and nonsmokers. For example, Hahn et al. (2012), did not find differences between patient smokers and nonsmokers on the CPT-IP, however, the majority (83%) of participants were inpatient. As such, there may also be differences between inpatient and outpatient status of nicotine effects on sustained attention. Clinical and demographic measures did not differ between the two groups, so our findings are not due to significant differences in these measures between the two groups. We also correlated COLevel before cognitive testing and the sustained attention measures that showed significant differences between smokers and nonsmokers, and found COLevel was not significantly correlated with any of the sustained attention composite scores. These findings suggest that the worsened sustained attention in smokers is not related to the recency of smoking. Our finding of more severe deficits of sustained attention in patient smokers does not support the self-medication theory, at least at its face value. The self-medication theory would predict that smokers to have improved sustained attention, because these smokers are not smoking-deprived (COLevel = 17). However, patient smokers may have worse sustained attention even before they become smokers, a possibility our study was not designed to refute or support.

The interpretation of the results in the current study is constrained by several limitations. First, patients who indicated smoking any amount of cigarettes every day for at least a year were considered smokers. As such, the range of cigarettes smoked per day ranged from 1 to 40. There may be differences of sustained attention when assessed on a light to heavy smoking continuum. Additionally, former smokers were entered as nonsmokers. It may be that former patient smokers behave more like patient smokers on measures of sustained attention; however, our design did not distinguish between former and never smokers. Additionally, we did not ask nor record the timing of the last cigarette smoked by patient smokers. Patient smokers were allowed to smoke ad libitum no sooner than 30 minutes before each CPT testing. Thus, to further control for smoking recency effects, it may have been beneficial to record COLevels before each CPT testing as well as upon arrival. Demographic information such as education level was not collected, and it may have been to correlate education status with performance on the attentional levels. Lastly, statistical interpretation may be compromised by the increased risk of making a Type 1 error due to performing 18 one-way ANOVAs as we did not correct for multiple comparisons.

In summary, there has been a considerable amount of study dedicated to understanding the neuropsychological functioning of the schizophrenic population (Hong et al., 2011; Barr et al., 2008). There may be pre-existing differences in nAChR between patient smokers and nonsmokers that account for differences in neuropsychological functioning. To our knowledge, this is the first direct evidence that sustained attention deficits may be more impaired in outpatient smokers compared to outpatient nonsmokers. The present study is also the first to concurrently compare the ability of the C-CPT to the CPT-IP to distinguish between smokers and nonsmokers with schizophrenia. Our results suggest that the CPT-IP is a more sensitive tool for this purpose. These differences may be important for researchers studying neuropsychological functioning in schizophrenia when selecting assessment instruments. Controlling for smoking status may also be warranted.

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Table 1

Descriptives and Results of Clinical Baseline Measures

Measure	Non-smoking N= 22 Mean (sd)	Smoking N= 31 Mean (sd)	F	Sig
Gender (% male)	14 males (64%)	22 males (71%)	X2 = .03	.874
Age	41.09 (9.71)	40.23 (11.13)	.09	.770
CPD ^a	-	17.00 (13.11)	-	-
CoLevel	-	17.58 (10.70)	-	-
SANS ^b	20.23 (9.50)	24.48 (13.30)	1.65	.205
GAF ^c	49.77(10.01)	47.58 (9.74)	.63	.430
BPRS ^d	57.17 (27.80)	47.44 (21.07)	.02	.968
HAMD ^e	6.05 (3.82)	5.10(3.62)	.84	.363

^aCPD= Cigarettes per Day

^bSANS= Schedule for Negative Symptoms

^cGAF= Global Assessment of Functioning Scale

^dBPRS= The Brief Psychiatric Rating Scale

^eHAMD= The Hamilton Scale for Depression

Table 2

Descriptives and ANOVA Results of Patient Smokers vs. Patient Nonsmokers on the C-CPT^a, CPT-IP^b, and CPT-IP 3^c

Measure		Non-smoking Mean (sd)	Smoking Mean (sd)	F	p-value	d
d'						
	C-CPT	1.02 (.44)	.82 (.46)	2.54	.117	.501
	CPT-IP	2.39 (.74)	1.89 (1.01)	3.97	.052	.677
	CPT-IP 3	1.53 (.81)	.93 (.76)	7.63	.008	.817
Hit Rate						
	C-CPT	312.50 (15.64) 97%	307.35 (22.78) 95%	.84	.364	.670
	CPT-IP	24.21 (4.89) 81%	20.75 (6.32) 69%	4.62	.036	.790
	CPT-IP 3	22.36 (5.70) 75%	17.61 (6.43) 59%	7.71	.008	.966
Hit Response Time						
	C-CPT	435.98 (119.75)	463.53 (113.68)	.72	.399	.168
	CPT-IP	535.11 (64.55)	547.73 (96.43)	.29	.596	.238
	CPT-IP 3	541.58 (78.85)	554.21 (111.35)	.21	.650	.000
Hit Response Time SD						
	C-CPT	9.11 (4.72)	12.19 (7.74)	2.74	.104	.403
	CPT-IP	129.52 (26.99)	164.20 (48.30)	9.25	.004	.725
	CPT-IP 3	127.78 (35.76)	171.37 (69.07)	7.34	.009	.094
Commission Errors						
	C-CPT	8.91 (5.14)	12.77 (6.89)	4.96	.030	.089
	CPT-IP	4.09 (2.71)	4.80 (3.83)	.55	.462	.006
	CPT-IP 3	8.05 (5.18)	8.29 (5.76)	.032	.860	.001
Response Style/ Randoms						
	C-CPT	1.46 (1.52)	1.04 (1.14)	1.29	.261	.033
	CPT-IP	1.56 (2.07)	4.59 (4.58)	8.37	.006	.126
	CPT-IP 3	2.14 (3.71)	6.74 (8.08)	6.20	.016	.093

Bolded items indicate significant differences between patient smokers and patient nonsmokers.

^aC-CPT= Conners' Continuous Performance Task

^bCPT-IP= Continuous Performance Task- Identical Pairs

^cCPT-IP 3= Third, and most difficult, block of the Continuous Performance Task- Identical Pairs

Table 3
Correlations Between CPD^a, COLevel, COLevel & Significant C-CPT^b and CPT-IP 3^c Measures

	CPD	d' CPT-IP 3	Hit Rate CPT-IP 3	Hit Rate SD CPT-IP 3	Commission Errors C-CPT	Random Errors CPT-IP 3
COLevel (n=31)	r= .61 p= .000	r= -.13 p= .477	r= .19 p= .494	r= .14 p= .444	r= -.00 p= .996	r= -.29 p= .112
d' CPT-IP 3	-		r= .70 p= .000	r= -.31 p= .024	r= -.30 p= .031	r= -.54 p= .000
Hit Rate CPT-IP 3			-	r= -.39 p= .004	r= -.25 p= .075	r= -.37 p= .007
Hit Rate SD CPT-IP 3					r= .24 p= .088	r= .59 p= .000
Commission Errors C-CPT						r= .24 p= .084

Bolded items reflect significant correlations

^aCPD= Cigarettes per Day.

^bC-CPT= Conners' Continuous Performance Task

^cCPT-IP 3= Third, and most difficult, block of the Continuous Performance Task- Identical Pairs