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Carry-over effects of smoking cue exposure on working memory performance

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The present study investigated the effects of drug cue exposure on working memory performance in cigarette smokers. Adult smokers ($N=23$) deprived for 12 hr performed a working memory task during which they were exposed to three types of task-irrelevant stimuli: Pictures containing smoking related-content, pictures devoid of smoking content, and a fixation cross. Consistent with prior research, we found that drug cue exposure affected the processing of subsequent items (i.e., carry-over effects). Specifically, we found that working memory performance was worse on trials containing neutral pictures preceded by trials containing smoking cues compared with performance on trials containing neutral pictures preceded by trials not containing smoking-related stimuli. Previously observed effects of smoking cue exposure on cognitive processing were replicated but only after removing trials subject to carry-over effects. These results replicate and extend previous research demonstrating similar effects and highlight the significant methodological and conceptual implications of carry-over effects.

Introduction

Converging evidence indicates that exposure to drug-associated stimuli produces in substance users systematic biases in the processing of information in a manner that increases the likelihood of drug use (Sayette, 2004). Accordingly, interest in understanding the effects of drug cue exposure on cognitive processing has grown. Numerous investigations have used mixed randomized or quasi-randomized (i.e., ''unblocked'') presentations of drug-related and nondrug stimuli during performance on standard paradigms thought to assess one or more cognitive functions. For example, several studies have used the unblocked format of the Stroop paradigm to study attentional bias for drug cues in substance users (e.g., Bauer & Cox, 1998; Wertz & Sayette, 2001). To assess attentional bias, these studies used a modified version of the Stroop paradigm in which participants are required to disregard the meaning of drug-related (e.g., cigarette) and neutral (e.g., citizen) words while identifying the color in which the words are printed (e.g., by vocalizing the color). Typically, a difference is calculated between average performance on trials involving exposure to putatively neutral cues and average performance on trials involving drug cue exposure to quantify cue-elicited changes in cognitive performance.

Waters and colleagues (Waters, Sayette, Franken, & Schwartz, 2005; Waters, Sayette, & Wertz, 2003) have demonstrated that exposure to salient stimuli in the unblocked format of the Stroop task can affect performance on subsequent task events (see also McKenna & Sharma, 2004). That is, the attentional effects elicited by exposure to salient stimuli ''carry over'' to influence the processing of the following trial. Specifically, Waters et al. (2003, Studies 1 and 2) found that smokers responded more slowly to words appearing after smoking-related items than to words appearing after neutral items. Subsequent work across multiple laboratories replicated and extended the generalizability of carry-over effects in the Stroop paradigm. Heroin users, but not nonusers, responded more slowly to words appearing after

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heroin-related words than to words appearing after neutral items (Waters et al., 2005, Study 1). These effects also generalized to nonaddicted populations; participants expecting to deliver a stressful self-disclosing speech about their physical appearance responded more slowly to words following those associated with the speech stressor than to items coming after nonspecific stress words or neutral words (Waters et al., 2005, Study 2).

Taken together, these data provide strong evidence for the existence of carry-over effects in the unblocked format of the Stroop paradigm. However, it is unknown whether similar effects are found in cognitive tasks other than the Stroop. Conceptually similar effects in other response domains suggest that carry-over effects may indeed be widespread. For instance, elevations in self-reported urge to smoke are associated with cue exposure carry-over when smoking cues are removed and replaced with putatively neutral periods or cues (Hutchison, Niaura, & Swift, 1999; Rickard-Figueroa & Zeichner, 1985; see also Heishman, Saha, & Singleton, 2004). Similarly, prior exposure to drug-associated stimuli appears to influence neurobiological responses under purportedly neutral conditions (Breiter et al., 1997). Thus carry-over effects potentially are of methodological and conceptual importance, particularly given the rapidly growing body of studies using standard cognitive paradigms to investigate drug cue reactivity. Carry-over effects, if present, might reduce the magnitude of differences between performance on drug-related and nondrug items under certain circumstances (e.g., when stimulus presentation is not completely random; McKenna & Sharma, 2004; Waters et al., 2003), reducing the likelihood of detecting cue-elicited effects on cognitive performance. Carry-over effects therefore raise important questions about research designs involving multiple interleaved presentations of drug and nondrug stimuli, a frequent practice in cue exposure research. Moreover, identifying carry-over effects in other cognitive domains may help further characterize the dynamics of the cognitive processes influenced by drug cue exposure.

Working memory performance is one domain of cognitive functioning that has received little attention in examinations of drug cue exposure. Recent research suggests, however, that working memory impairments may play a significant role in the development and maintenance of addiction (e.g., Bechara & Martin, 2004; Finn, 2002). One aim of the present study was to investigate the effects of drug cue exposure on working memory performance in cigarette smokers. One challenge in conducting this research concerns the approach to administering the cues. On the one hand, repeatedly exposing participants to both control and drug cues in a within-participant design has been argued as providing maximal power for detecting effects of drug cue exposure (e.g., Tiffany, Carter, & Singleton, 2000). For example, it is common to administer in random order a series of a dozen or more visual images or scripts associated with drug use (i.e., drug cue) and nondrug use (i.e., control cue; e.g., Conklin & Tiffany, 2001). Presumably this approach provides a more reliable assessment of the effects of drug cues than is found in studies that include only a single exposure to the drug and control cue (e.g., Sayette, Martin, Hull, Wertz, & Perrott, 2003). On the other hand, the research described above suggests that repeated exposures to drug cues may produce carry-over effects that can cloud interpretation of the study.

In summary, the improved reliability of a multitrial, repeated-exposure design was attractive to us, provided it did not also introduce carry-over effects. The present study aimed to examine working memory performance in deprived smokers and to determine if a multitrial paradigm would be vulnerable to carry-over effects in an investigation of this domain of cognitive performance. Although prior research using different cognitive tasks suggested a risk of carry-over, the advantages of such a method led us to evaluate this risk (of carry-over effects) empirically. Related to this latter aim, we also tested whether potential carry-over effects would obscure the effects of smoking cues on working memory. Finally, we sought to examine the degree to which carry-over effects, if present, would be moderated by the properties of the target item and the executive demands of the task. This last aim was based on findings from Stroop (MacLeod, 1991) and working memory tests (e.g., de Fockert, Rees, Frith, & Lavie, 2001; McConnell & Quinn, 2004; Quinn & McConnell, 1996) that performance varies as a function of both difficulty level of the primary task and complexity of task-irrelevant stimuli. To test these various aims, we administered a delayed-response working memory task adapted from prior research (D'Esposito, Postle, Ballard, & Lease, 1999) in which participants performed multiple trials involving exposure to smoking cues.

Method

Participants

Adult cigarette smokers ($N=23$; 14 male, 9 female) not currently interested in quitting were recruited through newspaper advertisements. Exclusion criteria included illiteracy and medical conditions that ethically contraindicated smoking. To be eligible, participants had to report smoking 10–30 cigarettes/day for at least the past 24 months continuously.

Participants' mean age was 33.9 years (SD=11.5). They reported an average of 12.7 years of formal education (SD=1.7), 17.5 years of smoking (SD=11.8), and 19.8 cigarettes/day (SD=5.7). All procedures were approved by the institutional review board of the University of Pittsburgh. Written informed consent was obtained from all participants, who received US$20 for their involvement.

Materials

Baseline assessment measures. Demographic information and information regarding smoking patterns were assessed with standard forms (Sayette, Martin, Wertz, Shiffman, & Perrott, 2001).

Smoking urge assessment. Participants' self-reported urge to smoke was assessed using a single-item rating scale (Sayette & Hufford, 1994). This scale ranged from 0 (no urge to smoke at all) to 9 (very strong urge to smoke). Participants were prompted to enter urge ratings into the computer immediately prior to and following completion of the working memory task. Because of technical error, the urge ratings provided by four participants were not collected properly. Urge data are reported for the remaining 19 participants.

Task and stimuli. Participants completed several trials of a delayed-response working memory task adapted from previous research (D'Esposito et al., 1999). At trial onset, a set of five English letters was presented simultaneously for 2,500 ms. This set was constructed by sampling five items in random order (without replacement) from the consonants B, F, H, J, K, L, M, Q, R, S, T, and Y. Subsequently, the set of letters was removed and an instruction cue (Forward or Alphabetize) was presented for 1,500 ms, indicating whether participants should maintain the memory set in the order in which it was presented (forward task trials) or reorder the memory set alphabetically and maintain the set in alphabetical order (alphabetize task trials).

The instruction cue was followed by an 8-s delay period during which one of three events was presented: (a) A fixation cross, (b) a picture containing smoking-related content (smoking picture), or (c) a picture containing no smoking-related content (neutral picture). Following the delay period, a memory probe consisting of a letter from the memory set and a number from 1 to 5 was presented for 3,000 ms, during which participants responded to indicate whether the letter was in the ordinal position represented by the number by pressing computer keys labeled "yes" or "no." For forward trials, which did not require reordering of the memory set, participants responded to indicate whether the letter was in the ordinal position in the memory set as it was presented initially. For alphabetize trials, which required reordering of the originally presented memory set, participants responded to indicate whether the letter would be in the ordinal position represented by the number if the items in the memory set were rearranged into alphabetical order. Trials were separated by 4,000 ms, during which a fixation cross was displayed.

Participants completed five blocks of trials. Each block consisted of 24 randomly presented trials: 4 forward trials and 4 alphabetize trials of each delay cue condition (fixation cross, smoking picture, neutral picture). Thus participants completed a total of 120 trials. E-prime software (Psychological Software Tools, Pittsburgh, Pennsylvania) was used to control computerized stimulus presentation and the collection of responses and response latencies.

The picture stimulus set consisted of 40 smoking-related and 40 neutral pictures. Each picture was presented once during the experiment. The smoking pictures were adopted from those shown in previous research to elicit robust cue-reactivity (Mucha, Geier, & Pauli, 1999; Mucha, Geier, Stuhlinger, & Mundle, 2000; Mucha, Pauli, & Angrilli, 1998). Similar stimulus items have been shown to produce responses in multiple response systems (Ehrman et al., 2002; Field, Mogg, & Bradley, 2004; McDonough & Warren, 2001; Mogg, Bradley, Field, & De Houwer, 2003). In addition, a large set of neutral pictures (over 100) consisting of pictures similar in general content to the smoking-related pictures, but devoid of smoking-related stimuli, were obtained from the Internet. These neutral pictures were piloted with smokers to derive a set of 40 neutral pictures that elicited minimal cue-reactivity as indicated by self-reported urge to smoke. Similar procedures have been used to generate picture stimuli in previous research (Field et al., 2004; Mogg et al., 2003).

Procedure

Participants who responded to the advertisements completed a preliminary screening interview over the phone. Eligible participants visited the lab for two sessions: An initial screening session and the experimental session. During the screening session, participants provided an expired-air carbon monoxide (CO) sample, which was used to verify smoking status ($\geq$10 ppm; BreathCo, Vitalograph, Lenexa, Kansas) and to provide a baseline for comparison with levels obtained at the start of the experimental session. Subsequently, all participants were permitted to leave the laboratory after being instructed not to drink alcohol or use tobacco products or other drugs for 12 hr prior to arriving at the laboratory to participate in the experiment.

Experimental sessions were scheduled to begin between noon and 3:00 P.M. To check compliance with deprivation instructions, participants reported the last time they smoked a cigarette and a second CO sample was obtained. For the second CO assessment, samples exceeding half of the initial CO level or 16 ppm resulted in exclusion from the study, based on criteria derived from similar deprivation periods in comparable smoking samples (e.g., Sayette et al., 2001). (Seven potential participants failed to meet this CO requirement and were excluded from the study. These participants were not included in the previously described sample of 23 participants.) Following CO verification, participants were instructed that they would not be able to smoke during the experiment and were given instructions about how to perform the working memory task. Participants were informed that their main task was to try to remember the list of letters in the instructed manner (i.e., either as presented or reordered alphabetically), but that they also would be presented with pictures during the delay period of some trials (they were not informed that some of the pictures would have smoking-related content). To reduce the likelihood that they would try to avoid viewing the pictures (e.g., by turning away or shutting their eyes), participants were told to look at each picture because they would be asked some questions about them after completing the memory task. (We do not have data indicating the degree to which participants actually viewed pictures during the study.) Participants were instructed that they did not have to do anything else regarding the pictures but look at them.

Participants then completed a set of practice trials to ensure understanding of the task demands. The practice set included both forward and alphabetize trials with only fixation crosses and neutral picture presented during the delay period; no smoking pictures were presented during practice trials. (Additional pictures without smoking content that were not part of the previously described set of 40 neutral pictures were used for practice trials.) Participants were then prompted to enter their urge to smoke into the computer and then completed the working memory task. After completing the task, participants were prompted to enter their urge to smoke and were subsequently debriefed.

Results

CO assessment

All participants included in the study satisfied CO criteria for smoking status and abstinence compliance verification, as described earlier. Experimental session CO levels ($M=5.2$, $SD=2.1$) were significantly lower than screening session CO levels ($M=16.7$, $SD=6.8$), $F(1, 22)=100.60$, $p<.0001$, effect size $d=4.28$.

Smoking urge

Participants reported their urge to smoke on two occasions: Prior to completing the working memory task and just after completion of the task. Results indicated that post-task smoking urge levels ($M=7.4$, $SD=1.9$) were significantly greater than pretask levels ($M=6.6$, $SD=2.4$), $F(1, 18)=7.04$, $p=.016$, $d=1.25$.

Working memory performance

We first conducted a 2 (task: Forward, alphabetize) by 3 (before: Fixation cross, neutral picture, smoking picture) by 3 (target: Fixation cross, neutral picture, smoking picture) repeated-measures analysis of variance with mean accuracy as the dependent measure (with the first trial of each task block—which could not be affected by an immediately preceding stimulus—omitted from analysis). (Analyses utilizing response latency as the dependent measure yielded no significant findings and are not discussed here.) We observed a significant effect of task, $F(1, 22)=15.61$, $p<.001$, $d=1.68$. As expected, participants performed better in the forward condition ($M=79.2\%$ accuracy, $SD=14.8$) than in the alphabetize condition ($M=67.1\%$, $SD=18.8$).

One aim of the present study was to investigate the effects of drug cue exposure on working memory performance. A nonsignificant effect of target suggests that working memory performance was not affected by the type of distractor presented during the current trial, $F(2, 21)=1.73$, $p>.2$. A second objective was to determine whether working memory performance was affected by the content of the preceding trial (i.e., whether it contained a smoking cue). Related to this aim, we observed a significant before × target interaction, $F(4, 19)=4.07$, $p=.015$. Separate follow-up analyses were conducted for each of the three types of target stimuli. Of central interest, results revealed that performance on trials containing neutral pictures was worse when the preceding trial contained smoking pictures than when the prior trial contained a fixation cross, $F(1, 22)=5.46$, $p=.029$, $d=1.00$ (Table 1). The size of this carry-over effect (mean accuracy for targets containing neutral pictures preceded by trials in which a fixation cross was presented minus mean accuracy for targets containing neutral pictures preceded by trials in which smoking pictures were presented) was not reliably correlated with the change in smoking urge from pretask to post-task, $r(19)=.34$, $p>.1$.

We also observed a trend indicating that performance on trials containing neutral pictures was worse when the preceding trial contained smoking

Table 1. Means (and standard deviations) for percent accuracy as a function of the content of the previous trial.

	Content of preceding trial		
Target trial	Fixation cross	Neutral picture	Smoking picture
Fixation cross	77.2 (20.2)	71.2 (19.0)	74.9 (17.2)
Neutral picture	76.6 (15.8)*	76.0 (19.5)	69.8 (16.8)*
Smoking picture	70.8 (22.4)	71.3 (21.0)	71.3 (18.0)

Note. [a]Indicates that values in row are significantly different from one another ($p<.05$).

pictures than when the prior trial contained neutral pictures, $F(1, 22)=3.17$, $p=.089$, $d=.76$. In contrast, performance for trials in which a fixation cross or smoking stimulus served as the target were not significantly affected by the content of the previous trial (all p-values $>.1$). No other effects were significant: Main effect of before, $F(2, 21)=1.96$, $p>.1$; task × before interaction, $F(2, 21)=.28$, $p>.7$; task × target interaction, $F(2, 21)=1.19$, $p>.3$; task × before × target interaction, $F(4, 19)=1.44$, $p>.2$.

To test whether the difference in performance on smoking versus neutral targets may have been obscured in part because of carry-over effects, we next examined the effect of smoking targets versus neutral targets on working memory performance for only those trials preceded by nonsmoking stimuli so that we could exclude trials subject to carry-over effects. This analysis is consistent with the a priori aims of the present study and provides a reasonable assessment of whether significant effects of cue exposure would have been observed in the absence of carry-over effects. Results indicated that, when considering only "pure" trials (i.e., those not preceded by smoking-related content), accuracy during smoking targets was poorer than during neutral targets, $F(1, 22)=6.44$, $p=.019$, $d=1.08$.

Discussion

The present study investigated the effects of smoking cue exposure on working memory performance in deprived cigarette smokers. In addition, the study examined whether previously demonstrated carry-over effects would be observed in a delayed-response working memory task involving multiple smoking cue exposures.

Consistent with prior research, we found carry-over effects such that drug cue exposure affected the processing of subsequent items. Specifically, working memory performance on trials containing neutral pictures preceded by trials containing smoking cues was worse than performance on trials containing neutral pictures preceded by trials not containing smoking-related stimuli.

These carry-over effects obscured the ability to detect cue-elicited disruption of working memory performance. That is, conventional analyses suggested that working memory performance was not affected by the type of distractor presented during the current trial (i.e., whether the current trial contained a smoking cue). The failure to detect a significant main effect of smoking cue exposure on working memory performance may have been related to specific aspects of the paradigm used in the present study. For instance, a more difficult version of the task involving explicit recall, rather than a simple binary response, may have been more sensitive to such effects. Nonetheless, if we had examined the current data without consideration of the presence of carry-over effects, we would have concluded incorrectly that smoking cue exposure has little impact on working memory. Upon taking into account carry-over effects, however, we found that smoking cues impaired working memory functioning but only relative to "pure" neutral comparators. These results highlight the potential methodological implications of carry-over effects for research designs involving multiple interleaved presentations of drug and nondrug stimuli.

Our findings are consistent with previous research demonstrating similar carry-over effects in the unblocked format of the Stroop task (Waters et al., 2003, 2005). Our results also extend this prior research in two important ways. First, the present data indicate that, in addition to affecting performance on tasks thought to index attentional processing, recently presented drug-related information can affect subsequent working memory processing several seconds after such information is removed. Attention and working memory, themselves interrelated processes, are used to support a wide variety of tasks demanding nonautomatic cognitive resources (Kane & Engle, 2002). Thus the observation that carry-over effects occur in both attention-demanding and working-memory-demanding tasks suggests that performance on a variety of cognitive tasks is likely to exhibit similar effects. As noted, carry-over effects also appear when using self-report (Hutchison et al., 1999; Rickard-Figueroa & Zeichner, 1985; see also Heishman et al., 2004) and neurobiological (Breiter et al., 1997) indices of cue reactivity, suggesting the impact of the phenomenon across multiple response systems.

Second, our results suggest that carry-over effects are moderated by properties of the target item. As noted, research suggests that stimulus complexity affects the impact that task-irrelevant information has on performance. For instance, the latency to name the color of a stimulus in the traditional Stroop task increases as the stimulus becomes more wordlike and more semantically related to the concept of color, whereas little color-naming interference is produced by nonlexical items (MacLeod, 1991). Similarly, working memory performance becomes more impaired as the complexity of concurrently presented visual distractors is increased (McConnell & Quinn, 2004). In accord with such findings, we found carry-over effects for trials containing relatively complex visual properties (i.e., those in which nonsmoking pictures were the target stimuli) but not for trials lacking such stimuli (i.e., those in which a simple fixation cross was the target).

We did not observe significant carry-over effects for trials in which smoking pictures served as target stimuli, suggesting that the presentation of consecutive smoking cues does not result in a cumulative disruption of performance. This result differs from the additional interference found on the emotional Stroop task following exposure to two consecutive drug cues (e.g., Waters et al., 2005). Perhaps with the presentation of several consecutive drug cues, carry-over effects would emerge for smoking stimuli (possibly explaining the robust Stroop effects found in blocked designs; Waters et al., 2005). Alternatively, though speculative, the presence of smoking stimuli—during either the preceding or current trial—may have been sufficient to disrupt ongoing working memory performance in the current task for trials that themselves had distracting information (neutral or smoking pictures), whereas the paradigm (unlike the Stroop task) was relatively insensitive to any additional effects resulting from consecutive smoking cues (i.e., a floor effect).

The present study does not permit specification of the mechanisms underlying observed carry-over effects. It is possible, for example, that presentation of smoking-related information affected the encoding or maintenance of memory items (or both) on the subsequent trial, making performance more susceptible to disruption from distracting events. Alternatively, carry-over effects may have been specific in some way to the type of nonsmoking pictures used in the present study (e.g., perhaps the neutral pictures, which were matched in general content to smoking-related pictures, elicited additional smoking-related thoughts when following smoking cue trials). Given the broad range of stimuli across multiple studies showing carry-over effects, however, we view this latter possibility as unlikely. Future research is needed to clarify the way in which prior smoking content influences subsequent working memory. Indeed, understanding the mechanisms underlying carry-over effects in different cognitive domains may help characterize the manner in which cue-elicited shifts in cognitive processing contribute to drug use and addiction (Waters et al., 2005). For instance, it is possible that carry-over effects may predict relapse independent of more traditional measures of cognitive performance, perhaps by identifying differences in ability to disengage from salient information (Waters et al., 2005).

The results of the present study add to prior research demonstrating carry-over effects in several independent datasets (McKenna & Sharma, 2004; Waters et al., 2003, 2005). It has been suggested that "all other things being equal," the inclusion of multiple cue presentations should increase the power of cue-reactivity studies (Tiffany et al., 2000). Although this suggestion is based on established psychometric principles, it now seems clear that all things may not be equal when it comes to cue-elicited effects. Rather, converging evidence indicates that exposure to salient (e.g., drug-related) material can cause detectable changes in the processing of stimuli presented shortly thereafter, even when such events are theoretically neutral. As noted above, this appears to be true even when self-reported urge is the measure of interest. As found in the present study, unnoticed carry-over effects can interfere with detection of actual cue-elicited effects. Thus failing to appreciate the impact of such effects may have significant implications for studies using multiple intermingled presentations of drug-related and non-drug stimuli (particularly for designs in which stimulus presentation is not fully random; McKenna & Sharma, 2004; Waters et al., 2003). Future research is needed to investigate the ways in which carry-over effects influence different cognitive operations. It is likely, for example, that duration of intertrial interval will affect carry-over differently depending on the particular cognitive task. Elucidating the mechanisms underlying carry-over may offer insight into the nature of the cognitive biases associated with drug addiction.

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