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Testing the left hemisphere activation hypothesis in psychopathic offenders using the Stroop task



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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Response modulation Selective attention Psychopathy checklist revised Attention	Prior investigations of selective attention using the Stroop task have indicated individuals with high levels of psychopathic traits show reduced Stroop interference only when there is spatial separation of conflicting information. However, theories of psychopathy such as the left hemisphere activation hypothesis make specific predictions regarding the impact of rewards which have yet to be tested. Ninety-nine incarcerated male participants were assessed for psychopathy trait levels using the Psychopathy Checklist-Revised (PCL-R Hare, 1999) and completed four Stroop task variants, in which the spatial separation of conflicting information and the presence of financial reward/punishment contingencies varied. While the study failed to replicate previous findings of reduced interference on spatially separated Stroop tasks in individuals with high levels of psycho-

hemisphere activation hypothesis of psychopathy.

1. Introduction

Despite the prominence of conceptualizations of psychopathy that emphasize emotional deficits, the past quarter century has been characterized by a large increase in studies reporting cognitive dysfunction in individuals with psychopathic traits. Numerous studies have reported reduced responsiveness to peripheral contingencies, deficient learning of stimulus-reinforcement associations, and poor performance under conditions placing differential demands on left hemisphere attention and motor system resources (Finger et al., 2011; Riser & Kosson, 2013; Zeier, Maxwell, & Newman, 2009).

These studies have led to a resurgence of interest in cognitive perspectives on psychopathy, and among these, perhaps the most influential theoretical perspective is the response modulation hypothesis, which posits that psychopathic offenders are characterized by a reduced attention to peripheral cues that signal the need to change behavior in the midst of a dominant response (e.g., Patterson & Newman, 1993).

Among the many paradigms employed to test this hypothesis, studies using the Stroop task have proven especially useful, based in part on the extensive literature addressing the mechanisms underlying the Stroop task effect. In the classic version of the Stroop task, participants are asked to name the ink color of a word that spells a color name. In some cases, the color of the ink and the word are congruent; in other cases; they are incongruent. More difficulties are experienced during the incongruent condition, and this can be measured as an increase in reaction times, or a decrease in accuracy rates (the Stroop interference effect). In contrast, reaction times are decreased and accuracy increased in the congruent condition compared with a neutral condition (in which the word does not refer to a color). This is known as the Stroop facilitation effect. The implications of these differences is that task-irrelevant semantic information (i.e., the meaning of the word "BLUE") is processed despite the deployment of voluntary attention to processing stimulus color.

pathy, the novel finding of reduced facilitation under reward conditions provides evidence corroborating the left

Newman and colleagues have demonstrated that psychopathic offenders and non-psychopathic offenders exhibit comparable interference on the traditional Stroop task (Hiatt, Schmitt, & Newman, 2004; Smith, Arnett, & Newman, 1992). However, when completing a variant of the task in which participants name the color of a rectangular frame that surrounds color words presented in black (the box Stroop; see Fig. 1), non-psychopathic offenders continue to display substantial interference when the color of the rectangular frame differs from the meaning of a color word despite the spatial division between the color

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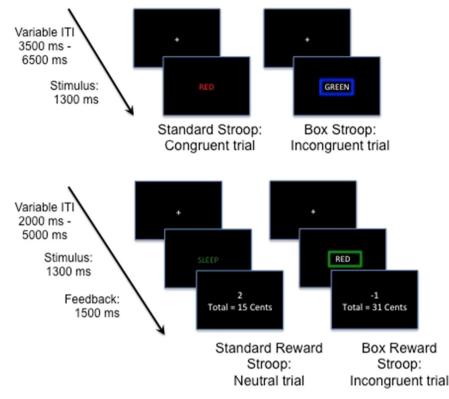


Fig. 1. Examples of trials presented.

word and the distracting information – the frame color. In contrast, psychopathic traits have been linked to lower levels of such interference relative to non-psychopathic offenders. In the first study exploring the Stroop effect in psychopathic offenders, reduced interference was found only in psychopathic offenders with low levels of negative affectivity (Hiatt et al. (2004). In a replication, Hamilton, Baskin-Sommers, and Newman (2014) reported a direct relationship between psychopathic traits and reduced interference. This relationship has been interpreted as consistent with the proposal that psychopathic individuals allocate less automatic attention to semantic processing when their task set prompts them to attend to information even only slightly separated from word stimuli.

As described, within the Stroop task, attentional interference effects can be differentiated from facilitation effects, and these processes appear to depend on different mechanisms (e.g., Brown, 2011). Both prior studies of psychopathy that have addressed the interference-facilitation distinction have suggested that psychopathy is associated with reduced interference but not with increased facilitation (Hamilton et al., 2014; Hiatt et al., 2004).

The Stroop paradigm could potentially be manipulated to test other models of psychopathy. In particular, the left hemisphere activation hypothesis suggests that several psychopathy-related performance deficits depend on manipulations that induce approach motivational states (that is, states in which people are motivated to approach rewarding stimuli, e.g., Kosson, Miller, Byrnes, & Leveroni, 2007; Lopez, Kosson, Weissman, & Banich, 2007), with a large body of research suggesting that the left hemisphere is specialized for approach motivational states and the right hemisphere specialized for avoidance states (e.g. Harmon-Jones, Gable, & Peterson, 2010; Spielberg, Heller, & Miller, 2013). According to this perspective, psychopathic offenders are characterized by performance inefficiency under conditions that place differential demands on left hemisphere-lateralized resources. Studies employing a variety of different paradigms (divided visual field studies, dichotic listening studies, global-local paradigms) have provided evidence for impairments specific to conditions placing greater demands on left

hemisphere attention and motor resources. In most of these studies, participants have been incentivized through the use of performancebased incentives. Moreover, several studies suggest that psychopathic offenders' behavioral deficits may be especially robust in situations involving concrete rewards and punishments (Arnett, Smith, & Newman, 1997; Newman, Kosson, & Patterson, 1992).

These perspectives raise questions about the impact of task parameters and rewards on the performance of individuals high in psychopathic traits, with the left hemisphere activation hypothesis predicting that psychopathic offenders will perform especially inefficiently under conditions presenting tangible performance-based rewards. However, no prior Stroop studies examining psychopathic offenders have used rewards to test these hypotheses. As a better understanding of the nature of attentional differences associated with psychopathic traits, the current study was designed to address: 1) the specificity of reduced interference to Box Stroop conditions; 2) the generalizability of the observed effects to a new sample of offenders; 3) the impact (or lack thereof) of an incentive manipulation designed to increase approach motivation, and therefore elicit abnormalities in individuals high in psychopathic traits.

2. Methods

2.1. Participants

Participants were 99 incarcerated males recruited from a mediumsecurity North American correctional facility that volunteered for the study and provided informed consent. Procedures were approved by the Institutional Review Board of [identifying information removed]. Participants received monetary compensation for participation. Participants qualified for inclusion in the study if they were aged 18–55, had been convicted of felonies, were fluent in English, had a reading level of at least 4th grade and an IQ of at least 70. Additionally, since the data were collected as part of a larger study with included magnetic resonance imaging, participants with a history of serious brain injury/disease, loss of consciousness for over 5 min, or any MRI contraindications were excluded from taking part.

2.2. Measures

All participants were rated on the Hare Psychopathy Checklist-Revised (PCL-R; Hare, 1999) by trained staff following a semi-structured interview covering school, employment, relationship and criminal history and review of institutional files. The PCL-R is a 20-item checklist of personality and behavior characteristics, each scored on a 3-point severity scale (0–2), with a maximum score of 40. A score of 30 or higher is the recommended cutoff for a categorical operationalization of psychopathy. The PCL-R also provides a dimensional assessment of psychopathic traits, divided into two factors. Factor 1 scores correspond to affective/interpersonal characteristics, whereas Factor 2 scores correspond to antisocial characteristics associated with impulsive violence and socially deviant lifestyles. Extensive evidence documents the reliability and validity of PCL-R ratings as indices of the clinical construct of psychopathy (Hare & Neumann, 2008).

Since Hiatt et al. (2004) found abnormalities only for low anxious psychopathic offenders, the Welsh Anxiety Scale (WAS; Welsh, 1956), a widely used trait measure of proneness to experience negative affect (Watson & Clark, 1984) was also administered. As in Hiatt et al. (2004), median splits on the WAS were used to create high- and low- anxious groups for statistical analysis.

As the comorbidity of psychopathy and substance use is high, substance abuse history is therefore a possible confound which may affect task performance. In order to control for this potential confound, substance use was assessed using a modified version of the Addiction Severity Index (ASI; McLellan et al., 1992). The ASI is scored based on a short interview about the duration, frequency and amount of use of multiple types of drugs, and was used to calculate the cumulative years of regular use (i.e., three or more times per week) for all substances (alcohol, heroin, cocaine, methamphetamine, cannabis, hallucinogens, and inhalants) combined.

Demographic and assessment information for the sample is provided in Table 1. There were no significant differences on demographic characteristics, PCL-R scores or substance use between the high and low anxiety groups.

2.3. Tasks

All tasks were presented using *E*-Prime Studio (Version 2). Four variants of the classic Stroop task were administered during two fMRI scanning sessions; standard Stroop, box Stroop, standard reward Stroop and box reward Stroop. Imaging results will be presented separately, in a later manuscript. During the first testing session, participants performed the two non-reward versions of the task, and returned approximately a week later to perform the two reward variants of the task. Non-reward variants were administered first in all participants to

Table 1

Demographic and assessment characteristics of sample.

ensure that experiencing performance-based incentives did not alter performance in subsequent administration of tasks. Additionally, during each session, participants completed the standard variant of the task first, followed by the box variant. For each of the conditions, participants were given a short practice outside of the scanner before completing the main task to ensure that participants were familiar with the task and using the response pad.

Participants completed one run of each of the four task variants, each including 60 trials and lasting 6 min 30 s. Each run was comprised of 20 congruent, 20 incongruent, and 20 neutral trials presented in a random order. Each trial began with a white central fixation cross presented on a black background. Specific parameters of the four task variants are detailed as following, and a schematic showing the time course of trials on each task variant is shown in Fig. 1.

2.3.1. Standard Stroop

Participants were presented with a series of words, in red, blue, or green upper case letters on a black background, and asked to indicate the color of the text by pressing one of three buttons with the index, middle or ring fingers of their right hand. Three different trial types were presented: congruent, incongruent and neutral. During 'congruent' trials the printed word and the color of text matched (e.g. the word 'RED' presented in red). During 'incongruent' trials, the printed word was presented in an incongruent color (e.g. the word 'BLUE' presented in green). During neutral trials, one of three non-color words (i.e. 'EAT', 'WALK' or 'SLEEP') was presented in one of the three colors (e.g. 'SLEEP' presented in blue). Words presented during neutral trials were matched to the color words in terms of length and abstract/concreteness. A fixation cross was presented for a jittered period of 3500 ms to 6500 ms (with a mean of 5000 ms). Following this, the trial stimuli were presented for 1300 ms.

2.3.2. Standard reward Stroop

Parameters were similar to that of the standard Stroop, with the addition of monetary rewards/punishments based on performance. Participants earned 1–3 cents for correct answers, with the amount depending on speed of response (3 cents for responses under 475 ms, 2 cents for responses 475–575 ms, and 1 cent for responses over 575 ms) and lost 1 cent for every incorrect answer. Similar methods have been used to incentivize participants and elicit approach motivation in other studies (Kleinsorge & Rinkenauer, 2012; Llanes & Kosson, 2006). Each trial began with a fixation cross presented for 2000 ms–5000 ms, followed by stimulus presentation for 1300 ms, and ended with feedback regarding earnings on the current trial, and on the task so far, for 1500 ms.

2.3.3. Box Stroop

A spatially separated color-word Stroop task based on that of Hiatt et al. (2004) was administered. The Box Stroop used parameters almost identical to those in the Standard Stroop, with the key difference that all trials words were presented in a white text, with colored rectangular

	Full group (n = 99)		Low anxiety $(n = 42)$		High anxiety $(n = 47)$		Difference between groups	
	Mean	SD	Mean	SD	Mean	SD	t	р
Age	31.81	8.15	33.00	8.55	30.74	7.71	1.31	.19
WAIS	97.98	13.55	100.44	13.73	95.79	13.13	1.63	.11
Education (years)	10.98	1.12	10.83	1.21	11.11	1.03	1.15	.25
WAS	12.63	8.74	5.21	4.02	19.26	6.07	12.71	.00
Total PCL-R	22.79	7.14	23.72	7.93	21.95	6.32	0.25	1.77
PCL-R Factor 1	8.82	3.10	9.24	3.59	8.45	2.56	0.23	.79
PCL-R Factor 2	12.00	4.44	12.63	4.57	11.53	4.33	1.10	.28
Substance use (cumulative years across drugs)	14.11	15.04	12.75	14.45	15.30	15.60	-0.79	.43

WASI = Wechsler Abbreviated Scale of Intelligence; WAS = Welsh Anxiety Scale, PCL-R = Psychopathy Checklist - Revised;

frames (red, blue or green) surrounding the words. Participants were asked to indicate the color of the rectangular frame, ignoring the word presented.

2.3.4. Box reward Stroop

Task parameters were the same of those for the Box Stroop, with the addition of the same reward contingencies as those in the Standard Reward condition.

2.4. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics (Version 21). For each Stroop task variant (standard, standard reward, box, box reward), reaction times (RT) for each condition (congruent, incongruent and neutral) were calculated for each participant. Interference was calculated for each participant by subtracting mean RTs on neutral trials from those on incongruent trials. Facilitation was measured for each participant by subtracting RT on congruent trials from those on neutral trials.

To examine whether overall Stroop effects were present, and also to investigate differences resulting from the demands of the task variants, response times were entered into separate repeated measures ANOVAs, with three within group factors; trial type (congruent, neutral and incongruent), Stroop design (standard, box) and incentive (reward, no reward). For trial type, planned comparisons were calculated, as linear trends were expected for response time (incongruent > neutral > congruent).

To investigate relationships between psychopathic traits and effects of the Stroop task, separate repeated measures ANOVAs were conducted to analyze facilitation and interference. Stroop design (box, standard), incentive (reward, no reward), and trial type were included as within group factors, with congruent and neutral trials included in the ANOVA investigating facilitation, and incongruent and neutral trials included in the ANOVA investigating interference. Mean centered PCL-R scores were included as a continuous covariate. Initially, total PCL-R scores were included in the model; analyses were then repeated separately for PCL-R Factor 1 and Factor 2 scores, to investigate the unique variance accounted for by each factor. To investigate the influence of anxiety, as in prior studies of the response modulation hypothesis (e.g., (Hiatt et al., 2004; Zeier, Baskin-Sommers, Hiatt Racer, & Newman, 2012), anxiety was also included as a between subjects factor (high, low). To control for the potential confounding effects of substance use on any findings, the analyses were repeated, with the inclusion of mean centered total ASI as a covariate.

3. Results

Due to incomplete sessions, data were obtained from 99 participants in the standard Stroop, 97 participants in the standard reward Stroop, 95 for the box Stroop, and 97 for the box reward Stroop.

3.1. Correlations between demographic factors and PCL-R ratings

Correlations between PCL-R scores and demographic variables were calculated, to determine any significant relationships. There was a significant negative correlation between total PCL-R and years of education ($r_{89} = -0.23$, p < .05) and a significant positive relationship between total PCL-R score and substance use ($r_{89} = 0.34$, p < .001). Correlations between total PCL-R score and age, IQ and WAS score were non-significant (all rs < 0.10).

3.2. General effects for the Stroop tasks

Response times and accuracy rates for the three trial types across the group are presented in Table 2. There was a significant main effect of design ($F_{1.88} = 88.33$, p < .001), with response times during the box

Table 2			
Performance	on	Stroop	variants

	Trial types							
	Congruent		Neutral		Incongruent			
	Mean	SD	Mean	SD	Mean	SD		
Reaction times (ms)								
Standard	755.93	87.69	782.19	90.44	842.14	95.72		
Standard reward	603.40	80.71	615.63	83.19	652.35	107.07		
Box	742.00	93.17	758.37	92.75	786.10	98.16		
Box reward	554.74	85.86	568.68	87.17	582.46	95.11		
Accuracy (%)								
Standard	95.28	5.90	93.76	6.32	89.86	10.40		
Standard reward	95.14	4.10	93.99	4.72	91.97	5.58		
Box	95.51	5.35	95.39	5.19	92.78	8.71		
Box reward	95.76	4.48	94.69	4.72	94.80	5.20		

Stroop faster than during the standard Stroop, and also a significant main effect of incentive ($F_{1,88} = 644.99$, p < .001), with response times faster during reward variants of the task than the standard variants. A significant main effect of trial type was present ($F_{2,176} = 171.10$, p < .001). Planned comparisons indicated a significant linear trend ($F_{1,88} = 233.18$, p < .001), with response times increasing from congruent trials, to neutral trials, to incongruent trials.

3.3. Speed-accuracy trade-offs

Correlations between response times and accuracy are presented in Table 3. Significant negative correlations between response times and accuracy during incongruent trials in all four variants of the task suggest that there were no speed-accuracy tradeoffs. Additionally, response time/accuracy correlations were examined separately for the high and low anxiety groups, and are also presented in Table 3.

3.4. Relationships between Stroop performance and PCL-R and anxiety

A similar profile of results was found for analyses that included, and did not include years of regular substance abuse (as assessed using ASI) as a covariate. However, where the inclusion of this covariate had an impact on results, both results are noted. Full results of the ANOVAs investigating facilitation and interference in reaction times and accuracy rates are included in Supplementary Tables 1 and 2.

3.4.1. Facilitation effects

The ANCOVA investigating facilitation effects revealed a significant Trial type × Incentive × Total PCL-R interaction ($F_{1,86} = 4.21$, p < .05, $\eta^2 = 0.05$) and a Trial type × Design × Incentive × Total PCL-R interaction ($F_{1,86} = 4.74$, p < .05, $\eta^2 = 0.05$). Both interactions were significant only when total PCL-R was included in the model, and were not significant when only Factor 1 or Factor 2 ratings were included.

A series of interaction contrasts was conducted to unpack the

Table 3

Correlations between reaction times and accuracy on incongruent trials on all four Stroop task variants.

	Full sample $(n = 99)$		Low anxie $(n = 42)$	Low anxiety $(n = 42)$		ety
	r	р	R	р	r	р
Standard	-0.60	.000	-0.60	.000	-0.59	.000
Box	-0.56	.000	-0.56	.000	-0.59	.000
Standard reward	-0.37	.000	-0.17	.28	-0.50	.000
Box reward	-0.37	.000	-0.49	.001	-0.29	.05

interactions. These revealed that the Trial type × Incentive × Total PCL-R score interaction was significant for the Box Stroop condition ($F_{1,86} = 8.35$, p = .005, $\eta^2 = 0.09$) but not for the Standard Stroop ($F_{1,86} < 1$, *ns*). Further analyses showed that the Trial type x Total PCL-R score interaction was significant for the reward condition ($F_{1,86} = 8.33$, p = .005, $\eta^2 = 0.09$) but not for the no-incentive condition ($F_{1,86} < 1$, *ns*). More specifically, under incentive conditions, PCL-R total scores were associated with reduced facilitation scores on the Box Stroop (r = -0.28, p < .01); however, PCL-R scores were not associated with facilitation scores under no-incentive conditions (r = 0.09, *ns*). There were no significant effects in the analyses of facilitation using Factor 1 or Factor 2 scores.

3.4.2. Interference effects

Analyses investigating interference yielded no effects involving total PCL-R or Factor 2 scores. However, the analyses involving Factor 1 revealed a Trial type \times Design \times Factor 1 interaction which closely approached significance ($F_{1,86} = 3.92$, p = .05). There was an additional interaction effect which involved the Trial type \times Design \times Incentive \times Factor 1 interaction $(F_{1.86} = 4.11,$ p < .05). In the analyses that controlled for substance abuse, both these interactions were significant $(F_{1,84} = 4.70, p = .033,$ $F_{1.84} = 5.24, p = .025$).

Interaction contrasts revealed that the Trial type × Design × Factor 1 interaction was significant under non-incentive conditions ($F_{1,86} = 6.44$, p = .01) but not under incentive conditions ($F_{1,86} = 6.44$, p = .01) but not under incentive conditions ($F_{1,86} = 1.7$, ns). Further analyses revealed a non-significant Trial type × Factor 1 interaction in the standard Stroop ($F_{1,86} = 3.56$, p = .06) but not in the box Stroop ($F_{1,86} = 1.54$, p > .20). Within the standard Stroop, the relationship between Factor 1 scores and interference under non-incentive conditions approached significance (r = -0.18, p < .10) but not under incentive conditions (r = -0.10, ns). In the analysis that controlled for substance use, the F1-interference correlation under non-incentive conditions approached significance (r = -0.21, p = .05) whereas this correlation did not approach significance under incentive conditions (r = -0.11, p = .29).

3.4.3. Anxiety effects

There were no significant main effects of Anxiety nor any Psychopathy \times Anxiety interaction effects for the analyses investigating either facilitation or interference.

4. Discussion

While Newman and colleagues demonstrated that psychopathic offenders demonstrate reduced interference during a variant of the Stroop task in which conflicting information was spatially separated, this finding has, to the best of our knowledge been replicated only once, and only partially. As such, this study aimed to examine the robustness of the reduced interference effect, as well as the specificity of the effect to interference (rather than facilitation) and to the box Stroop (and not the standard Stroop). Additionally, the impact of adding concrete incentives on Stroop task performance was examined.

Across all participants, and all task variants, the results from the Stroop tasks suggest that a Stroop effect was successfully elicited. We observed a linear trend in reaction times, increasing from congruent trials, to neutral trials, to incongruent trials, indicated that task-irrelevant information, when presented, was processed. As response times were quicker on the Box Stroop compared with the Standard Stroop, it appeared that spatially separating the task-irrelevant, distracting information reduced its influence. Faster response times during reward variants of the task also suggested that the inclusion of financial rewards successfully motivated the performance of participants, consistent with the expectation that tangible rewards would increase approach motivation. not provided tangible incentives such as financial rewards, we first discuss findings under standard, non-reward conditions. Replicating both Smith et al. (1992) and Hiatt et al. (2004) there was no evidence of a relationship between psychopathy and reduced color-word inference during standard conditions. We did not replicate Hiatt et al.'s (2004) finding of reduced interference on the standard (non-reward) box Stroop variant of the task. Rather, we found no relationship between total PCL-R scores and facilitation or interference on standard Stroop variants. Although there was a Factor 1 x incentive x Design interaction, none of the individual component effects proved reliable in analyses that did not control for substance abuse. Even so, the negative correlation between Factor 1 scores and interference on the non-reward standard Stroop is at least consistent with the notion of reduced interference associated with psychopathic traits under some conditions. Even so, finding this relationship in the standard Stroop but not in the box Stroop and for Factor 1 rather than total PCL-R score raises some questions about the robustness of the reduced interference effect previously reported. Consequently, additional studies are needed to examine whether the difference in the reduced interference effects across studies reflects a lack of robustness in the effect, or some other difference between the programming or administration of the task in the present study versus the earlier studies of Newman and colleagues.

We observed novel psychopathy effects in the Box Stroop variant under reward conditions, where total PCL-R scores were associated with reduced facilitation. The evidence for impaired performance associated with psychopathy that is specific to conditions designed to instantiate approach motivation is consistent with the LHA hypothesis and provide the first evidence of an association between psychopathic traits and Stroop task performance impairments under LHA conditions. It is worth emphasizing that the impairment was limited to a reduction in facilitation, with no evidence for an increase in interference associated with psychopathy under incentive conditions.

An additional discrepancy between our findings and those of the earlier studies that we have reviewed, is that we found no significant main effects of anxiety or interactions between levels of psychopathy and anxiety. This is consistent with Hamilton et al. (2014), but unlike Hiatt et al. (2004) who found individuals who were both high in psychopathic traits and low in anxiety exhibited reduced interference on a picture-word variant of the Stroop task.

There are several possible drivers of the discrepancy between the findings of Hiatt et al. (2004) and those of the current study. Firstly, although both studies utilized color-word Stroop tasks, administration was very different. While Hiatt et al. (2004) used handheld stimulus cards to investigate the standard Stroop task, they used a computerized single-trial box Stroop with a verbal response. The current task used a computerized, single-trial task with a button press response for all Stroop variants. Previous research has indicated that there is evidence to suggest interference but not facilitation is reduced when a manual response is used rather than an oral response (MacLeod, 1991). Additionally, the current task was part of a large imaging study, and the task took place within an MRI scanner under loud noise conditions, whereas Hiatt et al. (2004) did not. There is mixed literature on the impact scanner noise has upon task performance, with evidence to suggest performance may decrease (Mazard et al., 2002), increase (Hommel, Fischer, Colzato, M, & Cellini, 2012) or remain the same (Jacob et al., 2015; Tomasi, Caparelli, Chang, & Ernst, 2005), it is possible that this difference in experimental environment may have influenced findings.

In conclusion, while the current study fails to replicate previous findings of reduced interference on Stroop task variants in individuals with high levels of psychopathic traits, we reveal a novel impairment associated with psychopathy which is consistent with the left hemisphere activation hypothesis – i.e. there were deficits during task variants that included reward.

As previous investigations of the Stroop effect in psychopathy have

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.paid.2018.07.020.

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