

## RESEARCH LETTER

# Stroop performance in drug users classified by HIV and hepatitis C virus serostatus

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## INTRODUCTION

Hepatitis C virus (HCV) can be detected in the brain (Radkowski et al., 2002) and investigators speculate that HCV has neuroinvasive properties (Forton et al., 2003) with direct effects on cerebral function.<sup>1</sup> MRS studies show that the basal ganglia and white matter of individuals with HCV have abnormal choline/creatine ratios, indicating CNS inflammation or infection (Forton et al., 2003). Patients with HCV show defects in working memory and information processing speed (Forton et al., 2003; Hilsabeck et al., 2002), similar to patients with basal ganglia disorders and HIV (e.g., Heaton et al., 1995).

Eighty to 90% of injection drug abusers are infected with HCV and 30 to 40% of HCV+ drug abusers are coinfecting with HIV (Thorpe et al., 2000; Sherman et al., 2002). These findings raise the question of whether HCV and HIV exert additive effects on brain dysfunction. No studies of HCV infection and cognition have targeted HCV+ or HIV/HCV coinfecting drug users. However, findings from neurocognitive studies of HIV-infected drug users can inform the development of similar investigations of HCV and cognition.

We present preliminary findings using a reaction time (RT) version of the Stroop task sensitive to HIV-associated cognitive dysfunction (Martin et al., 1992). We hypothesized that dually infected subjects would perform the RT Stroop more slowly compared with monoinfected persons or those seronegative for both viruses.

## METHODS

### Research Participants

We tested 159 males with known HCV and HIV serostatus enrolled in an ongoing study of neurocognition and HIV disease in drug users. Subjects were recruited from the Chicago-West Side VA Medical Center, community addiction treatment programs and shelters. All subjects carried at least one DSM-IV substance dependence diagnosis and 91% were African American. Eighty-four percent of subjects had a history of dependence on cocaine, 52% heroin, 50% cannabis, and 75% alcohol. Fifty-one percent of subjects reported a history of injection drug use. All subjects' urine toxicology screens and Breathalyzer results were negative at testing.

Table 1 shows demographic data for subjects grouped by HIV and HCV serostatus. HCV+ subjects were significantly older ( $p < .001$ ), had used drugs for a significantly longer time period  $F(1,155) = 8.35, p < .005$ , and reported a history of injection drug use significantly more frequently than HCV- subjects,  $\chi^2 = 33.4, p < .001$ . The mean estimated verbal IQ was slightly higher for HCV+/HIV- subjects compared with HCV-/HIV- controls ( $p < .05$ ). Groups did not differ in mean years of education or scores on the Beck Depression Inventory,  $F < 1$  for each comparison. HIV disease characteristics did not differ significantly between the two HIV+ groups, including CD4 count, AIDS diagnosis at testing percent of undetectable viral loads, or prevalence of antiretroviral therapy. None of the HCV+ subjects were receiving antiviral therapy at testing.

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**Table 1.** Participant characteristics

	HIV Serostatus				<i>F</i>	<i>p</i>
	Negative		Positive			
	HCV–	HCV+	HCV–	HCV+		
n	69	20	39	28		
Age	40.0 (10.6)	44.9 (4.3)	41.6 (5.0)	45.2 (4.2)	9.75	.005
Education	12.2 (1.8)	12.6 (1.1)	12.6 (1.9)	12.3 (1.4)	<1	.720
Years of Drug Abuse	21.5 (7.6)	24.9 (6.0)	18.3 (7.4)	23.2 (7.0)	8.35	.005
Estimated VIQ	100.6 (9.9)*	104.4 (5.4)	104.4 (11.0)	101.4 (8.7)	4.02	.05
Mean CD4 count	—	—	498 (382)	495 (326)	<1	.970
	HCV–	HCV+	HCV–	HCV+	$\chi^2$	<i>p</i>
% IDU	36	85	34	86	33.4	.001
% Undetectable HIV RNA	—	—	22	35	1.17	.280
% Antiretroviral Therapy	—	—	66	81	1.79	.180

\*versus HCV+/HIV–

## Procedure

RT Stroop procedures have been described in detail elsewhere (Martin et al., 1992). Briefly, the task consists of 192 voice-activated RT trials. On each trial a colored word appears at central fixation and the participant must name the display color and ignore the word. Twenty-five per cent of trials are color-congruent (e.g., “GREEN” in green), 50% are neutral (animal names in color) and 25% are color-incongruent (e.g., “BLUE” in red). The computer records voice-activated reaction times and errors.

## RESULTS

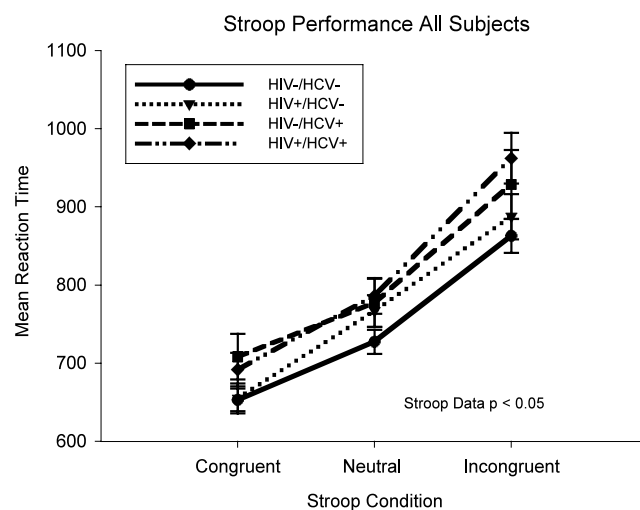
We analyzed median RTs for each condition using a mixed design ANOVA, with HCV and HIV serostatus as between-group factors and Stroop condition (Congruent, Neutral, or Incongruent) as the within factor, controlling for age, IQ, years of drug use, and history of injection drug use. The main effect for HCV Serostatus was significant  $F(1, 148) = 5.56, p < .05$ , with HCV+ subjects responding more slowly than HCV– groups. The Stroop  $\times$  HCV interaction was marginally significant,  $F(2, 296) = 2.85, p < .06$ ; HCV+ subjects showed a trend toward greater RT slowing in the Congruent and Incongruent conditions compared with the Neutral condition,  $p = .06$ . The Stroop  $\times$  HIV interaction was significant,  $F(2, 296) = 3.25, p < .05$ . Compared to HIV– subjects, HIV+ subjects showed significantly more RT slowing in the Incongruent condition ( $p < .05$ ) but not in the Congruent or Neutral conditions. (see Figure 1).

We computed a measure of overall Stroop performance for each subject by averaging RTs from the three separate conditions and compared the performance of seronegative, singly infected (HIV+ or HCV+ but not both) and dually infected subject groups using the Jonckheere–Terpstra statistic which tests for evidence of a monotonic trend in data from ordinaly classified independent subject groups (Jonck-

heere, 1954; Terpstra, 1952). This revealed a significant monotonic trend for poorer performance among subject groups ordered hierarchically according to infection status, (seronegative, monoinfected, dually infected),  $J\text{-}T \text{stat} = 2.95, p < .005$ . Exploratory analyses of data from separate Stroop conditions indicated that the monotonic trend was significant for Congruent and Incongruent conditions, all  $p$ 's  $< .05$ .

## DISCUSSION

We studied Stroop performance in a group of drug-dependent men monoinfected with HIV or HCV, dually infected, or seronegative for both viruses. We replicated a pattern of Stroop effects observed in our previous HIV studies. Spe-



**Fig. 1.** Mean RTs for HCV–/HIV–, HCV+/HIV–, HCV–/HIV+, and HCV+/HIV+ subject groups in Congruent, Neutral and Incongruent testing conditions.

cifically, HIV+ persons performed the RT Stroop significantly more slowly compared with HIV− controls in the Incongruent condition, which places maximal demand on controlled processes, but not in the Neutral or Congruent conditions, which rely on more automatic processes (Tzelgov et al., 1990). In addition, we found evidence of overall slowed RTs among HCV+ compared with HCV− subjects regardless of Stroop condition. These findings suggest that HIV+ subjects were impaired primarily on the “executive” component of the Stroop while HCV+ subjects’ performance was consistent with overall slowed information processing.

Finally, we observed a monotonic increase in overall Stroop RTs when comparing data from seronegative, singly infected, and coinfecting subject groups, consistent with hypothesized additive effects of HIV and HCV on neurocognition. These retrospective findings require replication, and prospective studies are underway.

Neurocognitive studies of drug abusers infected with HCV or dually infected with HCV and HIV pose significant challenges due to multiple comorbid conditions that can confound effects on cognition. Carefully designed cognitive neuropsychological measures developed to study HIV-associated cognitive impairment among drug users are also effective in the study of HCV and cognition. The Stroop task may be useful for isolating different types of neurocognitive deficits and have potential utility as neurocognitive probe in functional neuroimaging studies of patients with HIV and HCV.

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