Journal of the International Neuropsychological Society (1999), **5**, 579–592.

The impact of HIV-related neuropsychological dysfunction on driving behavior

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(RECEIVED July 2, 1998; REVISED February 10, 1999; ACCEPTED February 25, 1999)

Abstract

HIV infection often results in neuropsychological (NP) impairment. In order to assess the impact that HIV-related NP deficits may have on automobile driving, we evaluated 68 HIV-seropositive drivers using an NP battery and two PC-based driving simulations. Thirty-two participants were classified as NP impaired; most (72%) evidenced only mild impairment, and none met criteria for HIV-associated dementia. After controlling for degree of immunosuppression and disease stage, NP-impaired participants failed a previously validated driving simulation at a much higher rate than cognitively intact participants [OR = 5.3, 95% CI (1.7, 17.0), $p = .006$]. Similarly, on a simulation of city driving, NP impaired participants were more likely to fail based upon the number of accidents [OR = 6.1, 95% CI (1.5, 24.6), $p = .01$]. Simulator performance was predicted by functioning in a number of NP domains, with NP tests accounting for 13–30% of the variance on the simulations. Although it would be premature to extrapolate these findings to impairment in on-the-road driving, they do argue for greater attention to the impact that even mild HIV-related NP deficits may have on driving skills. (*JINS*, 1999, *5*, 579–592.)

Keywords: HIV infection, AIDS, Driving, Neuropsychological impairment

INTRODUCTION

HIV infection frequently is associated with brain dysfunction and cognitive impairment (Bornstein et al., 1992; Grant et al., 1987; Heaton et al., 1995; McArthur et al., 1993; Stern et al., 1991). The latter can range from subtle deficits that have no discernible impact on everyday functioning, to HIV-associated dementia with profound limitations on activities of daily living (Grant et al., 1995). Research addressing the impact that HIV-related neurocognitive impairment has on everyday functioning, however, has been limited. Most studies of the real-world implications of HIV-related neuropsychological (NP) impairment have focused on vocational functioning and found that NP impairment is associated with increased unemployment and complaints of difficulty in job performance, even after adjusting for medical symptomatology (Albert et al., 1995; Heaton et al., 1994b). Heaton et al. (1996) also have demonstrated that individuals with HIV-related NP impairment perform more poorly than their well-matched, unimpaired peers on standardized measures of vocational performance (work samples).

Driving an automobile is an everyday task requiring a complex combination of cognitive and perceptual–motor abilities. These include perception, attention, continuous tracking, choice reactions, sequential movements, judgment, and planning. If an individual is unable to adequately perform these tasks, this can result in serious public safety risks, as well as the loss of the person's license and subsequent diminished mobility.

What constitutes a person's driving ability, and how one goes about assessing it, are complex questions. Assessment approaches include reviewing driving histories (Dubinsky et al., 1991) and performing on-road evaluations (both closed-course; Fitten et al., 1995, and in-traffic assessments; Hunt et al., 1993). Driving simulators provide an opportunity to assess individuals in a standardized manner, as well as the unique ability to safely place individuals into emergency situations. Many studies have utilized the Doron

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Dr. Erin D. Bigler served as Action Editor during the course of this review.

Simulator (e.g., Galski et al., 1992; Rebok et al., 1995), in which a scene is projected onto a screen and the participant must use a driving console to react appropriately (e.g., press the brakes to make an emergency stop). Data from this simulator have been shown to be predictive of on-road scores (Galski et al., 1992). Most other simulations, on the other hand, are best characterized as reaction-time measures, in which the participant must, for example, press the accelerator pedal in response to a green light on the computer screen. These systems are frequently used as outcome measures in order to demonstrate that a patient population shows decreased driving skills, although the face validity of these instruments remains somewhat suspect. The simulation to be described in the present study expands upon prior methodologies by incorporating a prolonged (12-min), interactive drive in which the participant must constantly respond appropriately to environmental cues.

Research into the impact of medical conditions on driving have typically focused on older persons, especially patients with Alzheimer's disease or vascular dementias, and patients with traumatic brain injuries. Alzheimer's disease is generally accompanied by NP deficits that are of a "cortical" nature (e.g., deficits in language abilities, visuospatial skills, and memory), while impairments associated with cerebrovascular accidents and traumatic brain injury often have mixed cortical and subcortical features (Cummings & Benson, 1992). These driving studies have generally found that patients with these disorders are at increased risk for automobile accidents (e.g., Dubinsky et al., 1992b; Friedland et al., 1988) and perform worse in on-the-road tests (e.g., Fitten et al., 1995; Hunt et al., 1993), although a subset may retain adequate driving skills. Findings regarding NP predictors of driving abilities have been mixed as a result of varying methodologies, but the available evidence suggests that attentional and visuoperceptual–visuospatial deficits are significantly related to impaired driving skills (Johannson & Lundberg, 1997; Parasuraman & Nestor, 1993). The degree to which these findings are specific to these patient populations is unclear, however.

In contrast to the above-mentioned disorders, HIV-related NP impairment has a characteristic "subcortical" presentation (Becker et al., 1995; Martin, 1994; Monsch et al., 1995; Peavy et al., 1994). Most frequently affected are attention/speed of information processing, learning, and psychomotor skills (Heaton et al., 1995). Brain imaging (Jernigan et al., 1993; Rottenberg et al., 1987; Stout et al., 1998; Van Gorp et al., 1992) and neuropathology studies (Navia et al., 1986; Price & Brew, 1988) have shown that HIV has an affinity for subcortical gray and white matter, although the neocortical regions also are affected (Masliah et al., 1992; Wiley et al., 1991) and synaptodendritic integrity in the frontal cortex, assessed at autopsy, appears to be strongly related to *in vivo* NP functioning (Masliah et al., 1997).

Research on driving abilities in individuals with subcortical dementias has been limited to Parkinson's and Huntington's disease patients. Epidemiological studies of Parkinson's disease have found cognitively impaired persons to have significantly more motor vehicle accidents than cognitively intact individuals with Parkinson's disease (Dubinsky et al., 1991). Investigations utilizing driving simulators have suggested that slowed reaction time in some of these patients may place them at higher risk for accidents (Lings & Dupont, 1992; Madeley et al., 1990). In a study of patients with Huntington's disease, those who were still driving were more likely than controls to have been involved in an automobile accident in the previous 2 years (58 *vs.* 11%, respectively), and to perform more poorly on a driving simulator (Rebok et al., 1995).

To our knowledge, there is no research examining the effect that HIV-related cognitive deficits may have on driving abilities. Since HIV infection occurs primarily in relatively young individuals who are likely to be driving, this appears to be an important scientific and public health issue. The objectives of the current study were (1) to determine whether HIV-related cognitive impairment results in poorer driving abilities as assessed with a driving simulator, and (2) to identify specific NP abilities that are predictive of driving performance in this patient population. We hypothesized that individuals with NP impairment would perform more poorly on the driving simulator, and that, based upon prior research with other disorders, deficits in attention and complex perceptual–motor (including visuospatial) functioning would be most strongly associated with driving performance.

METHODS

Research Participants

Participants consisted of 68 HIV seropositive individuals enrolled in the San Diego HIV Neurobehavioral Research Center, an NIMH-funded study of the prevalence, features, course, and pathogenesis of HIV involvement in the CNS. All participants completed comprehensive medical, neurological, neuroradiologic, psychiatric and neuropsychologic assessments. Since the HNRC is a longitudinal study, some study participants had multiple NP evaluations prior to the simulator assessment (see Results). In all cases, we used the NP assessment closest to the time of the driving simulator evaluation. Exclusion criteria included history of non-HIV-related neurological disorder or medical disorder affecting the nervous system (e.g., head trauma with greater than 30 min loss of consciousness, epilepsy), schizophrenia, and active substance abuse. No participant had evidence of an HIV-related central nervous system opportunistic infection at the time of evaluation. The overall sample had a mean age of 37.0 (SD = 6.4) years and a mean of 13.4 (SD = 2.2) years of education. Eighty-four percent were male, and 16% female. Sixty-two percent were White, 21% African American, 13% Hispanic, and 4% of other ethnicity. The mean CD4 cell count for the sample was 270.8 cells/mm^3 (SD = 255.5). Thirty-one percent were medically asymptomatic or had generalized lymphadenopathy [Centers for Disease Control (CDC) Stage A], 43% had minor

https://doi.org/10.1017/S1355617799577011 Published online by Cambridge University Press

opportunistic infections, constitutional symptoms, and/or peripheral neuropathies (Stage B), and 26% had a history of an AIDS-defining illness (Stage C). Half of the sample ($n = 34$) met the diagnostic criteria for AIDS, either due to an AIDS-defining illness or a CD4 cell count below 200 (Centers for Disease Control, 1992).

All participants in this study had routinely driven an automobile. The mean number of years driving was 21.4 ($SD = 7.5$), with a range of 7 to 38 years of driving experience. The two participants with less than 10 years of driving experience were less than 25 years of age and had been driving since they were license-eligible. Ten participants were no longer routinely driving, either because they no longer owned a car ($n = 6$), had their license suspended ($n = 2$), or needed corrective lenses ($n = 1$). One participant did not provide information as to why he was no longer driving.

Procedure

Neuropsychological testing

All participants completed a detailed neuropsychological test battery administered by trained psychometrists. The 4-hr battery consisted of measures assessing the following eight domains:

1. *Verbal*: Boston Naming Test (Kaplan et al., 1983), Thurstone Word Fluency (Pendleton et al., 1982; Thurstone, 1938; Thurstone & Thurstone, 1962), Letter and Category Fluency (Borkowski et al., 1967)
2. *Abstraction*: Category Test (Halstead, 1947; Reitan & Davison, 1974), Trail Making Part B (Reitan & Davison, 1974; U.S. War Department, 1944)
3. *Perceptual–motor*: Trail Making Part A (Reitan & Davison, 1974; U.S. War Department, 1944), WAIS–R Block Design and Digit Symbol (Wechsler, 1981)
4. *Attention–speed of information processing*: Paced Auditory Serial Addition Test (Gronwall, 1977), WAIS–R Digit Span and Arithmetic (Wechsler, 1981)
5. *Learning*: Story Learning and Figure Learning (Heaton et al., 1991), California Verbal Learning Test (CVLT) Trials 1–5 (Delis et al., 1987)
6. *Memory*: Story Retention and Figure Retention (Heaton et al., 1991), CVLT Retention [1 − (long-delay recall/Trial 5) × 100; Delis et al., 1987]
7. *Motor*: Finger Tapping (Halstead, 1947; Reitan & Davison, 1974), Grooved Pegboard (Kløve, 1963)
8. *Sensory*: Sensory–Perceptual Exam (Reitan & Davison, 1974).

In keeping with the recommendations of the NIMH Working Group on Neuropsychological Assessment Approaches with HIV patients (Butters et al., 1990), a senior neuropsychologist (R.K.H.), blinded to HIV serostatus as well as the participant's performance on the driving simulations, rated NP test performance using demographic information, raw test scores and age-, education-, and gender-corrected standard scores (*T* scores; Heaton, 1992; Heaton et al., 1991). The clinician was presented with all testing data, including any prior assessments, in order to account for practice effects and to determine whether there was a significant clinical change from the prior evaluation. Performance ratings in each of the eight domains were assigned using the following 9-point scale: 1 = *above average functioning*, 2 = *average*, 3 = *below average*, 4 = *borderline/atypical*, 5 = *definite mild impairment*, 6 = *mild to moderate impairment*, 7 = *moderate impairment*, 8 = *moderate to severe impairment*, and 9 = *severe impairment*. Participants were also assigned a global neuropsychological rating using the same scale, with a global rating of 5 or above indicating abnormal neuropsychological functioning; a global rating in this range required a rating of at least 5 on a minimum of two of the eight ability areas (i.e., a single, isolated ability deficit would not qualify for a global rating within the *impaired* range). Previous studies have shown NP clinical ratings to be reliable and sensitive to brain dysfunction in a variety of clinical populations (Filley et al., 1990; Heaton et al., 1981, 1983, 1994a, 1995), and in HIV-infected subjects to be strongly related to *post-mortem* neuropathology findings (Masliah et al., 1997). Participants with a global rating less than 5 were considered to be within normal limits neuropsychologically (the *NP normal group*), and those with a rating of 5 or greater were classified as neuropsychologically impaired (the *NP impaired group*).

In addition, participants received a clinical neurocognitive diagnosis based on their NP status and the impact that NP impairments had on their everyday functioning (American Academy of Neurology AIDS Task Force, 1991; Grant et al., 1995). This diagnosis was assigned following a review of all NP, clinical, and laboratory data by a consensus diagnostic team consisting of a neurologist, a neuropsychologist, and a research clinical nurse. Participants who had no objective evidence of NP dysfunction were considered unimpaired, and those with NP impairment, but with no concomitant deficit in everyday functioning, were classified as subsyndromically impaired. A diagnosis of minor cognitive motor disorder (MCMD) was reserved for participants who demonstrated (1) objective findings of at least mild overall NP impairment, (2) symptoms of cognitive decline, using a standardized history and questionnaire regarding everyday functioning (Chelune et al., 1986), and (3) mild-to-moderate functional disability (such as impaired performance at home or work), present for at least 1 month, and not attributable to comorbidities. These consensus diagnoses were made prior to, and without knowledge of, driving simulator performance.

Driving simulations

Participants completed two PC-based driving simulations based on System Technology, Inc.'s STISIM (Rosenthal

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et al., 1995; Stein et al., 1992). The hardware consisted of a steering wheel with turn signal indicator, an accelerator pedal and a brake pedal. Simulated roadways, buildings, cars, and pedestrians were displayed on a VGA monitor. In order to minimize the effect that the novelty of the computer-based simulator might have on performance, participants underwent training to a specified criterion prior to taking each of the simulations. For example, they did not start the *Routine and Emergency Driving* simulation until they demonstrated that they could successfully pass a car and stop at a traffic light. Participants were presented with each of these scenarios individually, and were required to show proficiency by successfully completing each task three consecutive times.

The first simulation, *Truck Operator Performance System* (TOPS), is an 8-min program in which the participant is to drive down a straight highway, maintain a speed of 55 mph, and respond to occasional divided attention tasks in the upper corner of the screen (by using the turn signals). No other images (e.g., cars, pedestrians, etc.) are included in this simulation. At the conclusion of the simulation, the program identifies whether the participant passed or failed. This test is an abbreviated version of a simulation developed by Systems Technology, Inc. (Stein et al., 1992) which utilized performance data from fatigued truck drivers and drivers who had experimentally induced high blood alcohol levels to create five discriminant functions for the identification of impaired drivers. The investigators in the above study then established cutpoints for each of the discriminant functions; respondents were considered to have failed the simulation if they scored beyond the established cutpoint on any of the five functions. The procedure was then validated in a follow-up study using fatigued truck drivers. The current simulation utilizes similar discriminant functions provided by Systems Technology to determine failure.

The second program, *Routine and Emergency Driving*, was designed by the first author to simulate city–country driving. The participant drives at both city (35 mph) and highway (55 mph) speeds. During the course of the 12-min simulation drivers must pass cars, stop at traffic lights, follow a curving road, drive around stalled automobiles, and avoid potential accidents (e.g., a pedestrian stepping onto the road, a car in front slamming on its brakes). To ascertain how individuals perform with respect to accident avoidance, we included four scenarios in which the participant is placed in a situation requiring an aggressive maneuver to prevent an accident. Data regarding speed and accidents were automatically collected by the program, and the examiner made behavioral notes to clarify the conditions under which accidents occurred. To increase the utility of the instrument, we established a cutpoint for failing the simulation. Previous NP research has shown that a cutpoint in which 15% of normal controls are classified as impaired (85% specificity) provides an optimal trade-off between sensitivity and specificity in detecting individuals with and without brain lesions (Heaton et al., 1991). We therefore planned *a priori* to identify a cutpoint, based on the number of accidents, such that approximately 15% of NP normal participants were classified as impaired. In addition, we used this cutpoint in the analyses rather than the raw scores because of the relatively limited distribution of the number of accidents (0–5) on this brief simulation.

Statistical analyses

All variables were assessed for the presence of outliers and non-normal distributions prior to analysis. In the case of outliers, operationalized as 3.0 standard deviations from the group mean (Tabachnick & Fidel, 1989), the deviant score was modified (Winsorized) to be one measurement unit further from the mean than the next most deviant score in the distribution (Hawkins, 1980; Tabachnick & Fidel, 1989). The outlier thus remains usable for analysis and the extreme score in the distribution, but exerts less influence on the analyses. The following variables were Winsorized (1 case for each unless noted otherwise): Boston Naming Test, Tapping–Dominant Hand, Grooved Pegboard–Dominant Hand, Grooved Pegboard–Nondominant Hand (2 cases), Figure Retention, Trail Making Part B (2 cases), Sensory score (2 cases) and standard deviation of lane position on the TOPS program (3 cases). Because even limited missing data would significantly hamper multivariate analysis of potential predictors of driving abilities, missing NP test scores were imputed *via* estimates based on regression equations incorporating the other NP tests. The following variables include imputed values: Category errors (3 cases), FAS (5 cases), PASAT (6 cases), Tapping–Nondominant Hand (1 case), Figure Retention (1 case), Figure Learning (1 case), CVLT Sum of Trials 1 to 5 (9 cases), CVLT Retention (9 cases), Trail Making Part B (1 case), Arithmetic (4 cases), Digit Span (6 cases), Digit Symbol (4 cases), and the Sensory score (7 cases). The following variables were not normally distributed and were transformed: Boston Naming Test (square root of the reflected score), Sensory score (common log), and standard deviation of lane position (square root).

The odds ratio, or the probability of an event occurring versus the event not occurring, was calculated using logistic regression, with the NP normal subjects serving as the reference group. The "event" in these analyses was failure on TOPS or *Routine and Emergency Driving*. CD4 cell count and AIDS/non-AIDS status were included as control variables. Since none of the demographic variables (age, education, sex, and ethnicity) were associated with failure on either of the simulations, they were not included in the model.

Discriminant analysis was used to separate simulator failure from passing on NP tests. The groups being classified were pass–fail on TOPS and pass–fail on *Routine and Emergency Driving*. Potential predictors were first separated into groups of variables governed by a common theme (i.e., related NP tests). Multiple discriminant analyses were performed with each outcome of interest using each of the groups of related NP predictors. Each of those variables that showed significance in every group were then combined for the final analyses.

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Group comparisons on continuous variables were performed using analysis of variance. Chi-square analyses were used for categorical, nonparametric comparisons, with Fisher's exact test utilized when the expected cell frequency fell below 5. Since the hypotheses for this study stated that NP deficits would be associated with poor driving performance, analyses examining the relationship between NP performance and driving skills were performed using a one-tailed test. All other analyses are two-tailed tests. Statistical analyses were performed using SPSS (SPSS, 1994) and S-Plus (S-Plus, 1995).

RESULTS

Sixty-four participants had *Routine and Emergency Driving* data, 60 had TOPS data, and 56 had data for both simulations. Failure to have useable data on a simulation was primarily due to software or equipment malfunction on these relatively new tests; there was no apparent systematic bias with respect to missing data. All of the participants appeared to take the task seriously and not treat it as a video game. The time between NP testing and assessment on the driving simulator ranged from zero to 4.4 months, with most (57%) completing both evaluations on the same day (M = 14.0 days, SD = 27.9).

The primary analyses for this study involved comparisons between participants with and without NP impairment. Thirty-two (47.0%) participants were identified as being neuropsychologically impaired (NP impaired). Table 1 shows the demographic characteristics of the NP normal and NP impaired groups; again, the NP classifications were made on the basis of demographically corrected test scores, so group differences on demographic variables would not be expected. As can be seen in the table, the two groups were similar across all relevant demographic factors as well as HIV-disease status, although there was a trend for the NP normal group to be more immunosuppressed (i.e., to have a lower CD4 count) than the NP impaired individuals. Of the NP impaired participants, 23 (72%) were classified as mildly impaired (global rating of 5), 8 (25%) had mild-to-moderate impairment, and 1 (3%) was rated as moderately impaired. Twenty-five of the impaired participants received a diagnosis of subsyndromic impairment, and 7 were diagnosed with MCMD. None met criteria for HIV–associated dementia. The number of days between the NP and simulator evaluations for the NP normal and NP impaired groups was not significantly different (M = 9.9 and 18.6, respectively; p = .20). In this longitudinal cohort, the NP normal group had a higher number of previous exposures to the NP tests (M = 4.0, SD = 2.6) than the NP impaired group (M = 2.0, SD = 1.6; $p < .001$). NP test scores for the total NP impaired and NP normal groups are presented in Table 2; although group differences obviously do not constitute a finding, because participant grouping was based on presence or absence of NP impairment, the level and pattern of deficits in the NP impaired group are shown here.

Global NP Impairment and Simulation Performance

TOPS simulation

The NP impaired group had a higher failure rate than the NP normal group on the TOPS simulation [61.5 *vs*. 23.5%; $\chi^2(1, N = 60) = 8.8$, $p < .001$; Figure 1]. This difference does not appear to be due to any general severity of illness confound: even after controlling for level of immunosuppression (CD4 count) and disease status (AIDS–non-AIDS), NP impaired participants were significantly more likely to fail the TOPS simulation than were the NP normal participants [OR = 5.3, 95% CI (1.7, 17.0), p = .006]. NP impaired participants also were more likely than the NP normal participants to have difficulty maintaining their lane position (i.e., swerving) as assessed by the (square-root transformed) standard deviation of the lane position [M = 1.09 (SD = .16) *vs*. 1.0 (SD = .13); $t(58) = 2.5$, p = .008]. There were no significant group differences on the divided atten-

Table 1. Demographic and HIV disease characteristics for neuropsychologically normal (*NP normal*) and impaired (*NP impaired*) participants

Characteristic	NP normal (N = 36)		NP impaired (N = 32)		t	DF	p
Age**	36.3	(5.8)	37.7	(6.9)	−.85	66	.40
Education**	13.2	(2.2)	13.6	(2.2)	−.69	66	.50
CD4†	212.3	(176.3)	324.3	(322.5)	1.78	66	.08
Male‡	30	(84.4%)	27	(83.3%)			.91*
Non-White‡	12	(33.3%)	14	(43.4%)			.38*
CDC Stage							
A‡	12	(33.3%)	9	(28.1%)			
B‡	14	(38.9%)	15	(46.9%)			
C‡	10	(27.8%)	8	(25.0%)			.80*
AIDS‡	20	(55.6%)	14	(43.8%)			.33*

*Chi-square analysis. **Years; M (SD). †Cells/mm^3; M (SD). ‡n (%).

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Table 2. Group comparisons of participants rated as neuropsychologically normal (*NP normal*) and impaired (*NP impaired*) on neuropsychological tests

Score	NP normal ($N = 36$)		NP impaired ($N = 32$)		t	p
Verbal Clinical Rating	2.4	(1.0)	3.6	(1.4)	4.1	.0001*
Boston Naming	78.8	(6.9)	75.4	(7.6)	6.0	.02
Thurstone Word Fluency	59.6	(19.9)	46.1	(18.0)	8.6	.005
FAS	48.4	(10.8)	40.5	(11.2)	8.6	.005
Abstraction Clinical Rating	2.1	(.8)	4.1	(1.3)	7.6	<.0001*
Category Test (errors)	19.1	(15.6)	52.9	(25.8)	43.7	<.0001*
Trail Making Part B	58.5	(23.2)	79.4	(21.8)	14.6	.0003*
Attention/SIP Clinical Rating	2.3	(1.1)	4.4	(1.3)	7.3	<.0001*
Digit Span (scaled)	11.6	(2.5)	9.2	(2.2)	18.1	<.0001*
Arithmetic (scaled)	10.9	(3.0)	8.2	(2.7)	15.4	.0002*
PASAT (number correct)	145.2	(29.2)	94.0	(34.0)	44.5	<.0001*
Perceptual–Motor Clinical Rating	2.3	(.9)	3.8	(1.1)	6.3	<.0001*
Block Design (scaled)	11.9	(3.3)	9.0	(3.0)	14.4	.0003*
Digit Symbol (scaled)	10.2	(2.5)	7.2	(2.1)	28.0	<.0001*
Trail Making Part A	23.1	(8.7)	30.7	(8.9)	12.6	.0007*
Learning Clinical Rating	2.6	(1.2)	4.9	(1.4)	7.5	<.0001*
Story Learning	16.7	(6.4)	9.9	(5.9)	20.7	<.0001*
Figure Learning	13.7	(4.9)	6.5	(3.6)	46.8	<.0001*
CVLT Trials 1–5	57.5	(12.6)	46.3	(10.0)	4.0	<.0001*
Memory Clinical Rating	2.3	(1.2)	3.1	(1.2)	2.6	.01
Story % Retention	10.2	(9.5)	15.6	(12.6)	4.2	.04
Figure % Retention	5.2	(8.6)	8.6	(9.8)	2.3	.13
CVLT % Retention	4.9	(8.6)	15.7	(13.7)	3.9	.0002*
Motor Clinical Rating	2.7	(1.0)	4.1	(1.3)	5.0	<.0001*
Grooved Pegboard (Dom)	60.1	(7.5)	73.6	(10.3)	38.7	<.0001*
Grooved Pegboard (Non-Dom)	68.4	(10.6)	80.9	(10.5)	23.8	<.0001*
Finger Tapping (Dom)	54.2	(5.6)	48.9	(7.9)	10.5	.002
Finger Tapping (Non-Dom)	49.6	(5.6)	45.6	(7.4)	6.4	.01
Sensory Clinical Rating	2.0	(1.1)	3.3	(1.9)	4.1	.001
Sensory–Perceptual (errors)	.4	(.3)	.8	(.4)	16.9	.0001*

*Significant following Bonferroni correction (.05/28 tests = .0018).

tion subtask on the TOPS simulation (e.g., incorrect responses or response latencies).

Routine and Emergency Driving

The NP impaired group had more accidents than the NP normal group [$M = 2.3$ ($SD = 1.3$) and 1.5 ($SD = .9$); $t(62) = 3.00$, $p = .002$]. The two groups did not differ with respect to their average speed, the number of times they exceeded the speed limit, or the rate of running traffic lights. As discussed in the Procedures section, we established a cutpoint for failure on this test by identifying the number of accidents that would generate 85% specificity in NP normal participants (i.e., classifying 15% as impaired drivers). More than two accidents occurred in only 14.7% ($n = 5$) of the NP normal group, and this was used as the cutpoint for impairment. Utilizing this criterion, 40% of the NP impaired group failed this simulation, which was significantly higher than that for the NP normal group [$\chi^2(1, N = 64) = 5.2$, $p = .01$; Figure 1]. After controlling for level of immunosuppression and disease status, NP impaired participants were still more likely than NP normal participants to fail this simulation [OR = 6.1, 95% CI (1.5, 24.6), $p = .01$]. Since AIDS participants had more accidents on the *Routine and Emergency Driving* simulation than did non-AIDS participants [$M = 2.3$ ($SD = 1.4$) *vs*. 1.4 ($SD = .79$); $t(62) = 2.8$, $p = .008$], we confirmed the above findings by analyzing the simulator performance of NP normal and NP impaired participants separately *within* non-AIDS and AIDS participants. As with the overall sample, NP impaired participants performed worse on the simulations than did NP normal participants in both groups.

An examination of the situations in which accidents occurred showed that NP impaired participants had a higher rate of accidents across most emergency or increased-risk situations. These included situations in which the participants must avoid pedestrians crossing the road (33.3 *vs*. 2.8%, $p < .0001$), pass a car (33.8 *vs*. 13.9%, $p = .02$), adjust for cross-traffic (26.7 *vs*. 11.1%, $p = .025$), and react to traffic lights (13.3 *vs*. 0.0%, $p = .01$). There was no significant

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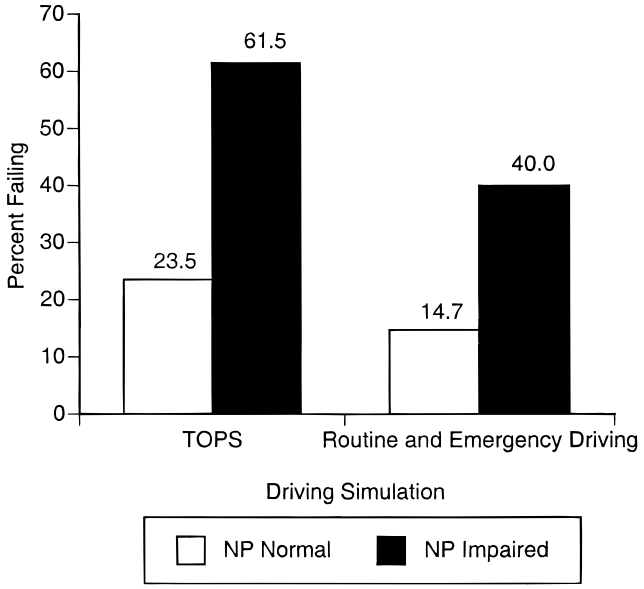

Fig. 1. Percent of neuropsychologically normal (NP normal) and impaired (NP impaired) participants failing each of the driving simulations.

difference in accident rates for the situation in which a car slams on its brakes in front of the participant (the task perhaps most dependent on reaction time). In this latter situation, two-thirds of both groups had accidents.

The Effect of Multiple NP Test Exposures

Because participants were assessed at different points during their involvement in the HNRC, and had varying numbers of exposures to the NP tests, we examined whether the relationship between NP impairment and driving performance varied as a result of the number of NP testings. A factorial analysis of variance using NP status (normal *vs*. impaired) and test exposure status (first exposure *vs*. follow-up testing) as the independent variables and simulator scores as the dependent variables showed that, while there was a significant main effect for NP status, there was no significant effect for exposure status nor was their an interaction between the two independent variables ($p > .5$). We also conducted an analysis of covariance using the number of exposures as a continuous measure in order to determine whether the *number* of exposures affected the relationship between global NP impairment and driving performance. As with the above analyses, the main effect for NP status remained significant. In each case, the p value for the covariate (number of exposures) was not significant ($p > .20$).

A similar set of analyses was completed for the impairment ratings on each of the eight NP domains. Of 32 analyses (eight domains, two simulator outcomes, and two types of analyses), an interaction ($p < .05$) between impairment classification and the number of exposures was found for only one NP domain (Learning). A correction for the multiple analyses would suggest that this finding should be given limited weight.

Relationship Between Neurocognitive Syndrome and Driving Performance

Again, the major difference between syndromic and subsyndromic NP impairment classifications is that the former require independent clinical evidence (i.e., independent of both NP testing and the simulator performance) that the participant's NP deficits are interfering with his or her everyday functioning. Since the number of participants in the current study diagnosed with MCMD was limited ($n = 7$ for TOPS, $n = 6$ for *Routine and Emergency Driving*), we only performed preliminary analyses examining global driving performance across neurocognitive classifications. There was no difference in the failure rates on TOPS between subsyndromically impaired and MCMD participants (57.1 and 63.2%, respectively; $p = .8$). However, on the *Routine and Emergency Driving* simulation, subsyndromically impaired participants had a mean of 2.1 ($SD = 1.3$) accidents, and participants with an MCMD diagnosis averaged 3.2 ($SD = 1.2$) accidents [$t(28) = 1.9$, $p = .035$, see Figure 2]. This simulation was failed by MCMD participants at twice the rate of subsyndromic participants (66.7 *vs*. 33.3%). Failure rates between subsyndromically impaired and MCMD participants did not differ significantly because of the small sample sizes ($p = .15$).

Concordance Among TOPS and Routine and Emergency Driving

The two simulations utilized in this study were designed to measure two very different aspects of driving: TOPS re-

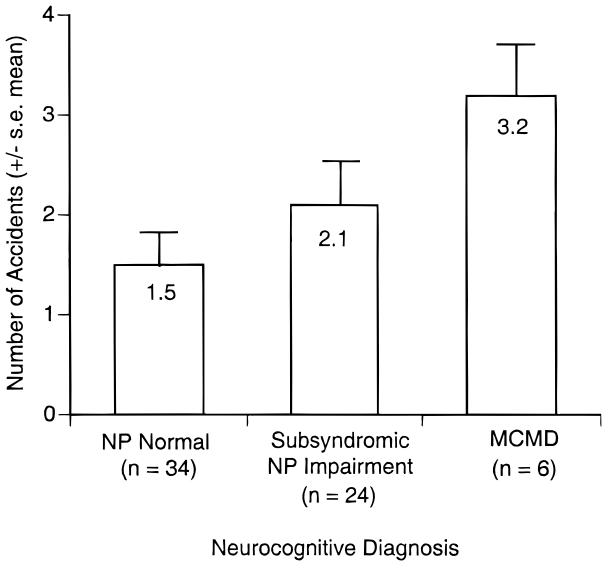

Fig. 2. Number of accidents on the *Routine and Emergency Driving* simulation by neurocognitive classification.

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quires the participant to perform straight-ahead, uneventful driving, while the *Routine and Emergency Driving* simulation is a more complex and difficult drive requiring accident avoidance maneuvers. Nonetheless, it is of interest to determine whether a participant who fails one simulation is likely to fail the other. We therefore compared *Routine and Emergency Driving* performance in participants who failed and passed the TOPS program. Despite the obvious differences in the nature of these simulations, a modest association in failure rates was found: Those who failed the TOPS simulation were more likely also to fail the *Routine and Emergency Driving* (using the cutpoint of more than 2 accidents) than those who passed the TOPS simulation [40.9 *vs*. 14.7%; $\chi^2(1, N = 56) = 4.9$, $p = .03$].

On-the-Road Driving History

NP impaired and NP normal participants drove a similar reported number of miles in the past year (*M*s of 8,213 *vs*. 9,118 miles, respectively; $p = .74$), The incidence of reported accidents in the last year did not differ between groups (11.1% for NP impaired, 17.1% for NP normal; $p = .50$). Of these accidents, only two were considered "not minor," both of which occurred in the NP impaired group. NP impaired participants were more likely to not be currently driving than the NP normal participants [27.6 *vs*. 5.7%; $\chi^2(1, N = 64) = 5.8$, $p = .02$], and the NP impaired participants who were not driving tended to perform worse on the simulations than those who still were driving (e.g., those who were no longer driving ($n = 7$) averaged 3.1 simulator accidents, compared to 2.1 simulator accidents for those who continued to drive ($p = .07$). Since it is possible that the reduced performance on the driving simulator in the NP impaired group was a result of less frequent driving, we reran the above analyses excluding those participants who were no longer driving. The same pattern of results was found, with NP impaired individuals having higher failure rates on both simulations.

Demographic and Clinical Predictors of Driving Performance

On TOPS, there were no significant differences between participants passing or failing the simulation with respect to age, education, sex, CD4 cell counts, percent with an AIDS diagnosis, or ethnicity. On *Routine and Emergency Driving*, there were no age, education, sex, or ethnicity differences. However, compared to participants who passed this simulation, those who failed had a higher prevalence of an AIDS diagnosis [76.5 *vs*. 38.3%; $\chi^2(1, N = 64) = 7.3$, $p = .007$], and a trend towards a lower CD4 count [$M = 178.9$ ($SD = 192.8$) *vs*. 314.7 ($SD = 277.6$); $t(61) = 1.9$, $p = .07$].

Clinical ratings of domain-specific functioning

We examined domain-specific clinical ratings in participants passing and failing the driving simulations in order to identify which NP ability areas were associated with performance on the computer simulations. Participants failing TOPS (24/60) had higher impairment rates than those passing this simulation in the areas of Abstraction [41.7 *vs*. 13.9%; $\chi^2(1, N = 60) = 5.9$, $p = .007$], Attention–Speed of Information Processing [43.5 *vs*. 16.7%; $\chi^2(1, N = 59) = 5.1$, $p = .012$], and Motor Abilities [41.7 *vs*. 11.1%; $\chi^2(1, N = 60) = 7.5$, $p = .003$], and there was a trend for a greater failure rate on Sensory [30.0 *vs*. 8.8%; $\chi^2(1, N = 54) = 4.1$, $p = .05$] and Complex Perceptual–Motor Abilities [29.2 *vs*. 11.1%; $\chi^2(1, N = 60) = 3.1$, $p = .08$; Figure 3]. Verbal Functioning, Learning, and Memory (retention over a delay) were not significantly associated with driving performance. Because poor motor and sensory functioning were related to poor performance on the simulator, we excluded those participants who were found to have a peripheral neuropathy during the medical examination ($n = 3$). This did not significantly alter the results.

Participants failing the *Routine and Emergency Driving* simulation had significantly greater impairment in the Abstraction domain [41.2 *vs*. 17.0%; $\chi^2(1, N = 64) = 4.1$, $p = .049$], as well as a trend for a higher impairment rate in Attention–Speed of Information Processing [41.2 *vs*. 21.7%; $\chi^2(1, N = 63) = 2.4$, $p = .11$; see Figure 4].

Specific NP tests as predictors of simulator performance

Although many of the individual NP tests correlated with performance on the simulations, we followed the procedures detailed in the Statistical Analysis section to identify which combinations of tests were the best predictors of simulator performance, controlling for shared variance. With respect to passing or failing the TOPS simulation, the final model accounted for 20% of the variance ($p = .002$) and

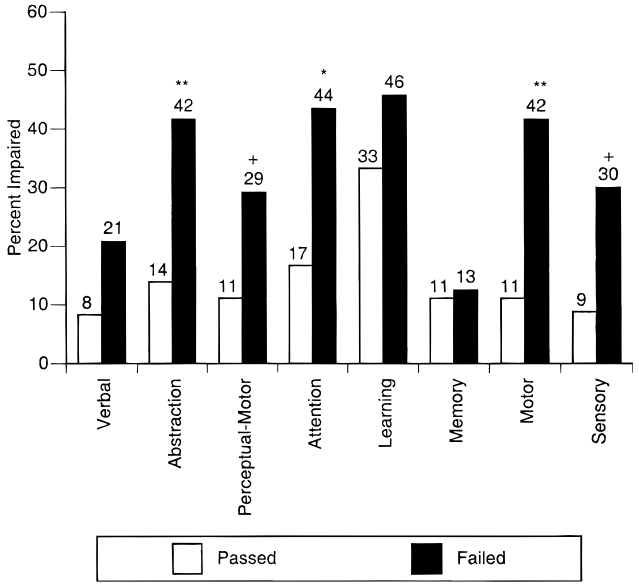

Fig. 3. Domain-specific impairment profiles for participants passing–failing TOPS.

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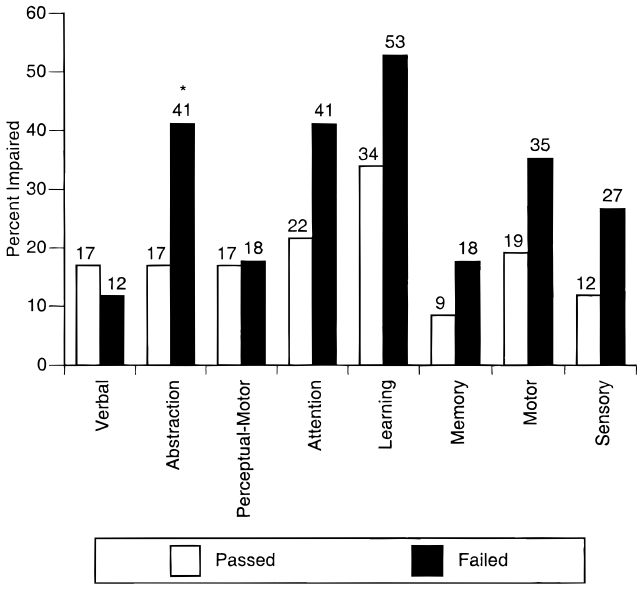

Fig. 4. Domain-specific impairment profiles for participants passing–failing *Routine and Emergency Driving.*

included a test of attention–speed of information processing (PASAT; $p = .007$) and motor skills (Finger Tapping; $p = .04$). The final model for predicting the amount of "swerving" (standard deviation of lane position) on the TOPS simulation consisted of measures of complex perceptual–motor functioning (WAIS–R Block Design, $p = .013$), fine motor skills (Grooved Pegboard, $p = .023$) and simple motor speed (Finger Tapping, $p = .14$), and accounted for 30% of the variance in this variable ($p < .001$).

Lastly, we sought to identify NP predictors of performance on *Routine and Emergency Driving* (pass–fail according to the number of accidents). Measures of Motor Functioning (Finger Tapping, $p = .024$), nonverbal memory (Figure Retention, $p = .071$), and Attention (WAIS–R Digit Span, $p = .13$) were included in the final model, which accounted for 13% of the variance in accidents ($p = .04$).

DISCUSSION

This study is the first to report on driving abilities in HIV-infected individuals. Our primary hypothesis, that individuals identified as having NP impairment would perform significantly worse on computerized driving simulations, was confirmed. The poor performance by the NP impaired individuals held even after controlling for medical symptomatology, suggesting that the decrement in driving skills is not simply the result of general disease progression. Those participants with a diagnosis of HIV-related minor cognitive motor disorder, in which NP impairment is coupled with other difficulties with everyday functioning, appeared to have the most difficulty on the simulations. In general, the impact of NP impairment on the *Routine and Emergency Driving* simulation was evidenced in driving tasks requiring the integration of complex cognitive and motor skills (e.g., passing a car), and not simply on accident avoidance tasks requiring intact reaction time.

The *Routine and Emergency Driving* simulation used in the current study differs from other simulator studies in that it involved a 12-min commute requiring negotiating situations involving other traffic, pedestrians, signal lights, and road signs. Most simulator studies typically present a series of brief, single-task driving situations in which the participant is to take only relatively simple decisive actions (e.g., turn the steering wheel). We would suggest that the simulation used in the present study, in which the person must navigate routine, albeit risky, situations (e.g., passing a car) and respond to sudden, unexpected hazards during a generally uneventful drive better mimics real-world driving and may potentially prove to be a better indicator of an individual's on-road performance. Maintaining concentration, reacting to pedestrians and other distractors (e.g., other cars and road signs), remembering speed limits, etc., during the 12-min drive may well stress an impaired individual's cognitive resources and reveal deficits that are not detectable under less taxing conditions.

On the other hand, the presentation of *four* emergency situations during a 12-min drive arguably stresses or challenges the driver more than anything typically encountered in real, on-road driving. In the design of this simulation, we attempted to obtain an adequate sampling of accident avoidance behavior within a relatively brief time period. We felt that fewer than four trials may not provide adequate sensitivity. The group differences obtained in this study provide some support for the sensitivity of this simulation. However, we emphasize that even NP normal, HIV-infected participants averaged 1.5 "accidents" (errors) on this task. Clearly, therefore, such errors by themselves cannot be interpreted as indicating unsafe driving in the real world.

The finding of reduced driving skills in this HIV-infected cohort is consistent with reports that individuals with other subcortical brain diseases such as Parkinson's disease (Dubinsky et al., 1991, 1992a; Lings & Dupont, 1992; Madeley et al., 1990) and Huntington's disease (Rebok et al., 1995) frequently evidence a decrement in driving abilities. These studies utilized simulators and/or driving histories in their analyses. In the current study, we found NP impairment to be associated with poor performance on the simulator, but not self-reported accidents in the past year. There are at least three possible reasons for this discrepancy between test performance and on-road driving history. It is not unusual for individuals with impaired driving abilities to limit or altogether stop driving, either of their own volition or with encouragement from significant others or medical professionals (e.g., Rebok et al., 1995; Trobe et al., 1996). This frequently has been cited as a factor in failing to find increased accident rates in demented individuals. Indeed, a larger percentage of NP impaired participants in this study had ceased driving and thus it was not possible to include these individuals in the analysis of recent driving history. Since these individuals did not cite neurocognitive or medical reasons for limiting their driving, however, the hypothesis that they

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have stopped driving due to declining driving abilities cannot be confirmed. It is also possible that since the participants in the current study had neurocognitive impairment in the mild or mild-to-moderate range, and none met criteria for HIV-associated dementia, the reduction in driving ability was not of sufficient severity to translate into a significant increase in on-road accidents. Accidents are relatively rare events, partly due to defensive practices of others on the road, and it would be difficult to ascertain a meaningful difference in this relatively small cohort. Lastly, of course, it is possible that the participants' self-reported number of accidents was not accurate, and this may be especially true of individuals with cognitive impairment.

Investigations of the relationship between specific NP tests and driving have met historically with mixed results. It has been posited that attentional abilities are a critical factor in driving (Parasuraman & Nestor, 1993), and many of the studies that utilize attentional measures have found them to be important predictors of driving performance. Visuoperceptual functioning is also frequently cited as an important predictor. Of the studies examining driving performance in subcortical diseases, only Rebok et al. (1995), in an investigation of Huntington's disease, attempted to predict simulator performance using NP tests. These authors found moderate correlations between test results on a driving-related cue recognition task (similar to a choice reaction time test) and performance on the Hopkins Verbal Learning Test and WAIS–R Block Design, but none of the tests in their NP battery was correlated with performance on a different driving simulation that more closely approximated an actual drive.

In a study with Alzheimer's patients, Hunt and colleagues (Hunt et al., 1993) found performance on a road test to be closely related to attention, language, and visuoperceptual abilities. Fitten et al. (1995) reported that short-term memory (Sternberg test), visual tracking, and Mini-Mental Status Exam scores were highly predictive of on-road drive scores for participants with Alzheimer's or vascular dementia. In another study, the performance of Alzheimer patients on the Iowa Driving Simulator was most strongly predicted by a single visuospatial task (the copy task of the Rey–Osterrieth Complex Figure Test; Rizzo et al., 1997). Odenheimer et al. (1994) related NP test performance of elderly and demented (AD and vascular dementia) patients to an on-road test and found strong correlations with visuospatial tasks and attentional measures. A number of these studies with older impaired individuals have also found correlations between language skills and on-road performance; most authors attribute this to difficulty following verbal instructions during the drive.

In the present study, the hypothesized relationship between driving performance and attention and visuospatial functioning was partially confirmed. Clinically rated impairment in Attention–Speed of Information Processing was related to poor performance on TOPS, and specific attentional measures (PASAT, Digit Span) contributed to the prediction of performance on the two simulations. Surprisingly, and in contrast to many of the studies previously cited, visuospatial (perceptual–motor) skills related only modestly to driving skills as assessed on the TOPS simulation.

Comparisons between studies are complicated by variations in NP test selection (most other studies utilized briefer test batteries), the use of different driving outcome measures (driving ability may be operationalized as performance on a simulator or road test, or a review of a person's driving history), cohort differences in the level of cognitive deficits (the present study examines performance in individuals with generally mild NP deficits), and, of course, the underlying neurological disorder.

The diversity of the tasks involved during the simulations in the current study, including accident avoidance maneuvers, likely draw on multiple cognitive domains and thus may hinder attempts to relate individual NP tests to driving performance. Furthermore, a characteristic of most neurobehavioral disorders (including those due to HIV infection) is that multiple abilities typically are affected. Considered together with the multiple abilities required to drive skillfully and safely, it may not be fruitful to look for a single most important ability or test: Different individuals may have different patterns of deficits, and may fail driving tasks for different reasons.

Consistent with this view, we found impairment in abstraction (executive functioning), attention–speed of information processing, complex perceptual–motor, motor, and sensory functioning to be associated with poor performance on the simulations. This suggests that several cognitive and noncognitive abilities must be intact for adequate driving skills, including the ability to pay attention, think–react quickly and plan and organize one's performance. Specific NP tests that related most to driving performance included the PASAT, Digit Span, Block Design, Finger Tapping, Grooved Pegboard, and Figure Retention. It was surprising to find the strong relationship between even a simple motor task (Finger Tapping) and performance on the simulators. HIV has a predilection for the subcortical brain structures, particularly the basal ganglia, and the concomitant motor slowing may significantly impact driving skills. Since other studies have not typically assessed motor and sensory functioning in this manner, at this point it is difficult to ascertain whether this is unique to HIV infection or simply an understudied phenomenon in other clinical disorders.

Different combinations of the NP measures accounted for 13 to 30% of the variance in simulator performance. This general range of predictability is consistent with findings of other studies with other neurologic diseases, although some studies (e.g., Fitten et al., 1995; Galski et al., 1992) have been able to use NP tests to predict a significantly greater amount of the variance in an on-road driving score (scores that often range from 0–40 or higher). The current analyses were likely limited in part by the fact that two of the three outcome variables were dichotomous (pass–fail). This was done both in order to increase the clinical interpretability of the analyses, and due to the limited number of accidents that occurred during the city driving simulation. A limita-

tion of pass–fail ratings was demonstrated by Fox et al. (1997), who examined how accurately clinicians (a physician and a neuropsychologist) could predict a participant's on-road performance. While NP performance tests and clinician predictions were marginally related to a continuous, on-road driving score, they were not predictive of whether an individual actually passed or failed the driving evaluation.

There are limitations to the present study. Using NP performance to predict driving was potentially hindered by the fact that many of the participants, all of whom were part of a longitudinal study, had been exposed to the NP tests numerous times and practice effects may have resulted in some attenuation in the correlation with driving performance. Thus, tests that have substantial practice effects on repeated administration (e.g., Category Test), may well be predictive of driving performance when given for the first time. Although it was not ideal that participants differed in terms of numbers of exposures to NP tests at the time of the simulator study, to the extent we could judge, it appears that the number of such prior exposures did not systematically influence the relationship between NP impairment and simulator failures. Regardless, it is unlikely that the repeated exposures resulted in measures being falsely identified as related to driving performance.

Unfortunately, there is only limited validation data on the TOPS program, and no normative data on these simulations, and thus we cannot equate simulator performance in the current cohort with what might be found in the general population. Although HIV-infected individuals with mild-to-moderate NP impairment may perform more poorly than their cognitively intact peers, it is possible that their driving is no worse than other, typically competent drivers (e.g., normal elderly individuals). And, importantly, these simulations have yet to been shown to be predictive of typical on-the-road driving. Although TOPS has been used to detect fatigue and alcohol effects in long-haul truck drivers, there is as yet no evidence regarding its utility for determining impairment in nonprofessional drivers. In addition, while efforts were made to create situations within the *Routine and Emergency Driving* simulation that mimicked real driving, no on-road validation of this program is currently available.

It should be noted, however, that simulators such as the one used in this project do offer some advantages over on-road tests. On-road evaluations of impaired patients can be dangerous, expensive in terms of time and money, and unreliable (Croft & Jones, 1987). In addition, while individuals may maintain adequate abilities for routine driving, subtle NP impairments may affect driving performance/safety when the person faces an emergency. It is not practical, or ethical, to create these situations utilizing a real vehicle with the risk of real accidents. The use of a computer driving simulator thus provides a safe, and perhaps sensitive, method of assessing the degree to which neurobehavioral deficits impair driving ability.

Recent estimates put the number of individuals with HIV–AIDS in the United States at 650,000 to 900,000 (Karon et al., 1996). If, as many researchers find, between 30 to 50% of these individuals, depending on stage of illness, have objectively determined cognitive deficits, then the public health impact of these deficits could be significant. However, clearly it would be inappropriate to make patient care or public health decisions based upon the current findings. An analogy can be found in studies of Alzheimer's patients and driving. Based on evidence that Alzheimer's patients were at a substantially increased risk of driving accidents relative to matched controls, Friedland et al. (1988) recommended that patients with this diagnosis not drive an automobile. A number of investigators called into question this recommendation and presented survey (Drachman & Swearer, 1993; Trobe et al., 1996) and road test (Hunt et al., 1993) data suggesting that a subset of patients continue to maintain acceptable driving skills. It was generally concluded that a diagnosis of Alzheimer's disease alone should not be considered adequate reason to rescind a patient's drivers license.

Similarly, in the current study only a subset of the HIV-infected individuals with documented NP impairment did more poorly on the simulations than neurocognitively intact subjects. NP impairment alone should not necessarily preclude driving in HIV-seropositive patients, although greater severity (especially in the ability areas mentioned above) should increase concern. Also, especially if there is independent clinical evidence that such deficits are affecting other aspects of everyday functioning, the presence of cognitive impairment might justify referral for on-the-road testing. Clearly, more research is needed to better establish the sensitivity and specificity of NP deficits in predicting driving impairment in HIV infection and other disorders.

ACKNOWLEDGMENTS

The authors wish to thank Theodore Rosenthal and Zareh Parseghian of Systems Technology, Inc. for their assistance with the driving simulator. The HIV Neurobehavioral Research Center (HNRC) is supported by Center award P50-MH 45294 from NIMH. The San Diego HIV Neurobehavioral Research Center (HNRC) group is affiliated with the University of California, San Diego, the Naval Hospital, San Diego, and the San Diego VA Healthcare System, and includes: Igor Grant, M.D., Director; J. Hampton Atkinson, M.D., Co-Director; Thomas D. Marcotte, Ph.D., Center Manager; James L. Chandler, M.D. and Mark R. Wallace, M.D., Co-Investigators Naval Hospital San Diego; J. Allen McCutchan, M.D., P.I. Neuromedical Component; Stephen A. Spector, M.D., P.I. Virology Component; Robert K. Heaton, Ph.D., P.I. Neurobehavioral Component; Terry Jernigan, Ph.D. and John Hesselink, M.D. ., Co-P.I.s Imaging Component; Eliezer Masliah, M.D., P.I. Neuropathology Component; J. Allen McCutchan, M.D., J. Hampton Atkinson, M.D., and Ronald J. Ellis, M.D., Ph.D., Clinical Trials Component; Daniel R. Masys, M.D., P.I. Data Management Unit; Ian Abramson, Ph.D., P.I. Statistics Unit; Julie Nelson, B.A., Data Manager. The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, nor the United States Government. Portions of this paper were presented at the Twenty-

fifth Annual Meeting of the International Neuropsychological Society, February 5–8, 1997, in Orlando, Florida.

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https://doi.org/10.1017/S1355617799577011 Published online by Cambridge University Press