

# Cognitive Complaints, Depression, Medical Symptoms, and Their Association With Neuropsychological Functioning in HIV Infection: A Structural Equation Model Analysis

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The main objective of this study was to use structural equation modeling (SEM) to clarify the relationship between subjective cognitive complaints and neuropsychological functioning in 160 adults with HIV infection. Participants completed questionnaires assessing cognitive complaints, symptoms of depression, and HIV-related medical symptoms. Neuropsychological tests included measures of attention, verbal fluency, psychomotor skills, learning, memory, and executive skills. SEM was used to test models of the relationships among cognitive complaints, mood, and medical symptoms with neuropsychological functioning. The model indicated that although depressed mood ( $\beta = 0.32, p < .01$ ) and medical symptoms ( $\beta = 0.31, p < .01$ ) influenced cognitive complaints, cognitive complaints were independently associated with poorer neuropsychological performance ( $\beta = 0.39, p < .01$ ). Mood and medical symptoms were significantly correlated but were not significantly associated with neuropsychological skills.

Self-reported cognitive symptoms, or cognitive complaints, are a potentially important indicator of neuropsychological functioning. They communicate an individual's perception of his or her neuropsychological impairments or deficits and their impact on everyday activities (Gordon, Haddad, Brown, Hibbard, & Sliwinski, 2000). Subjective cognitive complaints often affect both diagnosis and treatment decisions because clinicians rely on patient report as

an important source of information. Nonetheless, the clinical utility of subjective cognitive complaints as indicators of cerebral functioning has not been clearly established. Findings in the literature regarding the accuracy of cognitive complaints in predicting neuropsychological status have been inconclusive, and they suggest that cognitive complaints may stem from a number of different sources.

The present study was designed to clarify the relationship between cognitive complaints and neuropsychological skills in a sample of participants with HIV infection or AIDS by using a different, and potentially more robust, methodological approach than used in previous studies. Increased knowledge regarding the clinical significance of cognitive complaints in HIV/AIDS or in other neurological conditions will augment the ability of clinicians to identify early neuropsychological impairment in those individuals who are at risk, particularly when combined with results from a complete neuropsychological assessment. It is especially important to identify neuropsychological complications early in the course of a disease because the potential for effective rehabilitation may be greater than in more cognitively compromised individuals in whom there is often additional medical morbidity present.

The accuracy of cognitive complaints is particularly critical in persons with HIV infection because neuropsychological impairment in the initial stages of HIV infection is mild and "spotty" (Heaton et al., 1995; Hinkin, Castellon, Van Gorp, & Satz, 1998). Consequently, standard neuropsychological tests may not be sensitive enough to detect the subtle neuropsychological deficits present in the early stages of the

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disease (Sahakian et al., 1995). Subjective cognitive complaints may include decreased attention and concentration, forgetfulness, difficulty completing more than one task simultaneously, and slowed thinking (Gibbs, Andrewes, Sz mukler, Mulhall, & Bowden, 1990; Hinkin et al., 1998; Maj et al., 1994; Mehta et al., 1996). Such complaints tend to be more frequently reported in symptomatic individuals relative to asymptomatic individuals and relative to control participants who are HIV negative (Gibbs et al., 1990; Maj et al., 1994; Mehta et al., 1996; Saykin et al., 1991). In some cases, particularly when mood disturbance is present, individuals with HIV infection may continue to perform within normal limits on neuropsychological measures, despite the presence of significant cognitive complaints (Hinkin et al., 1998; Rourke, Halman, & Bassel, 1999a, 1999b). As in other populations, subjective cognitive complaints in HIV infection may be influenced by many variables; they may accurately reflect neuropsychological dysfunction, depressed mood, systemic medical illness, or combinations of these or other factors.

Research findings regarding the accuracy of subjective cognitive complaints in HIV infection have been mixed. Some research groups have reported good agreement between perceived neuropsychological functioning and performance on standardized neuropsychological tests (e.g., Mapou et al., 1993; Poutiainen & Elovaara, 1996; Rourke, Halman, & Bassel, 1999a). Other studies have demonstrated poor concordance between cognitive complaints and actual test performance; cognitive complaints were instead significantly related to psychiatric symptomatology (Moore et al., 1997; Van Gorp et al., 1991; Wilkins et al., 1991). Mixed findings may reflect both methodological differences across studies (Beason-Hazen, Nasrallah, & Bornstein, 1994; Heaton, Kirson, Velin, Grant, & the HIV Neurobehavioral Research Center [HNRC] Group, 1994; Van Gorp, Lamb, & Schmitt, 1993; Wilkins et al., 1990) and failure to consider the interrelationships among multiple factors contributing to cognitive complaints (Lopez, Wess, Sanchez, Dew, & Becker, 1998), such as neuropsychological impairments, mood, and systemic medical illness. Results of these studies suggest that there may be multiple sources of variance contributing to neuropsychological symptoms in HIV infection. Moreover, subgroups of individuals who are HIV positive may vary in the accuracy of their self-reported cognitive complaints (Hinkin et al., 1996; Rourke et al., 1999b).

In order to resolve discrepancies in the literature and clarify the nature of the relationship between subjective cognitive complaints and neuropsychological functioning in individuals with HIV infection, the present study examined the interrelationships among the multiple sources of variance potentially affecting cognitive complaints. The rationale was that the relationship between cognitive complaints and neuropsychological functioning would be less equivocal when the influence of additional factors (i.e., systemic medical illness and mood disturbance) was statistically taken into consideration. To address the main objective of this study, we constructed a model and tested it using multivariate modeling techniques (i.e., structural equation

modeling; SEM), which afforded the opportunity to examine both independent and interactive effects of variables influencing cognitive complaints.

We made the following predictions: (a) Depressed mood and medical symptoms would be significantly associated with each other, and both would be significantly associated with subjective cognitive complaints; (b) medical symptoms and mood would be significantly associated with neuropsychological skills indirectly through their influence on or relationship with cognitive complaints; and (c) cognitive complaints would be significantly associated with neuropsychological skills.

## Method

### Participants

Participants in the study were 160 adults with HIV infection (151 men and 9 women) who are part of an ongoing study of neurobehavioral functioning in a sample of over 250 cases of adults with HIV/AIDS at St. Michael's Hospital in Toronto, Ontario, Canada. Participants for this study were excluded if they had a history of central nervous system (CNS) opportunistic infection, neurological condition (e.g., seizure disorder), head injury with loss of consciousness exceeding 30 min, significant substance abuse or dependence in the past 3 months, or significant developmental problems (e.g., diagnosed learning disability). All participants had completed a 3–4 hr neuropsychological assessment that included several behavioral questionnaires, including self-report measures of depressive symptoms, HIV-related medical symptoms, and subjective cognitive complaints. Recruitment and testing of the participants was approved by the St. Michael's Hospital Research Ethics Board.

In the total sample ( $N = 160$ ), 17 were asymptomatic (CDC-A), 45 were mildly symptomatic (CDC-B), and 98 had AIDS-defining illnesses or CD4 counts less than 200 (CDC-C) as defined by the 1993 *Centers for Disease Control (CDC) Revised Classification System* (CDC, 1992) for HIV infection. Mean CD4 count and plasma viral load characteristics for the sample are presented in Table 1. Eighty-two percent of the sample was receiving antiretroviral treatment at the time of assessment, with 70% on highly active antiretroviral treatment (HAART) as defined by Carpenter et al. (2000).

Demographic characteristics of the sample, including age, education, and mean scores on questionnaires assessing mood, medical symptoms, and subjective cognitive complaints, are summarized in Table 1. The mean age was 40.86 years ( $SD = 7.89$ ), with a mean of 14.41 ( $SD = 2.73$ ) years of education. Mean Beck

Table 1  
*Demographic Characteristics and Symptoms*

Variable	<i>M</i>	<i>SD</i>
Age (years)	40.86	7.89
Education (years)	14.41	2.73
Recent CD4 lymphocyte count <sup>a</sup>	358.42	231.91
% with undetectable viral load (< 500)	48	
Beck Depression Inventory score	18.08	10.05
HIV medical symptom score	2.64	1.93
Cognitive symptom (PAOF) score	50.57	25.89

*Note.* PAOF = Patient's Assessment of Own Functioning Inventory.

<sup>a</sup>  $n = 156$ .

Depression Inventory (BDI; Beck & Steer, 1993) total score was 18.08 ( $SD = 10.05$ ), indicating that the group had mild to moderate depressive symptomatology. In comparison to the original study of the Patient's Assessment of Own Functioning Inventory (PAOF; Chelune, Heaton, & Lehman, 1986), mean cognitive complaints in the present sample were elevated relative to a neurologically normal control group but roughly comparable to a large comparison group of patients with neurological and psychiatric conditions.

Mean scores on neuropsychological measures are displayed in Table 2. Mean estimated Verbal IQ, based on the American National Adult Reading Test (ANART; Grober & Sliwinski, 1991), was in the high average range at 111.26 ( $SD = 26.54$ ). Mean scaled scores on the Information ( $M = 11.08$ ,  $SD = 3.33$ ) and Picture Completion ( $M = 10.30$ ,  $SD = 2.62$ ) subtests of the Wechsler Adult Intelligence Scale—Revised (WAIS-R; Wechsler, 1981) were in the average range. Cases with missing data on any variable included in the model were excluded from the analyses.

### Procedure

All participants in this study completed neuropsychological tests, the BDI, a 12-item HIV-related medical symptom inventory (modified from Gorman et al., 1991; Kalichman, Sikkema, & Somlai, 1995; and Rabkin, Ferrando, Jacobsberg, & Fishman, 1997), and the PAOF. We used the sum of the first 13 items of the BDI (i.e., the cognitive-affective symptoms) in the model as a measure of depression. We chose this constellation of symptoms because the latter items on the BDI (i.e., the remaining 8 somatic symptoms) may be confounded by the physical effects of HIV infection (Castellon, Hinkin, Wood, & Yarema, 1998; Kalechstein, Hinkin, Van Gorp, & Castellon, 1998). The medical symptom inventory assessed the presence or absence of common HIV-associated symptoms within the past week. Symptoms assessed included fatigue, oral thrush, night sweats, diarrhea, persistent fever, headaches, weight loss, skin rash, cough, sore throat or

mouth, skin abnormalities, and shortness of breath. Subjective cognitive complaints were assessed by the PAOF. The PAOF is a self-report questionnaire of symptoms in various neuropsychological domains that was "designed to elicit patients' self-perceptions regarding the adequacy of their functioning in various everyday tasks and activities" (Chelune et al., 1986, p. 96). Item selection for the PAOF was based on the neuropsychological domains typically assessed in neuropsychological test batteries, as well as common cognitive complaints identified through clinical experience. The items are arranged in eight scales, which were "rationally grouped . . . according to the general nature of the abilities" in question (Chelune et al., 1986, p. 96). These scales include memory (10 items), language and communication (9 items), motor and sensory-perceptual skills (5 items), and higher level cognitive and intellectual functions (9 items; Chelune et al., 1986). Participants rate the frequency of cognitive complaints on a 6-point Likert-type scale (with endpoints ranging from *almost never* to *almost always*). Scores can be tabulated for each of the four neuropsychological domains separately, and a total score is summed across neuropsychological domains.

Neuropsychological measures were selected according to guidelines developed by the National Institute of Mental Health Workshop on Neuropsychological Assessment Approaches of AIDS-related Cognitive Changes (Butters et al., 1990). Neuropsychological test data included scores on the ANART; WAIS-R Information, Picture Completion, Digit Span, and Digit Symbol subtests; Trail Making Test—Parts A and B (Reitan & Wolfson, 1993); Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983); phonemic fluency (*F*, *A*, and *S*) and category fluency (animals, fruits, and vegetables; Spreen & Strauss, 1991); Finger Tapping and Grooved Pegboard Test (Heaton, Grant, & Matthews, 1991); California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987); Figure Memory Test (Heaton, Grant, & Matthews, 1991); Wisconsin Card Sorting Test (Heaton, Chelune, Talley, Kay, & Curtiss, 1993); and Symbol Digit Modalities Test (Smith, 1982).

Clinical ratings of neuropsychological test performance (clinical NP ratings) were computed for each of the participants by a licensed psychologist specializing in clinical neuropsychology (Sean B. Rourke). The method for determining these ratings was outlined by Heaton, Grant, Anthony, and Lehman (1981), and their specific utility in the study of HIV infection was described in Heaton et al. (1994, 1995). Clinical NP ratings were based on a 9-point scale for six major skill areas: attention, learning efficiency, memory (i.e., retention), verbal skills, executive skills, and psychomotor skills. Global clinical NP ratings describe overall neuropsychological functioning, with ratings of 5 or greater indicating clinically significant neuropsychological impairment. Interrater reliability of the clinical NP ratings in this sample was assessed by randomly selecting a subset of 60 cases (38% of sample) to be rated by a second rater (Sherri L. Carter). Interrater reliability was evaluated for ratings dichotomized as neuropsychologically impaired (ratings of 5–9) or unimpaired (ratings of 1–4). Cohen's kappas were calculated for global clinical NP ratings and for ratings in each of the six neuropsychological domains. Kendall's tau correlation coefficients were also calculated to evaluate interrater agreement for the 9-point rating scale. Table 3 lists these values of agreement between the two raters for clinical rating scores in each domain. Cohen's kappa values indicate moderate to high agreement between the two raters for the dichotomous categories of impaired versus unimpaired. Perfect agreement was obtained for ratings of executive skills. Agreement was high in the domains of learning and psychomotor-motor skills. Kappa values for ratings of attention were considerably lower, although they still

Table 2  
Performance on Selected Neuropsychological Measures

Variable	<i>M</i>	<i>SD</i>
ANART	111.26	26.54
Information <sup>a</sup>	11.08	3.33
Picture Completion <sup>a</sup>	10.30	2.62
Digit Span <sup>a</sup>	10.61	2.72
Digit Symbol <sup>a,b</sup>	9.12	2.62
Boston Naming Test (no. correct)	54.68	8.17
Phonemic Fluency	45.54	11.35
Category Fluency	48.60	10.83
Symbol Digit Modalities Test	50.32	9.38
Trail Making Test, Part A (time) <sup>b</sup>	26.65	9.13
Trail Making Test, Part B (time) <sup>b</sup>	67.80	32.86
CVLT List A Trial 1	6.74	1.82
CVLT List A Trial 5	12.13	2.24
CVLT Total Trials 1–5	50.77	9.39
CVLT Long Delay Free Recall	10.56	3.01
CVLT Discriminability	94.03	5.73
WCST Categories	5.34	1.45
WCST Perserverative Responses	12.99	11.29

Note. With the exception of Wechsler Adult Intelligence Scale—Revised scaled scores, all scores listed are raw scores. ANART = North American Reading Test; CVLT = California Verbal Learning Test; WCST = Wisconsin Card Sorting Test.

<sup>a</sup> Wechsler Adult Intelligence Scale—Revised scaled scores. <sup>b</sup>  $n = 159$ .

Table 3  
*Interrater Agreement for Neuropsychological Clinical Ratings*

Neuropsychological domain	$\kappa$ (Impaired vs. unimpaired)	Kendall's $\tau$ (Ratings 1–9)
Global	.79	.87
Attention	.57	.77
Learning	.89	.76
Memory	.70	.73
Verbal	.64	.85
Executive	1.00	.81
Psychomotor	.83	.83

represent moderate levels of agreement according to criteria specified by Landis and Koch (1977). Kendall's tau correlation coefficients indicated good agreement between the two raters on the 9-point clinical rating system.

### Statistical Analyses

Hypotheses were addressed by constructing a model of the relationships among cognitive complaints, neuropsychological skills, mood, and medical symptoms using SEM. SEM is particularly suited to this type of analysis, because it simultaneously accounts for multiple interactive relationships among variables, easily handles multiple sources of variance, and permits testing of hypothesized directional relationships (Grimm & Yarnold, 2000; Kline, 1998). Consequently, the results of SEM analyses facilitate causal inferences regarding the relationships among variables (Francis, 1988). Overall, SEM is a more powerful statistical technique than multiple regression or path analysis, with more flexible assumptions (Garson, 2000). Unlike more traditional statistical approaches, SEM also accounts for measurement error (Hoyle & Panter, 1995; Kline, 1998). This issue is particularly important in neuropsychology, where multiple sources of error may occur because of the sheer number of tests and questionnaires used.

Maximum-likelihood estimation was used in the Analysis of Moment Structures (AMOS) module (Version 4.0; Arbuckle & Wothke, 1995) of the SPSS statistical package, to complete the analyses. Although using polychoric correlation matrices with the weighted least squares (WLS) method is usually preferred for ordinal variables, this approach was not used in the present study because of the very large sample size requirements (e.g., 2,000 cases). Furthermore, maximum-likelihood estimation and WLS methods appear to generate comparable values for fit indices and result in few interpretative differences (Garson, 2000). In SEM, the hypothesized model proposed by the researcher is evaluated for its "goodness of fit" with the actual observations in the sample data. Methods of assessing model fit include examining various indices of fit, such as parameter estimates and covariance residuals, and considering the parsimony of the model in question. The reader is referred elsewhere (e.g., Francis, 1998; Kline, 1998) for more detailed descriptions of evaluating model fit in SEM. In the present study, fit indices to evaluate model fit were selected based on criteria previously established in the literature (Bentler, 1989; Browne & Cudeck, 1993; Kelloway, 1998; Kline, 1998).

A partial hybrid model was constructed, with both unobserved (i.e., latent) and observed (i.e., measured) variables. Cognitive complaints and neuropsychological skills were represented as underlying constructs that were measured by multiple observed variables (i.e., indicators). Summary scores for the four neuropsychological

domains of the PAOF (i.e., memory, language and communication, motor/sensory-perceptual, and higher level cognitive and intellectual functions) were used as indicators of the construct *cognitive complaints*. Clinical neuropsychological rating scores for each of the neuropsychological domains assessed by the neuropsychological test battery (i.e., attention, learning, memory, verbal skills, executive skills, psychomotor skills) were used as indicators of the construct *neuropsychological skills*. Mood and medical symptoms were specified as observed variables in the model. Mood was measured by scores on the cognitive-affective items of the BDI (i.e., the first 13 items) and medical symptoms were measured by scores on the HIV-related medical symptom inventory. The endogenous (i.e., dependent) variable in the model was neuropsychological skills in order to determine the utility of cognitive complaints in predicting neuropsychological performance in HIV infection. The construct cognitive complaints was both an exogenous variable (predictor of neuropsychological skills) and an endogenous variable predicted by both mood and systemic illness. The feasibility of a model incorporating feedback loops (i.e., a nonrecursive model) was considered. However, nonrecursive models are more problematic, often requiring additional statistical assumptions and specialized statistical techniques; it is more difficult to achieve model identification in nonrecursive models, a requirement that produces a unique solution for each model parameter (Kline, 1998). These issues, combined with the relatively small sample size for an SEM study, resulted in the decision to use a simpler model that did not specify any feedback loops (i.e., a recursive model).

Version 10.0 of the SPSS statistical software package was used for all statistical analyses. Statistical significance was set at .05 for all analyses.

### Results

The resulting model, with accompanying path coefficients (i.e., regression weights), squared multiple correlations, and correlations among variables, is presented in Figure 1. The construct of cognitive complaints was significantly predictive of neuropsychological skills; the path coefficient of .39 indicated a moderate-sized effect ( $p < .01$ ; Kline, 1998). Cognitive complaints, however, accounted for only 13% of the variance in neuropsychological skills. Whereas both mood ( $\beta = .32, p < .01$ ) and medical symptoms ( $\beta = .31, p < .01$ ) also had moderate-sized effects on cognitive complaints, neither variable significantly predicted neuropsychological skills. Although mood ( $\beta = .12, p < .02$ ) and medical symptoms ( $\beta = .12, p < .02$ ) had small indirect effects on neuropsychological skills through cognitive complaints, total effects on neuropsychological skills were negligible for mood ( $\beta = -.01, p > .05$ ) and for physical symptoms ( $\beta = .15, p > .05$ ). As expected, mood and medical symptoms were significantly correlated ( $r = .43, p < .01$ ).

Factor loadings on the construct of cognitive complaints ranged from .59 to .88. Factor loadings on the construct of neuropsychological skills ranged from .52 to .68. Loadings in these ranges indicated that the constructs were relatively well-defined. Measurement error for neuropsychological clinical ratings of learning and memory were significantly correlated ( $r = .28, p < .01$ ), likely because ratings for these neuropsychological domains are partially derived from the same measures (i.e., California Verbal Learning

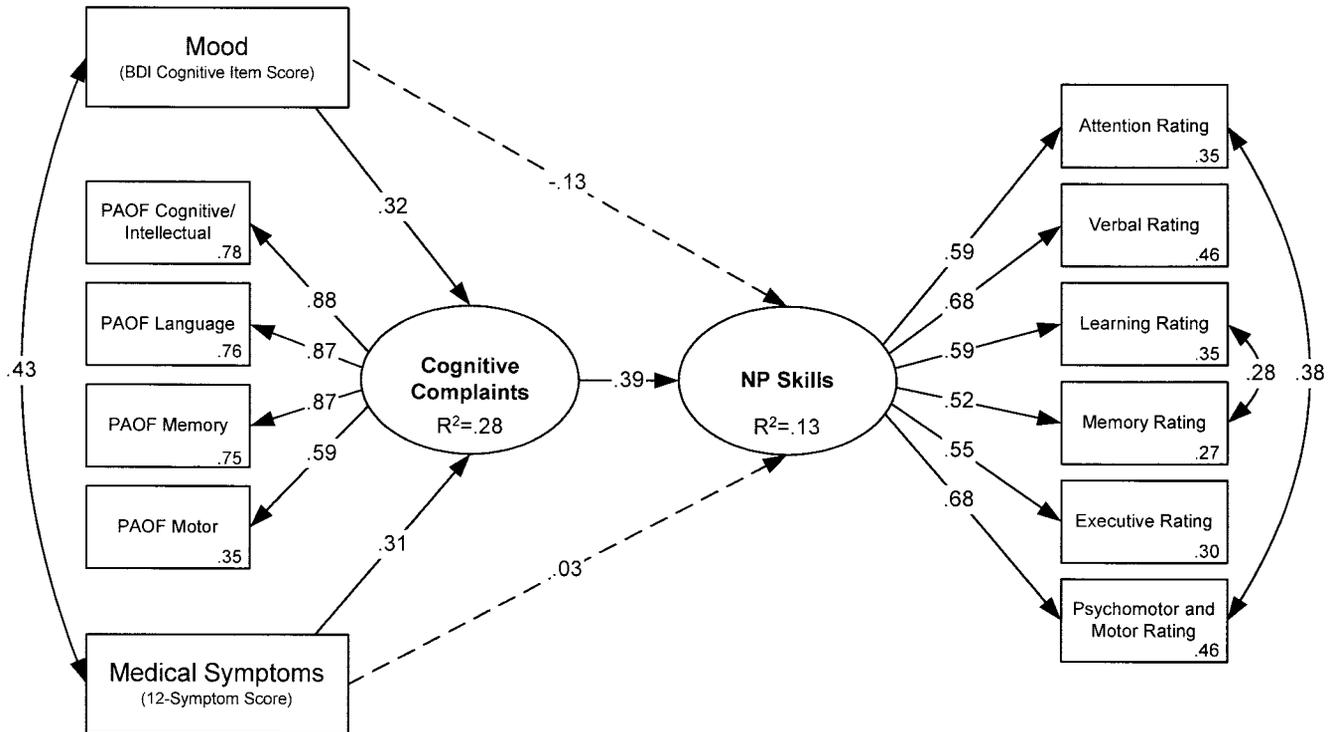


Figure 1. Model of relationships among cognitive complaints, neuropsychological (NP) skills, mood, and medical symptoms of HIV infection. Ovals represent unobserved variables; rectangles represent observed variables. Values embedded in unidirectional arrows are standardized regression weights. Values embedded in bidirectional arrows are correlations. Values within variable ovals or rectangles are squared multiple correlations. Note that error terms have not been depicted for simplification. BDI = Beck Depression Inventory; PAOF = Patient's Assessment of Own Functioning Inventory.

Test; Figure Memory Test). Measurement error for neuropsychological clinical ratings of attention and psychomotor speed were also significantly correlated ( $r = .38, p < .01$ ).

The fit indices generated by AMOS were examined to assess model fit (see Table 4). Most fit indices were well within expected guidelines. The chi-square value was not significant ( $p = .19$ ), indicating acceptable fit between the hypothesized (implied) model and the observed data. Chi-square/ $df$  was below the recommended value of 2 (Ullman, 2001). With the exception of parsimony fit indices, standard fit indices were above .90. The Tucker–Lewis index was

.98. The root-mean-square error of approximation was below .05, and a test of its significance was not significant, indicating an acceptable fit between model specification and the observed data ( $p = .78$ ).

Several alternative models were compared and evaluated for fit to determine the model that most accurately depicted the relationship between cognitive complaints and neuropsychological skills. Four of the models that were compared are listed in Table 4. Model 1 was the simplest model, including only cognitive complaints and neuropsychological skills. This model was compared with models including

Table 4  
Fit Indices for Models Tested in Structural Equation Model Analyses

Model	Cognitive complaints	Neuropsychological skills	Mood	Physical symptoms	$\chi^2$	$\chi^2/df$	GFI	TLI	RMR	RMSEA	AIC	BIC
1	+	+	–	–	36.2	1.1	.96	.99	.61	.03	82.2	205.9
2	+	+	+	–	50.1	1.3	.95	.98	.86	.04	102.1	244.4
3	+	+	–	+	41.2	1.0	.96	1.00	.56	.01	93.2	235.5
4	+	+	+	+	56.5	1.2	.91	.98	.81	.03	116.5	283.3

Note. GFI = goodness-of-fit index; TLI = Tucker–Lewis index; RMR = root-mean-square residual; RMSEA = root-mean-square error of approximation; AIC = Akaike information criterion; BIC = Bayes's information criterion. A plus (+) sign indicates variable was included in the model; a minus (–) sign indicates variable was not included in the model.

the additional contributions of either mood or physical symptoms (Models 2 and 3). All four of the models showed acceptable model fit. Fit indices for Model 1 indicated better model fit than the other models tested, likely because it was a more parsimonious model (i.e., it had fewer parameters). Fit indices for Model 2 (including mood but not medical symptoms) indicated less acceptable fit than those for Model 3 (including medical symptoms but not mood). Model 3 fit the data almost as well as Model 1. In each case, the size of path coefficients did not change substantially across models, indicating good model stability. Removing the contributions (i.e., paths) of mood and/or medical symptoms to neuropsychological skills did not significantly alter the model fit, confirming the minimal contribution of these variables in predicting neuropsychological skills. Overall, differences between models were not large. The modest size of the relationships among the variables examined may have limited the improvement gained by specifying additional variables in the model. Selection of the final model was based on fit indices, residuals, and theoretical soundness. Although all four models were acceptable, lower Akaike information criterion and Bayes's information criterion values were likely due, in part, to the greater parsimony of Models 1–3 relative to Model 4. Model 4 was selected for theoretical reasons to illustrate the minimal impact of mood and medical symptoms on neuropsychological skills and their significant effect on cognitive complaints in HIV infection.

### Discussion

This investigation is the first multivariate study to examine both the independent and interactive effects of variables affecting the relationship of cognitive complaints with neuropsychological skills. The use of SEM enabled this study to delineate the relationships among these variables, including the possible influences of depression and medical symptoms, more precisely than in previous investigations. This change in methodological approach advanced our knowledge of the complicated interrelationships among factors impinging on cognitive complaints, specifically in individuals with HIV infection.

A primary goal of this investigation was to determine whether, in fact, a relationship existed between cognitive complaints and neuropsychological skills when potential confounding factors were taken into account. The principal finding from the model was that cognitive complaints predicted neuropsychological skills, independently of the effects of depressed mood and medical symptoms on cognitive complaints. Overall, this investigation suggests that increased cognitive complaints are associated with poorer neuropsychological performance. Although mood and medical symptoms contributed to cognitive complaints, the relationship between cognitive complaints and neuropsychological skills was not solely due to their influence. The results of the model supported predictions that cognitive complaints would be significantly related to neuropsychological test performance, symptoms of depression, and medical symptoms.

The finding that cognitive complaints are independently related to neuropsychological performance in HIV infection is consistent with the findings of several previous investigations (Beason-Hazen et al., 1994; Mapou et al., 1993; Poutiainen & Elovaara, 1996; Rourke et al., 1999a; Stern et al., 1991), as well as with those of studies of memory symptoms in older individuals (Jonker, Geerlings, & Schmand, 2000; Jonker, Launer, Hooijer, & Lindeboom, 1996; Schofield et al., 1997; Sunderland, Harris, & Baddeley, 1983; Zelinski, Gilewski, & Anthony-Bergstone, 1990) and in other populations (Hertzog, Park, Morrell, & Martin, 2000).

Both depression and medical symptoms were associated with increased cognitive complaints. Contrary to expectations, however, their influence on cognitive complaints yielded only a small, indirect relationship with neuropsychological performance. These findings are consistent with those of other studies demonstrating that increased cognitive complaints in HIV infection are associated with increased symptoms of depression and systemic medical illness (Claypoole et al., 1998; Lopez et al., 1998; Moore et al., 1997; Van Gorp et al., 1991; Wilkins et al., 1991), but they are also associated with neuropsychological functioning.

The clinical implications of these findings are that increased cognitive complaints can reflect neuropsychological impairment even in individuals who are depressed or medically symptomatic. In clinical practice, it appears that a correction factor for the degree of depressed mood or medical illness is not required when assessing whether cognitive complaints are associated with neuropsychological performance. Nevertheless, individuals with depressed mood or increased medical symptoms are also more likely to report neuropsychological difficulties. Further studies are needed to differentiate between symptoms that reflect neuropsychological impairment and those that stem from other causes such as depressed mood and systemic medical illness.

Previous studies have typically related cognitive complaints in HIV infection to either neuropsychological impairment or depression. The structural equation model suggests that cognitive complaints may be related to (a) neuropsychological performance, (b) depressed mood, or (c) systemic medical illness. The current findings suggest that any of one of these three factors may lead to increased cognitive complaints in HIV infection. These variables are unlikely to be mutually exclusive causes of cognitive complaints, and their contribution to cognitive complaints probably varies across individuals. The number and type of cognitive complaints reported may be directly related to different combinations of these variables, although it is unclear whether their combined effect is directly additive or varies in systematic patterns. Individuals who are both depressed and neuropsychologically impaired, however, would be expected to report more cognitive complaints than individuals with only one of these clinical characteristics.

Furthermore, in agreement with the literature, depressed mood was not useful in predicting neuropsychological performance in HIV infection. Most previous studies have shown little relationship between depression and neuropsychological performance.

chological impairment in HIV infection (Bornstein et al., 1993; Goggin et al., 1997; Kalechstein et al., 1998), although depression may affect neuropsychological performance in other populations (Cassens, Wolfe, & Zola, 1990). In confirmation of previous findings, depression does not appear to complicate neuropsychological test result interpretation for individuals with HIV infection.

This study is one of few investigations to examine the impact of systemic medical symptoms on cognitive complaints in HIV infection. Systemic medical symptoms appear to interact with depressive symptoms in HIV infection (Fawzy, Namir, Wolcott, Mitsuyasu, & Gottlieb, 1989; Goggin et al., 1997; Hays, Turner, & Coates, 1992) and are associated with symptoms of cognitive slowing (Lopez et al., 1998). In accordance with previous findings (Lopez et al., 1998), the present results indicated that increased medical symptoms contribute to increased cognitive complaints but that the former has a minimal or negligible role in neuropsychological performance. Our findings are also consistent with those of a large-scale study that reported minimal association between HIV-related symptoms and neuropsychological performance, particularly for asymptomatic individuals (Heaton et al., 1995).

The results of our study are open to other interpretations. Cognitive complaints accounted for a limited amount of variance in neuropsychological performance in the model. Although there appears to be a relationship between complaints and neuropsychological functioning, the strength of the relationship may be viewed as a relatively weak one. Some may interpret this finding as support for the limited utility of cognitive complaints in the prediction of cerebral function and as further evidence for the importance of relying on neuropsychological test results. This is a reasonable interpretation, although, in our view, knowledge regarding the value of cognitive complaints in predicting neuropsychological outcome is in early stages and future studies may provide results supporting their worth in specific populations and/or disease stages.

Previous studies across different populations have shown substantial variability in the accuracy of cognitive complaints, calling into question their reliability in predicting neuropsychological performance. To date, studies have investigated the relationship between cognitive complaints and neuropsychological skills in dementia, multiple sclerosis, head injury, chronic fatigue syndrome and Lyme disease, as well as in Gulf War veterans, patients undergoing hemodialysis, and older individuals. Some of these studies have demonstrated an association between cognitive complaints and poorer neuropsychological performance (Gass & Apple, 1997; Jonker et al., 1996; Schofield et al., 1997; Sunderland et al., 1983; Zelinski et al., 1990). Other studies have linked cognitive complaints to affective disturbances such as anxiety or depression (Bassett & Folstein, 1993; Binder, Storzbach, Anger, Campbell, & Rohlman, 1999; Brickman, Yount, Blaney, Rothberg, & De-Nour, 1996; Derouesne et al., 1989; Elkins, Pollina, Scheffer, & Krupp, 1999; Gass & Apple, 1997; Grut et al., 1993; Jorm et al., 1994; Levy-Cushman & Abeles, 1998; O'Connor, Pollitt, Roth, Brook, & Reiss, 1990; Schofield et al., 1997; Wear-

den & Appleby, 1996) and poor physical health (Bassett & Folstein, 1993; Levy-Cushman & Abeles, 1998).

The relationship between cognitive complaints and neuropsychological functioning appears to be complex and may be mediated by degree of insight into cognitive deficits, level of premorbid functioning (e.g., education level), and the rate and extent of neuropsychological decline (Jonker et al., 2000; Schofield et al., 1997). Studies of cognitive complaints have primarily examined their relationship to neuropsychological dysfunction and/or depression; discrepant findings, however, may be partly explained by stronger relationships to variables that have not yet been examined. Examples of such variables include type and course of disease process, personality, and coping style. Increasing the complexity of the present model in future studies to include additional predictors of cognitive complaints (e.g., disease type, stage, and/or measures of brain pathology) and hypothesized buffers or mediators of the relationship between cognitive complaints and neuropsychological functioning (e.g., personality, coping, social support) may shed light on this issue.

Measurement differences across studies have likely contributed to differing conclusions regarding the reliability of cognitive complaints. Variation in the method of assessing cognitive complaints, including different self-report questionnaires and interview formats, may, in part, account for discrepant findings across studies (Beason-Hazen et al., 1994). Hertzog et al. (2000) found that cognitive complaints in individuals with rheumatoid arthritis best predicted performance when assessed with questions regarding specific behaviors in a specific context; their results suggest that situation-specific cognitive complaints may show stronger predictive relationships with neuropsychological performance than do non-situation-specific ones. Measurement issues are particularly important to address as changes in methodology have recently been hypothesized to alter conclusions about the significance of memory symptoms in older individuals (Jonker et al., 2000). Specifically, recent studies that used community-based samples, used a longitudinal rather than a cross-sectional design, and controlled for the influence of other variables (i.e., depression, level of cognitive impairment, and education) have increased confidence in the neuropsychological significance of self-reported memory problems in this population. In HIV infection, longitudinal studies examining the value of cognitive complaints in predicting subsequent neuropsychological decline are notably absent, and future studies of this type would likely contribute valuable information in clarifying the clinical significance of such symptoms.

One caveat to the conclusions drawn from this study is that causality cannot be inferred in the relationship between cognitive complaints and neuropsychological skills in HIV infection. Whereas cognitive complaints predict neuropsychological performance, the relationship is likely reciprocal, with increases in either cognitive complaints or neuropsychological impairment leading to subsequent increases in the other variable. This possibility was not adequately in-

vestigated in this study because feedback loops were purposefully omitted from the SEM model developed.

Limitations to the study conclusions also stem from the characteristics of this sample. The sample used in this study consisted primarily of gay Caucasian men with an average of 2 years' postsecondary education. The reported results may differ in samples that are more ethnically diverse, are less educated, and include heterosexual individuals. Furthermore, the sample was relatively "clean," without a significant history of neurological or psychiatric conditions, including IV drug use. As a result, these findings may not apply to individuals who are HIV positive and have comorbid conditions or significant substance abuse, particularly IV drug use. Whereas screening the sample allowed a purer evaluation of the relationship between cognitive complaints and neuropsychological performance, it restricts the generalizability of these results to a large proportion of individuals with HIV infection. It is important to examine the relationship between cognitive complaints and neuropsychological functioning in individuals who have CNS involvement and other comorbid conditions; these issues are currently being pursued in our laboratory.

The conclusions of this study are also limited by the relatively small sample size used in sophisticated statistical procedures that often require larger samples. Although the sample size met minimum standards for SEM, larger samples are typically recommended for such techniques (Grimm & Yarnold, 2000; Kline, 1998). Additional investigations in this area will be needed to address some of the methodological shortcomings of this study. These findings require replication and cross-validation with larger samples and with more diverse samples with complicated medical or psychiatric histories, comorbid disorders, and/or IV drug use.

Further research is recommended to clarify and extend some of the findings of this investigation. The relationship between specific types of cognitive complaints and neuropsychological performance requires further exploration, particularly in prospective studies. Additional study in this area will permit increasingly refined hypothesis testing regarding the significance of cognitive complaints in predicting neuropsychological impairment. Other variables that were not examined in this study (e.g., coping style, personality, neuropsychological subtypes, presence and type of structural abnormalities in the brain) may mediate the relationship between cognitive complaints and neuropsychological skills and merit further exploration. The most promising direction for future studies would be to (a) account for the influence of additional variables on cognitive complaints, including the level and pattern of neuropsychological functioning; (b) compare the validity of cognitive complaints in groups of individuals who have limited versus more complicated medical morbidity; and (c) gather longitudinal data on the value of cognitive complaints in predicting neuropsychological impairment. Investigations of this nature would further elucidate the complex relationship between cognitive complaints and neuropsychological skills, both in populations with HIV infection and in other populations.

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