Working Memory Performance Predicts Subjective Cognitive Complaints in HIV Infection

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The authors examined the contribution of working memory performance to subjective cognitive complaints in HIV infection beyond the influence of depressive symptoms. Thirty-six adults with HIV infection were administered neuropsychological (NP) tests of working memory, complex psychomotor efficiency, verbal learning, delayed recall, and questionnaires measuring depressive symptoms and cognitive complaints. Working memory performance, depression scores, and complex psychomotor efficiency were most strongly associated with self-reported cognitive complaints, whereas verbal learning scores and simple psychomotor efficiency showed more modest associations. Regression analyses revealed working memory performance to be the strongest NP predictor of self-reported cognitive complaints, comparable with depression scores in the amount of variance explained. These results suggest that working memory performance may be well suited to reflect how patients function in their everyday environment.

There is controversy concerning the extent to which subjective cognitive complaints in adults with HIV infection are valid indicators of cerebral dysfunction. When neuropsychological (NP) testing is not available, this issue is important for the clinical management of patients with HIV infection because physicians may need to rely on subjective cognitive complaints (in addition to information about CD4 and plasma viral load) when making inferences about the presence of HIV-related brain impairment and when making decisions of when to initiate antiretroviral and/or neuroprotective medications. Several studies have begun to address this issue by examining the relationship between subjective cognitive complaints and performance on objective NP tests. Some studies have found a significant relationship between cognitive complaints and NP test performance (Beason-Hazen, Nasrallah, & Bornstein, 1994; Mapou et al., 1993; Poutiainen & Elovaara, 1996; Stern et al., 1991), whereas others have failed to find such an association (Hinkin et al., 1996; Moore et al., 1997; van Gorp et al., 1991; Wilkins et al., 1991). Common to many of these investigations is the observation that cognitive complaints are related to the level of self-reported mood symptoms (Hinkin et al., 1996; Moore et al., 1997; van Gorp et al., 1991; Wilkins et al., 1991).

A recent investigation by Rourke, Halman, and Bassel (1999a) suggests that NP test performance makes a small yet significant contribution to patients’ cognitive complaints in addition to the strong influence of depressive symptoms. This investigation also yielded the interesting finding that regardless of the specific type of cognitive complaint (i.e., memory, language, or executive function), significant associations were found with performance on tests of attention and complex psychomotor efficiency but not with tests of memory or conceptual/problem-solving ability (Rourke et al., 1999a). This result is consistent with Hermann’s (1982) suggestion that self-reported symptoms of cognitive dysfunction may be more valid as indicators of actual performance than previously thought and that lack of correspondence between symptoms and laboratory test performance may be due to poor scale-to-task isomorphism (i.e., laboratory tests chosen to investigate cognition may tap into different processes than those assessed by symptom questionnaires; Pollina, Greene, Tunic, & Puckett, 1992). Similarly, Helmstaedter and Elger (2000) suggested that the lack of correspondence between self-reported memory symptoms and performance on objective memory tests relates to a discrepancy between the implicit theories of memory that lay persons possess and neuropsychological definitions of memory. In patients with temporal lobe epilepsy, these authors observed that self-reported memory was more strongly related to measures of verbal fluency and vocabulary than to measures of verbal...
learning and memory (Helmstaedter & Elger, 2000). These observations imply that patients’ cognitive complaints may be predicted by performance on NP tests that do not necessarily correspond to the semantic content of those complaints. Thus, in HIV infection, there may be a particular set of NP measures that are sensitive to the everyday cognitive and memory symptoms experienced by some individuals.

The main purpose of this investigation was to determine whether working memory performance is related to subjective cognitive complaints in individuals with HIV infection beyond the influence of depressive symptoms. In general, working memory refers to an individual’s ability to temporarily store and manipulate information in an on-line fashion. The classic working memory model proposed by Baddeley (1986) posits two specialized short-term stores (for verbal and visuospatial information) and a central executive that allocates processing resources to manipulate information in these short-term stores. In recent years, models of working memory have been developed that make reference to the underlying neural systems that support the ability to temporarily represent and manipulate goal-relevant information (Goldman-Rakic, 1995; Petrides, 1995, 1998). Electrophysiological and neuroimaging studies have implicated a major role for the dorsolateral prefrontal cortex (Brod-trophysiological and neuroimaging studies have implicated a major role for the dorsolateral prefrontal cortex (Brod-mann Areas 46 and 9) and its connections (Goldman-Rakic, 1995; Petrides, 1995, 1998).

Several studies have reported working memory deficits in individuals with HIV infection (Bartok et al., 1997; Farin-pour et al., 2000; E. M. Martin, Pirak, Pursell, Mullane, & Novak, 1995; Sahakian et al., 1995; Stout et al., 1995), although these studies have more consistently revealed deficits in symptomatic patients, and there has been at least one failure to reveal deficits (Law et al., 1994). It is possible that the working memory deficits reported in symptomatic individuals with HIV infection may underlie other NP deficits (e.g., learning efficiency) as well as subjective cognitive complaints in this population.

If a relationship exists between working memory performance and subjective cognitive complaints in patients with HIV infection, then we also wished to determine whether working memory performance is superior to standard measures of attention, complex psychomotor efficiency, and verbal learning and memory at predicting patients’ cognitive complaints. Accordingly, we administered the Hopkins Verbal Learning Test (Brandt, 1991) to examine immediate registration and verbal learning efficiency, the Sentence Memory Test (Shimamura & Squire, 1986) to examine delayed recall performance, and the Trail Making Test—Parts A and B (Reitan & Wolfson, 1993) to measure attention and complex psychomotor efficiency.

In the present investigation, we chose the Self-Ordered Pointing Test (SOPT; Petrides & Milner, 1982) to measure working memory performance. The SOPT measures an individual’s ability to monitor a set of self-generated responses within working memory (Petrides, 1995; Petrides & Milner, 1982). We chose this test because it has previously proven to be sensitive to working memory impairments in patients with HIV infection (Farinpour et al., 2000) as well as in patients with Parkinson’s disease (Gabrieli, Singh, Stebbins, & Goetz, 1996) and Huntington’s disease (Rich, Bylsma, & Brandt, 1996), which are two other conditions that, like HIV infection, are known to involve pathophysi-ological changes in subcortical brain regions. In addition, we believed that the monitoring requirements of the SOPT closely resemble the information processing demands of every day life, thus enhancing our chances of finding an association with self-reported cognitive complaints. Finally, administration of the SOPT along with standard NP measures of attention and complex psychomotor efficiency in the present investigation allowed us to examine the issue of how a relatively process-pure measure (i.e., monitoring within working memory) would compare with measures that are more sensitive to general cerebral efficiency at predicting subjective cognitive and memory complaints, given that in the Rourke et al., (1999a) investigation it was the latter types of measures that were the strongest predictors of subjective cognitive complaints.

Method

Participants

Thirty-six adults with HIV infection (35 men, 1 woman) with no known history of neurological disease, developmental disorders, central nervous system opportunistic infection, head trauma with loss of consciousness exceeding 30 min, or recent substance abuse or dependence of alcohol or illicit substances within the last 2 months participated in this study. Three participants were asymptomatic (CDC93 A1 and A2), 14 were mildly symptomatic (CDC93 B1 and B2), and 19 had AIDS-defining illnesses or CD4 lymphocyte counts less than 200 (CDC93 A3, B3, and C1–C3; Centers for Disease Control, 1992). The sample had a mean age and education of 44.52 (SD = 9.27) and 15.44 (SD = 2.28) years, respectively. The majority of individuals in our sample (89%) were on antiretroviral therapy at the time of initial testing, with 64% on highly active antiretroviral therapy (HAART), 25% on suboptimal antiretroviral therapy, and 11% taking no antiretro-viral medication.

For the purpose of preliminary analyses examining the impact of disease status, we formed two groups: an HIV positive without AIDS group (including participants classified as asymptomatic, CDC93 A1/A2, and participants classified as mildly symptomatic, CDC93 B1/B2; n = 17) and an AIDS group (CDC93 A3/B3/C1-C3; n = 19). Independent samples t tests revealed that the group with AIDS had a significantly lower CD4 cell count and that the groups did not differ in age or education. Analysis of covariance (with age and education as concomitant variables) failed to reveal differences among the groups in performance on any of the NP measures or questionnaires (see Table 1). Supplementary analyses were conducted with the sample divided into disease status groups on the basis of information relevant to HIV clinical stage (asymptomatic and symptomatic vs. AIDS), without regard to CD4 cell count. Again, no performance differences among the HIV disease status groups were found. Consequently, we conducted all subse-quent analyses on the sample as a whole, without regard to HIV disease status.

Materials

We administered a series of NP tests and questionnaires that consisted of the following: Hopkins Verbal Learning Test (HVLT; Brandt, 1991), Trail Making Test—Parts A and B (TMT–A and
Table 1

Results for NP Tests and Questionnaires by CDC-93
HIV Disease Status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>HIV positive</th>
<th>AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 17)</td>
<td>(n = 19)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Age</td>
<td>46.24</td>
<td>8.59</td>
<td>42.37</td>
</tr>
<tr>
<td>Education</td>
<td>14.94</td>
<td>2.41</td>
<td>15.16</td>
</tr>
<tr>
<td>CD4 cell count</td>
<td>391.63</td>
<td>131.69</td>
<td>132.68</td>
</tr>
<tr>
<td>Depressive symptoms</td>
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<tr>
<td>BDI total</td>
<td>14.65</td>
<td>8.91</td>
<td>14.47</td>
</tr>
<tr>
<td>BDI modified (Items 1–13)</td>
<td>8.59</td>
<td>6.22</td>
<td>7.68</td>
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<tr>
<td>Cognitive complaints</td>
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<tr>
<td>CFQ Total score</td>
<td>48.94</td>
<td>15.47</td>
<td>46.53</td>
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<tr>
<td>CFQ Memory scale score</td>
<td>16.35</td>
<td>4.91</td>
<td>15.41</td>
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<tr>
<td>Verbal memory</td>
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<tr>
<td>HVLT total words recalled</td>
<td>26.19</td>
<td>5.98</td>
<td>23.25</td>
</tr>
<tr>
<td>HVLT Trial 1 correct</td>
<td>7.24</td>
<td>2.14</td>
<td>6.79</td>
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<tr>
<td>Sentence Memory total</td>
<td>13.65</td>
<td>4.72</td>
<td>14.67</td>
</tr>
<tr>
<td>Psychomotor efficiency</td>
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<td></td>
</tr>
<tr>
<td>Trail Making Test—Part A</td>
<td>26.06</td>
<td>10.03</td>
<td>24.70</td>
</tr>
<tr>
<td>Trail Making Test—Part B</td>
<td>64.12</td>
<td>23.99</td>
<td>63.97</td>
</tr>
<tr>
<td>Working memory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOPT total errors</td>
<td>5.35</td>
<td>3.18</td>
<td>4.95</td>
</tr>
</tbody>
</table>

Note. Analyses revealed significant differences between HIV disease status groups only in CD4 cell count, p < .001. The HIV positive without AIDS group included individuals classified as asymptomatic (CDC93-A1/A2) or mildly symptomatic (CDC93-B1/B2), whereas our AIDS group included CDC93-A3, B3, and C1-C3. Results were similar when HIV disease status was determined clinically without regard to CD4 cell count. BDI = Beck Depression Inventory; CFQ = Cognitive Failures Questionnaire; HVLT = Hopkins Verbal Learning Test; Sentence Memory = Sentence Memory Test; SOPT = Self-Ordered Pointing Test.

TMT-B; Reitan & Wolfson, 1993), Self-Ordered Pointing Test (SOPT; Petrides & Milner, 1982)—Abstract Design version (Shimamura & Jurica, 1994), Sentence Memory Test (SMT; Shimamura & Squire, 1986), Beck Depression Inventory (BDI; Beck & Steer, 1993), and the Cognitive Failures Questionnaire (CFQ; Broadbent, Cooper, Fitzgerald, & Parkes, 1982).

The SMT was taken from Shimamura and Squire’s (1986) feeling-of-knowing procedure. At encoding, participants were presented with sentences printed on cue cards (e.g., “Patty’s garden was full of marigolds”) while hearing each sentence read aloud by the experimenter. Twenty-four different sentences were presented. Half of the sentences were presented twice for a total of 36 presentations. The sentences were presented consecutively and in random order. After 1.5 hr had elapsed, the participant was presented with the same 24 sentences but with one word missing from each sentence (e.g., “Patty’s garden was full of ______”). The participant’s task was to report the identity of the missing word that had been presented during the encoding phase of the test.

In the SOPT, participants viewed consecutive visual arrays printed on 8.5 × 11.0 in. (21.6 × 27.9 cm) sheets of paper in a binder, each of which contained 16 different abstract patterns in a 4 × 4 item configuration. Participants were required to point manually to any pattern in the first array, then turn to the next page on which they viewed another array containing the same visual patterns placed in different locations. On this second trial, and on each of the following 14 trials, participants were required to point to a new pattern (i.e., one that had not been selected on a previous trial). The location of each visual pattern was randomly determined in each array. The test was entirely self-paced. On completion of the 16 trials, participants rested briefly, then completed a second block of 16 trials. Performance on the SOPT was determined by the total number of repetition errors committed (i.e., the number of times a design was chosen that had been selected on a previous trial).

The CFQ is a 25-item self-report questionnaire that requires participants to rate the frequency with which they experience everyday mistakes in perception, memory, and motor function (e.g., “Do you read something and find you haven’t been thinking about it and must read it again?”). Each item is rated on a 5-point Likert-type scale ranging from never to very often. Dependent measures include a total cognitive complaints score (CFQ Total) and the sum of scores from the 8 CFQ items pertaining to memory complaints (CFQ Memory: Items 2, 6, 12, 16, 17, 20, 22, and 23).

For analyses involving the BDI, we used a modified depression score reflecting the sum of Items 1–13 to ensure that somatic–vegetative items (14–21) that could be elevated secondary to systemic HIV infection would not confound our results.

Procedure

Individuals in the present investigation were randomly selected from an ongoing study of the natural history of neurobehavioral complications in HIV infection conducted at St. Michael’s Hospital (Toronto, Ontario, Canada). All participants were informed about the objectives of the study, and the participants provided written informed consent for participation. Testing was completed on a separate day from testing done for the natural history study and was done in a session that lasted 2.0–2.5 hr. An optional 10-min rest period was offered midway through the session. All questionnaires and interviews were administered at the beginning of the session followed by NP tests. The protocol was approved by the Wellesley Hospital Research Ethics Board.

Data Analyses

To determine whether NP tests contribute significant variance to cognitive and memory complaints (beyond the influence of depressive symptoms), we conducted hierarchical multiple linear regression (hMLR) analyses. In each hMLR analysis, age and education were entered in an initial variable block, modified BDI was entered in a second variable block, and NP tests were entered in a third variable block. Separate hMLR analyses were conducted using CFQ Total and Memory scale scores as dependent variables. Block 3 predictor variables were those NP tests that exhibited the strongest Pearson product-moment correlation coefficients with CFQ Total and Memory scale scores (and included at least one NP test from an ongoing study of the natural history of neurobehavioral complications in HIV infection conducted at St. Michael’s Hospital).
predictors has been removed from the predictor variable but not from the criterion (Licht, 1995). We conducted a second set of hMLR analyses in which individual NP predictor variables were entered into regression analyses in sequential blocks (and in alternate order in separate analyses) to examine the impact that shared variance may have had on the results. The change in $R^2$ was examined for each NP variable when it was the first predictor entered in the regression model and when it was the last predictor entered. For these analyses, a more conservative criterion for statistical significance ($p < .01$) was adopted to account for the multiple models being tested. For all other analyses, the criterion for statistical significance was set at $p < .05$. All variables were examined for deviation from normal distribution with one-sample Kolomogorov-Smirnov tests to determine whether parametric statistical tests were appropriate. No variables deviated from normal distribution. All data analyses were conducted using SPSS for Windows (Version 8.0).

### Results

**Neuropsychological Correlates of Subjective Cognitive Complaints**

We examined associations between cognitive complaints, depressive symptoms, and NP test performances using Pearson product–moment correlation coefficients. The results of these analyses are displayed in Table 2. Strong relationships were found between CFQ scores (Total and Memory scale), and BDI scores (total and modified). However, equally strong associations were found between CFQ scores (Total and Memory scale) and TMT–B scores, as well as between CFQ scores and SOPT performance (see Figure 1). A less strong but statistically significant association was found between CFQ scores and HVLT Trial 1 correct responses. TMT–A and HVLT total correct scores were significantly related to CFQ Memory scale scores but not to CFQ Total scores. However, differences in correlation coefficients across the two sets of analyses were negligible, and it is likely that the difference in associations that attained statistical significance is an artifact of the relatively small sample size. CFQ scores were not related to SMT performance.

### Associations Between NP Tests

We calculated Pearson product-moment correlation coefficients to examine the relationship between patients’ SOPT performance and their performance on other NP tests. Significant associations were found between SOPT performance and the following NP tests: HVLT total correct, $r = -.61, p < .01$; HVLT Trial 1 correct, $r = -.61, p < .01$; TMT–B, $r = .63, p < .01$; and TMT–A, $r = .41, p < .01$. SOPT performance was not significantly related to depressive symptoms (responses on the modified BDI scale; $r = .12, p < .49$) or to performance on the SMT ($r = -.26, p < .13$). In addition, significant associations were found between HVLT Trial 1 correct and the following NP tests: TMT–A, $r = -.50, p < .01$; TMT–B, $r = -.52, p < .01$; and SMT, $r = .48, p < .01$. HVLT total correct was significantly related to SOPT ($r = -.61, p < .01$), SMT ($r = .53, p < .005$), and TMT–B ($r = -.48, p < .01$) but not to TMT–A ($r = -.32, p < .10$). As expected, a significant relationship was found between TMT–A and TMT–B ($r = .68, p < .01$). None of the NP measures exhibited significant associations with modified BDI scores.

### Predictors of Subjective Cognitive Complaints: hMLR Results

In each hMLR analysis, age and education were entered in an initial variable block, modified BDI was entered in a second variable block, and the following NP variables were entered in the third variable block on the basis of having the highest bivariate correlations with CFQ scores within each information processing domain: (a) memory, HVLT Trial 1—correct responses, (b) working memory, SOPT total errors, and (c) complex psychomotor efficiency, TMT–B.

![Figure 1](image.png)

**Figure 1.** Linear relationship between Self-Ordered Pointing Test (SOPT) errors and Cognitive Failures Questionnaire (CFQ) Total scores.
The results from the hMLR analyses are presented in Table 3. The final model for the regression of the predictor variables on CFQ Total scores was highly significant, $F(6, 32) = 10.46, p < .001$, as was the regression of the predictor variables on CFQ Memory scale scores, $F(6, 32) = 8.28, p < .001$. Age and education (Block 1) did not account for a significant amount of variance in either analysis, although the beta weight for age was significant in each analysis. Modified BDI scores (Block 2) predicted a large and significant amount of variance in CFQ scores. When TMT–B was the first NP variable entered into the regression model, it accounted for a smaller (yet substantial) incremental percentage of explained variance: ($R^2 = .19$), $F(1, 34) = 15.14, p < .001$, for CFQ Total scores; and ($R^2 = .19$), $F(1, 34) = 12.70, p < .001$, for CFQ Memory scale scores. With the alpha level set at .01, the HVLT Trial 1 variable did not account for a significant incremental percentage of variance in CFQ Memory scale scores when it was entered as the first NP variable ($R^2 = .10$), $F(1, 34) = 5.65, p < .02$; and also failed to predict a significant amount of variance in CFQ Total scores ($R^2 = .07$), $F(1, 34) = 4.10, p < .06$.

Most important, the SOPT continued to account for a significant amount of variance in CFQ scores when the other NP predictor variables were previously accounted for in the regression model, SOPT ($\Delta R^2 = .10$), $F(1, 32) = 7.83, p < .009$, for CFQ Memory scale; and SOPT ($\Delta R^2 = .08$), $F(1, 32) = 7.82, p < .009$, for CFQ Total scores. In contrast, when TMT–B was entered into the regression model subsequent to the other NP variables, it did not account for a significant amount of variance, ($\Delta R^2 = .04$), $F(1, 32) = 3.37, p < .08$, for CFQ Total score; and ($\Delta R^2 = .03$), $F(1, 32) = 2.05, p < .17$, for CFQ Memory scale scores. These analyses indicate that the SOPT and TMT–B variables account for a large, yet overlapping amount of variance in CFQ Total and Memory scale scores; however, the SOPT is the best predictor.

### Supplementary Analyses

Previous research has revealed an increased incidence of intralist repetition responses during verbal learning tests in individuals with lesions of the right dorsolateral prefrontal cortex.
cortex (Stuss et al., 1994). This deficit may reflect the disruption of output monitoring processes similar to processes required for successful performance on the SOPT. We examined the association between SOPT performance and total number of HVLT intralist repetition responses, and a significant relationship was found (Kendall’s tau-b = 0.35, p < .027; we used a nonparametric correlation coefficient because examination of the distribution of intralist repetition scores revealed departures from normality). HVLT intralist repetitions were also marginally related to CFQ Total scores (tau-b = 0.293, p < .057).

Discussion

Consistent with our hypotheses, working memory (SOPT) performance was a significant predictor of subjective cognitive and memory complaints in individuals with HIV infection, even after depressive symptoms, age, and education had already been accounted for in the regression analyses. Tests of verbal memory (HVLT) and complex psychomotor efficiency (TMT–B) showed significant bivariate correlations with cognitive and memory complaints; however, they did not account for a significant amount of variance when entered into the regression analyses with SOPT performance. This, along with the observation that the SOPT exhibited higher semipartial correlation coefficients (with CFQ scores as the criterion), suggests that SOPT performance was the best NP predictor of cognitive and memory complaints.

Subsequent analyses revealed that working memory and complex psychomotor efficiency accounted for overlapping variance in cognitive and memory complaints. However, the SOPT accounted for the largest percentage of explained variance and was the only NP variable that accounted for a significant amount of variance in cognitive and memory complaints after all other NP predictors had been accounted for in the regression analyses. These observations confirm the SOPT as the best NP predictor of cognitive and memory complaints. In general, these results add to a growing body of research suggesting that cognitive and memory complaints in patients with HIV infection may be related to NP performance, in addition to the influence of concurrent depressive symptoms (Beason-Hazen et al., 1994; Mapou et al., 1993; Rourke et al., 1999a; Rourke, Halman, & Bassel, 1999b).

In the present investigation, measures of working memory (SOPT) and complex psychomotor efficiency (TMT–B) showed stronger associations with memory complaints than did objective measures of verbal learning (HVLT) and delayed recall performance (SMT). This is consistent with the results of Rourke et al.’s (1999a) investigation as well as with Helmstaedter and Elger’s (2000) investigation of temporal lobe epilepsy, in revealing that subjective memory complaints may be predicted by nonmemory NP measures. In Helmstaedter and Elger’s study, subjective memory complaints were predicted by verbal fluency and vocabulary performance rather than by measures of verbal learning and memory. These authors suggested that their result is indicative of a discrepancy between patients’ implicit theories of memory and NP definitions of memory. However, in Rourke et al.’s (1999a) previous investigation, complex psychomotor efficiency (as measured by the Wechsler Adult Intelligence Scale—Revised Digit Symbol scale; Wechsler, 1981) was found to be superior to measures of verbal learning at predicting all different types of cognitive complaints (including memory complaints). It is unlikely that our patients’ implicit theories of memory would encompass abilities such as psychomotor speed. Instead, it may be that some patients with HIV infection are sensitive to a general decline in cerebral efficiency and answer symptom questionnaires indiscriminately. This alternative interpretation of our findings suggests that everyday cognitive and memory failures in patients with HIV infection may result from compromised abilities in domains of information processing that do not necessarily correspond to the semantic content of the specific type of complaint. In other words, patients’ memory complaints may reflect decline in general cerebral efficiency, or working memory, rather than direct compromise in learning efficiency and memory processing systems.

It is surprising that measures of working memory and complex psychomotor efficiency were superior to verbal memory at predicting memory complaints given that theoretical models of memory performance often emphasize the contribution of both of these variables to successful memory performance. For example, Gabrieli et al. (1996) have postulated a model to explain the observed relationship among strategic memory performance, working memory span, and speed of information processing in patients with Parkinson’s disease. In Gabrieli’s model, the depletion of frontostriatal dopaminergic systems is thought to cause impairments in perceptual–motor processing speed, with a consequent reduction in working memory capacity. In turn, limitations of working memory capacity compromise reasoning ability and strategic memory performance. Consistent with Gabrieli’s model, in the present investigation, we found significant relationships among complex psychomotor efficiency (TMT–B), working memory (SOPT), and strategic verbal memory performance (HVLT Trial 1; HVLT total correct). However, if strategic memory performance depends on working memory processes, then we might have expected it to be related to memory complaints to the extent that a relationship was found between working memory and memory complaints. Instead, we found modest (though significant) bivariate correlations between strategic memory performance (HVLT total correct) and CFQ Memory complaints. Thus, it is unclear why these relationships are not as strong as the association between working memory performance and memory complaints.

We must consider the possibility that working memory is not a unitary construct but rather a system of related functions organized according to information domain (Gold-
In the present study, we found a significant positive relationship with activity in Brodmann’s Areas 46 and 9 in the mid-dorsolateral prefrontal cortex, whereas the working memory process involved in strategic memory retrieval is more a function of the mid-ventrolateral prefrontal cortex (Petrides, 1995, 1998). Thus, it is not surprising that SOPT and HVLT performance are differentially related to memory complaints, because the working memory function that contributes to successful performance in the tasks differ, and consequently, the variables represent different sources of variance. The relationship between strategic verbal memory and SOPT performance found in the present investigation may instead reflect the influence of a moderating variable that is a common cause (e.g., processing speed, attentional processes, or integrity of frontostriatal circuits). This issue could be examined with additional variables (including physiological measures), and multivariate statistical techniques, but is beyond the scope of the present investigation.

Petrides (1995, 1998) suggested that the task demands of the SOPT are more closely related to the output monitoring requirements of verbal memory tasks than to retrieval processes. This output monitoring function is compromised in patients with damage to the right dorsolateral prefrontal cortex and leads to intralist repetition in verbal learning tests (Stuss et al., 1994). Consistent with this explanation, in the present study, we found a significant positive relationship between SOPT performance and the total number of HVLT intralist repetitions. We also found a marginal relationship between HVLT intralist repetition errors and CFQ Total score, supporting the relevance of monitoring ability to everyday cognitive and memory complaints. It is possible that monitoring and verbal memory performance may account for unique, nonoverlapping variance in subjective cognitive and memory complaints.

The observation that working memory performance was superior to strategic verbal memory in predicting memory complaints can also be explained with reference to the information processing demands of everyday life. When a laboratory test of verbal learning is administered, a patient’s undivided attention is focused on the primary task if he or she is motivated to perform well and there are no distractions. In contrast, a person’s everyday environment is complex, and there are often multiple events and behavioral sequences that have to be attended to at any one time. The task demands of the SOPT seem to parallel the characteristics of a complex environment—both require individuals to hold several pieces of information in mind simultaneously, to monitor the status of that information, and to allocate attention (and action sequences) to stimuli that are relevant for current behavioral goals. A person suffering from an impairment in working memory or monitoring would be more susceptible to cognitive or memory failures in this scenario. When we examine the content of the CFQ, we find many items that seem to invoke this same ability to monitor sequences of intentional action or thought (e.g., “Do you find you forget why you went from one part of the house to another?”; “Do you start doing one thing at home and get distracted into doing something else [unintentionally]?”). Thus, what may at face value seem like an episode of forgetfulness may actually reflect a failure to monitor a sequence of intentional action or thought. However, a major caveat to these conjectures is the fact that we did not examine everyday functioning directly but rather used scores from a self-report questionnaire as a surrogate marker of cognitive failures in everyday life. To measure actual function in everyday life would require a diary study that documented cognitive failures as they occurred, or collateral information.

A final explanation for the stronger association between working memory and cognitive complaints concerns the use of compensatory strategies. Patients with impaired episodic memory may use mnemonic strategies and/or memory aids to help them overcome their difficulties. Thus, these patients may seldom experience cognitive failures that are related to the nature of their impairment. In contrast, it is more difficult to imagine an efficient memory aid that could help an individual with on-line monitoring of information within working memory. Thus, individuals with working memory impairments may report more cognitive and memory failures simply because these individuals are unable to compensate for their problems.

Although traditional NP tests (Butters et al., 1990; Grant & Martin, 1994; Heaton et al., 1995, 1996; White, Heaton, Monsch, & the HIV Neurobehavioral Research Centre Group, 1995) and reaction time measures (Law et al., 1995; A. Martin et al., 1992; A. Martin, Heyes, Salazar, Law, & Williams, 1993; E. M. Martin, Sorensen, Edelstein, & Robertson, 1992; Miller, Satz, & Visscher, 1991) have been used to detect brain dysfunction in HIV infection, NP test scores may not always relate to patients’ self-reported symptoms (Sunderland, Harris, & Baddeley, 1983). Some researchers have attempted to overcome this limitation by devising more environmentally relevant assessment methods, such as the Rivermead Behavioural Memory Test (Wilson, Cockburn, & Baddeley, 1985), whereas other researchers have heeded Hermann’s (1982) warnings of poor scale-to-task isomorphism and have attempted to provide a psychometric solution (Pollina et al., 1992). Our results suggest that another way to understand the relationship between NP test scores and everyday functioning is through consideration of the type of processing that may underlie everyday cognitive difficulties. Although we have applied this conceptual framework to a population of individuals with HIV infection in the present investigation, it is reasonable to assume that the issue is not specific to this population and can be generalized to other neurological conditions and to healthy individuals (Broadbent, Broadbent, & Jones, 1986; Meiran, Israeli, Levi, & Grafi, 1994). A logical follow-up to this research endeavor would be to study a group of HIV-negative depressed individuals.
Some individuals with HIV infection may have a compromised ability to monitor the contents of working memory because of the disruption of fronto-striatal circuits. Cummings (1993) has described the presence of five independent circuits linking discrete prefrontal and subcortical regions. The dorsolateral circuit begins on the lateral prefrontal cortex (Brodman's Areas 9 and 10) and projects to the dorsolateral head of the caudate nucleus. This area of the caudate projects to the globus pallidus internal segment and to the substantia nigra pars reticulata. These regions project to the dorsomedial and anterior thalamic nuclei, which in turn complete the circuit by projecting to the dorsolateral prefrontal cortex. Some evidence suggests that damage to any part of this circuit can lead to similar behavioral impairments marked predominantly by executive dysfunction and working memory impairment (Cummings, 1993). Even though the ability to monitor the contents of working memory is thought to be a function of the dorsolateral prefrontal cortex (Petrides, 1995, 1998), it is likely that disruption of one (or several) of these functionally related subcortical regions and pathways may lead to monitoring dysfunction. Thus, the observation that HIV-related brain pathology preferentially affects subcortical gray and white matter (Ekholm & Simon, 1988; Grant et al., 1987, 1988; Hall et al., 1996; Olsen, Longo, Mills, & Norman, 1988; Wiley et al., 1991) may explain the presence of compromise in working memory–monitoring ability in some individuals within this population.

We failed to find a difference in working memory (SOPT) performance between our HIV positive without AIDS group (individuals classified as asymptomatic, CDC93-A1/A2, or mildly symptomatic, CDC93-B1/B2) and our group with AIDS (CDC93-A3/B3/C1-C3). Results were similar when HIV disease status groups were formed without regard to CD4 cell counts. It is difficult to compare these results with previous research findings because most investigations that have examined the influence of disease status on working memory performance in HIV infection have made comparisons among control, asymptomatic, and symptomatic groups (e.g., Bartok et al., 1997; Farinpour et al., 2000; Sahakian et al., 1995). We were not able to make similar group comparisons because our sample was composed predominantly of individuals who were symptomatic or had AIDS, and this is a limitation of our study. One previous investigation that compared rates of impaired working memory performance in symptomatic and mildly symptomatic individuals found differences between these two groups only in the number of correct responses made on a reading span task but not in other measures of working memory (Stout et al., 1995). Thus, the published empirical literature has not consistently demonstrated an effect of disease status on working memory performance when patients are symptomatic, and our results are consistent with the hypothesis that there are no differences.

Another possible explanation for our failure to observe an effect of HIV disease status on working memory performance is that historically, disease status effects may have been more salient before the advent of HAART. Consistent with this notion, at least two studies have demonstrated that HAART results in improvement of cognitive function in individuals with HIV-related cognitive impairment (Chang et al., 1999; Suarez et al., 2001) and also reverses brain biochemical abnormalities identified by magnetic resonance spectroscopy (Chang et al., 1999; Stankoff et al., 2000). Given that 89% of the individuals in our sample were receiving antiretroviral therapy (64% were on HAART) at the time of their initial assessment, this is a plausible explanation for the lack of HIV disease status effects.

The present investigation was limited by a relatively small sample size and should be cross-validated in a larger sample. This may reveal different strengths in the associations between our variables. Also, the sample consisted of predominantly gay Caucasian men with no other known neurological conditions or recent substance abuse confounds. Further investigations are necessary to determine whether the reported results can be generalized to other groups of HIV-infected individuals (e.g., women and people of ethnicity other than Caucasian), to individuals with concurrent neurological conditions or substance abuse problems, and to individuals with other risk factors for HIV infection (e.g., injection drug users). The investigation was also limited by the self-paced nature of our working memory task (SOPT). Without a standardized presentation rate, we could not control for the possibility that some individuals may have used compensatory strategies related to the time taken to process stimuli during presentation. Another limitation involves the nature of the instruments used to assess memory. The validity of the HVLT has not been established as thoroughly as it has for measures such as the California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987) and the Rey Auditory Verbal Learning Test (Rey, 1964), although recent studies have lent support for the construct and concurrent validity of both the HVLT and the HVLT–Revised (Frank & Byrne, 2000; Lacritz & Cullum, 1998). The SMT was designed to assess a metamemory phenomenon called feeling of knowing, and the validity of this test as a measure of delayed recall is questionable. However, the nature of the memory impairment that has been associated with HIV infection involves difficulty with learning efficiency and retrieval rather than with encoding or retention (i.e., a subcortical memory profile; Becker et al., 1995; Peavy et al., 1994), so the measurement of delayed recall performance was not crucial for testing our hypotheses.

Our experimental design did not include an HIV-seronegative control group, and as a result, we could not determine whether HIV-infected individuals in our sample were impaired in their SOPT performance. We do not consider this to be a serious limitation because the purpose of our investigation was to determine whether working memory performance was a significant predictor of cognitive complaints rather than to determine whether working memory impairment was present. This places our study within the domain of research in individual differences rather than in group mean differences. A previous investigation has revealed SOPT performance deficits in HIV-seropositive drug users compared with HIV-seronegative drug users (Farinpour et al., 2000). Furthermore, the strong associations found be-
between SOPT performance and other standard measures of NP functioning (e.g., TMT–B) that have previously been shown to be sensitive to HIV-related brain dysfunction (Heaton et al., 1995) support the notion that the SOPT may also be a valid index of cognitive efficiency in HIV infection.

In conclusion, our findings suggest that it may not be appropriate to conclude that patients are inaccurate in their self-assessment when no relationship is found between subjective cognitive complaints and NP test performance. It may be that we have not measured performance in the domains of information processing that underlie difficulties that patients encounter in their everyday activities. Conversely, the assumption that patients are without brain dysfunction when they do not complain of cognitive and memory failures is also of questionable validity (Rourke et al., 1999b). Individual patients may differ in the complexity of their environments, their use of memory aids, and their insight into the meaning of their everyday cognitive performance (Janowsky, Shimamura, & Squire, 1989). The results of this investigation along with those of Rourke et al. (1999a, 1999b) suggest that although standard NP tests (Butters et al., 1990; Grant & Martin, 1994; Heaton et al., 1995, 1996; White et al., 1995) and measures of reaction time (Law et al., 1995; A. Martin et al., 1992, 1993; E. M. Martin et al., 1992; Miller et al., 1991) have been used to detect the presence of HIV-related brain dysfunction, tests of complex psychomotor efficiency and working memory may be well suited to address the issue of how patients function in their everyday environment, and this issue warrants further investigation.

References


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