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REVIEW

The Neuropsychology of HIV/AIDS in Older Adults

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Abstract Highly active antiretroviral therapy is allowing increasing numbers of adults to age with HIV. The neuropsychological effects of aging with HIV are reviewed through three types of studies. First, the separate effects of HIV and aging on cognition are examined in studies that compare younger adults with HIV with neurologically normal older adults. Second, studies examine the impact of aging within samples of adults with HIV only. Third, providing the most critical evidence, are studies that assess cognition in younger and older adults with HIV relative to younger and older adults without HIV. In general research findings are inconclusive. Large individual differences among older adults with HIV as well as co-factors (APOE4 and detectable viral load) may account for inconsistent findings in the literature. A subgroup of older adults with HIV may be at greater risk for cognitive impairment, especially in attention functioning.

Keywords HIV · AIDS · Aging · Neuropsychology · Cognition · Attention

Since the first report of what was eventually determined to be the Human Immunodeficiency Virus (HIV) (Gottlieb et al. 1981), the vast majority of cases in the HIV epidemic have been younger adults. However, with the advent of highly active antiretroviral therapy (HAART) in 1996 or 1997, the demographics of HIV-infection have been changing. HIV-positive adults are now living longer. In addition, while the number of HIV cases in general has leveled off, the proportion of HIV diagnoses in adults 50 years or older is steadily increasing (Centers for Disease Control and Prevention 2007) (see Fig. 1). Although a longer lifespan is a welcome outcome, the combination of aging with HIV may place some older adults at increased risk for cognitive impairment.

To date, no comprehensive review of the neuropsychological literature on HIV and aging has been conducted. The neuropsychology of HIV has been described for younger and middle-aged adults (for reviews see Grant and Martin 1994; Hinkin et al. 1998; McArthur and Grant 1998). Accordingly, HIV is associated with a variety of cognitive symptoms including problems in attention, concentration, learning, memory, psychomotor ability, and speed of processing. Clinical syndromes include Minor Cognitive Motor Disorder (MCMD) which is characterized as psychomotor slowing and tremor, and HIV-associated Dementia (HAD) if symptoms are severe enough and interfere with aspects of daily living. Likewise, a large body of literature shows that normal aging is associated with a variety of cognitive changes in similar cognitive domains (Craik and Salthouse 1992, 2000; Woodruff-Pak 1997), thus the potential greater risk in older adults with HIV.

Several studies have examined the possible mechanisms or causal factors that could mediate such exacerbated cognitive decline in older HIV-positive adults (Brew 2004; Ernst and Chang 2004; Hinkin et al. 2001; Stoff 2004; Stoff et al. 2004; Valcour, Shikuma, Watters et al. 2004; Vance 2004; Vance and Robinson 2004). One

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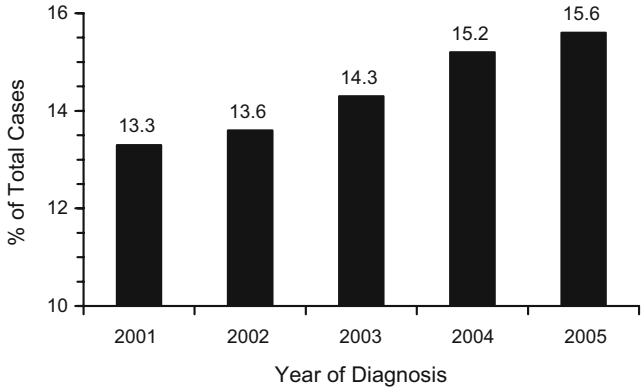

Fig. 1 Percentage of cases of HIV/AIDS in adults 50 years old or older. Based on data from the HIV/AIDS Surveillance Report, Centers for Disease Control and Prevention (2007)

possibility is increased risk for cardiovascular and cerebrovascular co-pathology that frequently accompany aging and HIV (Connor et al. 2000). This risk may be especially important if HAART includes a protease inhibitor which is known to increase cholesterol and compromise cardiovascular and cerebrovascular health. Immunological changes may be another possible factor, such as a reduction in CD4 lymphocyte cell count as well as proliferation and increase in macrophage activation. Exacerbated inflammatory glial activation has been shown in older HIV-positive adults beyond that of normal aging or in younger HIV-positive adults, particularly in frontal white matter (Ernst and Chang 2004). Expression of apolipoprotein E4 (APOE4) is another potential risk factor, considering its relationship with the occurrence of both Alzheimer's dementia (an age-related dementia) and HAD (Valcour et al. 2006). It is unclear if there is a primary causal mechanism for exacerbated cognitive deficiencies in older HIV-positive adults. The list of potential factors presented here is not exhaustive (for example, other factors include exacerbated testosterone deficiency, the advent of hepatitis C, etc.) but serves to show that there may be several interactive causative pathways by which older HIV-positive adults may be at risk for cognitive impairment.

The purpose of the present review is to examine the neuropsychological research on HIV and aging focusing closely on neurocognitive test performance. Three basic types of studies are examined. First, there are comparisons in test performance between younger HIV-positive adults and older clinically normal adults without HIV. These studies examine the similarity in cognition between these two groups, likening the impact of HIV to that of normal aging effects on cognition. Second, there are studies that examine age effects on cognition within groups of HIV-positive adults. Third, there are the more direct tests of the interaction between HIV and aging on cognition, where younger and older HIV-positive adults with corresponding HIV-negative control groups are compared. As a rule, the last group of studies provides the strongest evidence on the theoretical issue of whether HIV and aging interact resulting in exacerbated cognitive impairment. In addition, an important issue is that of within-group variability or individual differences. Because large amounts of individual differences in cognition are apparent both in HIV and in aging, the methodological distinction between group analyses versus the analysis of individuals is meaningful. Implications for research, prevention, and intervention in older adults with HIV are provided.

Comparing Younger HIV-positive Adults with Older HIV-negative Adults

There is a relatively long history of proposals characterizing the process of normal aging as alterations in a subcortical-frontal system (Bashore 1993, Hicks and Birren 1970; van Gorp and Mahler 1990), similar to that seen in HIV encephalopathy. Therefore, it is not surprising that early studies found a parallel pattern of cognitive impairment between HIV and aging. For instance, van Gorp et al. (1989) found a marked similarity in neuropsychological test performance between a sample of 14 younger HIV-positive men diagnosed with the Acquired Immune Deficiency Syndrome (AIDS) (mean age=37.5, *SD*=5.9) and 14 clinically older HIV-negative men (mean age=70.1, *SD*=6.0). No significant difference was found between the younger group with AIDS and the older control group on all 16 measures across five neuropsychological domains (attention and concentration, memory, visuospatial function, motor speed and cognitive flexibility, and language). Although care must be taken when drawing conclusions based on null results, the lack of a group difference on all test scores suggests a similar cognitive status. In an extension of this study, Hinkin et al. (1990) included 14 clinically normal younger males (mean age=35.9, *SD*=6.3) as an additional control group. Despite the large group difference in age, the pattern of performance on six neuropsychological tests was very similar between the younger AIDS group and the neurologically normal older group (see Fig. 2). As can be seen in this figure, the Trail Making Test Part B (a test of processing speed and attention) showed the largest deficit in the AIDS group and in the older adults. Lending quantitative and statistical support to the finding of a similar pattern of performance, a discriminant function analysis classified all 14 of the older adults into the same group as the HIV-positive patients in comparison to the younger control group. With no older HIV-positive group, the potential interactive effects of aging with HIV were not directly examined here. However,

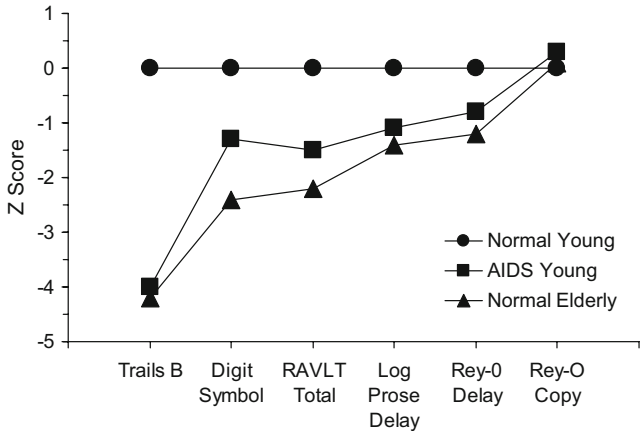

Fig. 2 Based on data from Hinkin et al. (1990). Z scores were originally computed using means and standard deviations from the normal young group

the results from these studies do suggest that because of the similarity in cognitive sequelae (in severity and pattern) between adults with HIV and normal older adults, HIV infection in older adults will result in a compounding or exacerbation of cognitive symptoms.

The Effects of Aging in Adults with HIV

Several studies have examined the role of aging on cognition within groups of adults with HIV. In a clinical sample of 257 HIV-positive men, the older adults (mean age=44.5, *SD*=6.8) performed worse than the younger adults (mean age=31.5, *SD*=3.5) on nine of nine neuropsychological test measures (Trail Making Test Parts A and B, three conditions on the Stroop test, Grooved Pegboard dominant hand, Symbol Digit Modalities Test, and two word fluency tests—the Controlled Oral Word Association Test, and an animal naming test) (Hardy, Hinkin et al. 1999). Furthermore, age-group differences were larger in the adults with AIDS versus the HIV-positive adults without AIDS on select test measures. This interaction between age and HIV severity was significant on the Trail Making Test Part B (p =.013), Grooved Pegboard dominant hand (p=.019), and a trend with the Symbol Digit Modalities Test (p=.066). It is not surprising that these were the tests that showed an interaction. Both HIV and aging are separately associated with a slowing in speed of processing (cognitive and motor performance). In addition, attention functioning (such as required on the Trail Making Test Part B) represents one of the more vulnerable cognitive domains in HIV and in aging. Although CD4 lymphocyte cell count in general was worse (lower) in the AIDS groups (both younger and older), CD4 lymphocyte cell count in the older adults with AIDS was no worse than in the younger group with AIDS. This suggests that the significantly worse test performance in the older AIDS group was due not to a more advanced clinical state per se but perhaps due to the concomitant effects of aging.

In a relatively large community sample of asymptomatic and symptomatic HIV-positive adults (N=199), Becker et al. (1997) found that age was negatively associated with a "speed" factor that in turn was negatively associated with four neuropsychological outcome variables (memory, frontal functioning, spatial ability, and fluency). This finding is noteworthy considering that the mean age of the sample was 38 years old with a standard deviation of 8.2 years. Thus, even a modest age difference within adults with HIV is associated with a decline in cognition that is mediated by a decline in speed of processing, a phenomenon that has also been found in much older normal adults (e.g., Salthouse 1994). In another study, the impact of age on divided attention or multi-task performance was examined in HIV (Hardy et al. 2004). In this experimental study, 32 HIV-positive adults (mean age=42.5, *SD*=9.9) between 25 and 70 years old performed on the MAT (Multi-Attribute Task) Battery, a fairly complex multi-task computer scenario developed by NASA researchers (Comstock and Arnegard 1992). In the MAT Battery, a tracking task was performed alone, concomitantly with one other task (a system monitoring task), and with two other tasks (a system monitoring task and a fuel management task). Increasing age was associated with worse tracking performance, and this relationship became progressively stronger (steeper slope values) from the single task (b=0.45, p=.08), dual-task (b= 0.85, p=.01), and three-task condition (b=1.28, p=.01). In other words, among this sample of HIV-positive adults, the older adults had the most difficulty in the tracking task, which required constant visual monitoring and motor-hand adjustments via a joystick (somewhat analogous to the demands of driving), and this difficulty was most apparent when having to attend to multiple tasks at the same time.

These three studies (Becker et al. 1997; Hardy, Hinkin et al. 1999; Hardy et al. 2004) indicate that older HIV-positive adults have deficits in specific cognitive abilities, particularly in various aspects of attention and cognitive and psychomotor speed. Compatible with these findings but at a more global level of cognitive functioning, in a preliminary report, Valcour, Shikuma, Watters et al. (2004) found that in a sample of 47 older HIV-positive adults (over 50 years of age) and 32 younger HIV-positive adults (between 20 and 40 years old), although 88% of the younger group were rated as normal or having equivocal neuropsychological status, only 58% of the older group were similarly categorized. In addition, unlike the younger group, a substantial proportion of the older HIV-positive adults had more severe Memorial Sloan Kettering ratings indicating dementia. In a subsequent report, Valcour et al. (2006) reported that after controlling for factors such as education,

race, depression, substance abuse, viral load, CD4 lymphocyte cell count, and antiretroviral medication status, the odds of having dementia (HAD) in the older adults was 3.26 times that of the younger adults. The proportion of adults with a diagnosis of HAD was 13.7% in the younger group and 25.2% in the older group.

By contrast, in an analysis of 50 HIV-positive adults (mean age=44.5, *SD*=5.7), Vance, Woodley, and Burrage (2007) found no significant correlations between age and performance on four neuropsychological tests (Rey-Osterrieth, Trail Making Test, WAIS Digit Symbol Substitution, and WAIS pattern comparison). Likewise, Cherner et al. (2004) examined a sample of 67 older HIV-positive adults (50 years or older, mean age=53.3, *SD*=3.7) and 52 younger HIV-positive adults (35 years or younger, mean age=31.8, *SD*=3.2). Although the prevalence of global impairment was 10% higher in the older group (64%) compared to the younger group (54%) with similar but smaller age-group differences on several specific cognitive domains, none of these differences were statistically significant. This null finding may be explained by there being significantly fewer younger adults on HAART than the older adults. Not being on HAART may have increased the level of HIV RNA in the cerebrospinal fluid (CSF), which may have made them more vulnerable to HIV-related cognitive impairments. In fact, of those with detectable CSF HIV RNA, 81% of the older group and 54% of the younger group were cognitively impaired; however, of those with undetectable CSF HIV RNA, 42% of the older group and 57% of the younger group were cognitively impaired. Logistic regressions predicting cognitive impairment showed an interaction between age group and CSF viral load on the cognitive domains of abstraction, attention/working memory, learning, and motor ability. Thus, with detectable levels of CSF HIV RNA, older adults may be more vulnerable than younger adults to the impact of HIV on cognitive functioning.

The findings of Cherner et al. (2004) highlight the importance of corollary factors that could significantly influence age group comparisons in HIV. Valcour, Shikuma, Shiramizu et al. (2004) examined another potentially influencing factor, APOE4. In a sample of 85 younger HIV-positive adults (between 20 and 39 years old, mean age=35.0, *SD*=5.0) and 97 older HIV-positive adults (50 years or older, mean age=55.6, *SD*=5.2), after controlling for age and diabetes status, having at least one E4 allele was associated with a 2.9 times greater chance of developing HAD in the older group but not in the younger group (OR=.33). This result mimics the pattern of the Cherner et al. (2004) results, where older adults with HIV appear to be more vulnerable than their younger counterparts to these corollary factors, resulting in greater cognitive deficits.

The Interaction Between HIV and Aging

To test directly whether HIV infection and aging have an interactive impact on cognition requires the examination of younger and older HIV-positive adults as well as younger and older HIV-negative adults. In one of the earliest studies, Arendt et al. (1993) examined auditory event-related brain potentials (ERPs) in 100 HIV-positive adults across a variety of clinical stages (mean age=35 years, *SD*=10.9) and in 43 HIV-negative adults (mean age=36 years, *SD*=10.4). ERPs were recorded during performance of a typical auditory "oddball" task. The main finding was that amplitude of P300, an ERP component that has been linked to cognition (see Rugg and Coles 1995), declined twice as fast as a function of age in the HIV group relative to controls. There is a large literature showing the sensitivity of ERP measures to aging (e.g., Czigler et al. 1997; El Yagoubi et al. 2005; Pfefferbaum et al. 1984; Picton et al. 1984; West and Schwarb 2006). ERPs have also been shown to be sensitive to HIV infection (Grotemeyer et al. 1991; Linnville et al. 1996; Polich et al. 2000; Takakuwa et al. 1993; Tartar et al. 2004). In the study by Arendt et al. (1993), there were no age-related effects on psychometric test performance. This finding suggests that cognition-related ERPs such as the P300, which did show an interaction between HIV status and age, may be a particularly sensitive marker to the interactive effects of HIV and aging on nervous system functioning.

Other studies have found minimal or no evidence for the interaction of HIV and aging on cognition. For instance, in a large sample from the Multicenter AIDS Cohort Study (MACS) with 1,066 HIV-positive adults (mean age=35.8, *SD*=6.5) and 1,004 HIV-negative adults (mean age=37.3, *SD*=7.5), van Gorp et al. (1994) found little evidence of an interaction between HIV status and age when comparing slopes of performance scores on a variety of standard neuropsychological tests and computerized reaction time tests regressed on age. Of 21 measures, only a single trend emerged, performance in executive function or attention, on the Trail Making Test Part B, became comparatively worse in the HIV-positive group (relative to the HIV-negative group) with advancing age (p=.056). In a second set of analyses using a similar test battery on a clinical sample of 76 HIV-positive adults (mean age=47.2, *SD*=13.0) and 47 HIV-negative adults (mean age=49.3, *SD*=13.8), only a single significant slope interaction between HIV and age emerged, and that was on the Grooved Pegboard nondominant hand (p=.015). A similar set of regression analyses was conducted in a study by Hardy, Satz et al. (1999), with no evidence of any interaction between HIV and aging on cognition. With clinical samples of 104 HIV-positive adults without AIDS (mean age=39.7, *SD*=7.6), 53 adults with AIDS (mean age=43.1, *SD*=10.1), and 100 HIV-

negative adults (mean age=44.7, *SD*=6.5), no group differences on slopes were found when regressing performance scores from a variety of standard neuropsychological tests on participant age.

The results from the van Gorp et al. (1994) and Hardy, Satz et al. (1999) studies are somewhat surprising considering that most of these HIV-positive adults did not yet have access to HAART. It is possible that the greater medical symptoms in these pre-HAART individuals may have obscured any age-serostatus interactions. In addition, although the average age in the van Gorp et al. (1994) study was comparable to the Arendt et al. (1993) study, only five HIV-positive individuals (out of a sample of 1,066) in the former study were 55 years of age or older. Older HIV-positive adults were infrequent in these early studies. Clinical or medical status could also be an issue. The majority of HIV-positive adults in the initial van Gorp analyses were asymptomatic. However, an analysis on a sub-sample of all symptomatic HIV-positive participants (n=185) also revealed no evidence of an age interaction with HIV status on test performance slopes.

More recently, Wilkie et al. (2003) also found no evidence of exacerbated cognitive deficits in older adults with HIV. Rather than comparing age by serostatus regression slopes, they compared test performance across four domains (attention, verbal learning and memory, speed of processing, and motor processes) among 54 younger HIV-positive adults (mean age=33.0, *SD*=5.5), 32 older HIV-positive adults age 50 or older (mean age=56.6, *SD*=5.0), 27 younger HIV-negative adults (mean age=33.0, *SD*=5.9), and 36 older HIV-negative adults (mean age=56.4, *SD*=6.2). Several cognitive measures showed no significant age by serostatus interaction, or surprisingly, showed that the younger HIV-positive group performed *worse* than the older HIV-positive group. For instance, on a simple visual reaction time test, although the younger HIV-positive group (377 ms) was slower than the younger HIV-negative group (298 ms), as could be expected, they were also slower than the older HIV-positive group (298 ms). When looking at individual's performance on the California Verbal Learning Test (CVLT), there was a greater number of severely impaired adults on learning and delayed recall in the younger HIV-positive group (51.8% and 53.6%, respectively) compared to the older HIV-positive group (33.3% and 41.7%, respectively). There were similar findings on other measures as well. Unfortunately, there were considerable demographic differences among the participant samples. Compared to the other groups, the younger HIV-positive group was significantly less educated (mean=11.7 years), they had a greater level of depression (via the Beck Depression Inventory), and a higher plasma viral load level. In addition, compared to the older HIV-positive group, the younger HIV-positive group included fewer European Americans (46.9% and 14.8%, respectively) and fewer males (81.3% and 44.4%, respectively). Despite including covariates in their analyses (e.g., education, gender, ethnicity, etc.), because of the considerable differences among groups, interpretation of the Wilkie et al. results remain difficult.

Becker et al. (2004) also found mixed results. They examined test performance across eight neuropsychological domains (verbal, attention, speed, verbal memory, non-verbal memory, visuospatial, fluency, and executive) in a community-based sample of 290 HIV-positive adults (mean age=38.3, *SD*=8.2) and 124 HIV-negative adults (mean age=34.3, *SD*=8.2). Although HIV serostatus groups differed on several domains, no serostatus by age group interactions emerged. Incidence of dementia was also examined in younger and older HIV-positive and control groups. At the baseline assessment, the proportion of HIV-positive adults under 50 years old categorized with dementia was 9% and with mild cognitive impairment was 22%; for individuals 50 years and older, 22% were categorized with dementia and 14% with mild cognitive impairment. Thus, in contrast to analyses on group scores (where no apparent age effect was evident), their examination of individuals showed that a larger subgroup of older HIV-positive adults were susceptible to dementia. Few HIV-negative adults in either age group showed signs of cognitive impairment. Using dementia as the outcome when examining the interaction between HIV and age may be of limited use considering the very low base rate of severe impairment in HIV-negative adults.

A more successful or complementary approach may be the examination of individual's outcomes on individual domains or tests (in contrast to or in addition to an aggregation of test scores indicating dementia). For example, in a second set of analyses in the Hardy, Satz et al. (1999) study, outliers per test (any score beyond two *SD* from the respective HIV-negative group mean–indicating poor performance) were assessed in the HIV-negative and HIV-positive groups across three age groups (30 to 39, 40 to 49, and 50+ years). Results are presented in Table 1. As can be seen, in general there are more outlier scores in the HIV-positive groups versus the HIV-negative groups, with the highest proportion of outliers usually in the adults with AIDS who are 50 years or older. Note that the largest proportion of older AIDS outliers was on the Trail Making Test Part B, a finding that is compatible with previous studies cited in this review showing the sensitivity of this test to the combined effects of HIV and aging on attention and speed of processing.

Conclusion

The variety of methods and approaches evident in the research on HIV and aging precludes a meta-analysis of the

Table 1 Percentage of outliers across three age groups

Test Measure	HIV-			HIV+ No AIDS			AIDS		
	30s	40s	50+	30s	40s	50+	30s	40s	50+
Stroop word reading	0.0	6.3	4.8	0.0	0.0	7.7	0.0	0.0	0.0
Stroop color naming	0.0	3.1	14.3	6.6	3.3	23.1	15.4	11.1	27.8
Stroop interference	0.0	3.1	9.5	9.8	13.3	46.2	23.1	22.2	38.9
Trail making test A	0.0	7.8	4.8	4.9	6.7	30.8	3.8	11.1	27.8
Trail making test B	0.0	3.1	9.5	18.0	20.0	23.1	26.9	22.2	61.1
Pegboard DH	6.7	9.4	0.0	3.3	0.0	15.4	19.2	11.1	27.8
Pegboard NH	0.0	4.7	4.8	3.3	3.4	15.4	11.5	22.2	44.4
Symbol digit	0.0	1.6	1.6	6.6	10.3	7.7	11.5	11.1	44.4
RAVLT recog	0.0	3.1	4.8	1.6	6.7	15.4	11.5	0.0	38.9
RAVLT recall	0.0	0.0	4.8	1.6	3.3	15.4	15.4	0.0	27.8
RAVLT delay	0.0	0.0	4.8	1.6	10.0	15.4	15.4	11.1	38.9

RAVLT=Rey Auditory Verbal Learning Test

literature at this point. Nonetheless, results from this qualitative review indicate that the effects of HIV and aging on cognition are not uniform. This finding is not surprising considering that there are known large individual differences in the cognitive status of HIV-positive adults (Hardy, Hinkin et al. 1999) as well as in older adults (Nelson and Dannefer 1992; Schaie 1996). Therefore, large individual differences would be expected in older HIV-positive adults. This expectation was directly examined and found in the study by Hardy, Hinkin et al. (1999). Comparing within-group test score standard deviations across nine tests, standard deviations were on average 84% larger in the older adults with AIDS compared to the younger AIDS patients. The difference was not so extreme in the younger and older HIV-positive groups without AIDS. Thus, disease severity in HIV combined with aging appears to be associated with increased heterogeneity in cognitive status. Two studies in the present review (Cherner et al. 2004; Valcour, Shikuma, Shiramizu et al. 2004) underscore the importance of co-factors (such as the presence of APOE4, or a detectable viral load) that affect cognitive functioning in HIV and aging, and can at least partly explain the mixed results in the literature.

There are other factors that could be causing large individual differences among older HIV-positive adults. For instance, some older adults with HIV may continue to work. The intellectual challenge of being employed, using existing skill sets, developing new skills sets, and socially interacting with colleagues and clients obviously encourages positive neuroplasticity, allowing the brain to maintain optimal cognitive ability (Mahncke et al. 2006; Vance and Burrage 2006). Likewise, with low levels of intellectual challenge that can occur with disability and lack of employment opportunities, negative neuroplasticity can occur resulting in less optimal cognitive ability.

Also relevant in the neurocognitive examination of older HIV-positive adults are potential age-related differences in alcohol and substance abuse and dependence. Alcohol abuse and dependence has been shown to be highly prevalent in HIV-positive adults (Conigliaro et al. 2006; Cook et al. 2001; Galvan et al. 2002). Alcoholism itself is associated with impaired motor function, working memory, sustained attention, and visuospatial skills (Fama et al 2004; Gordon et al. 1988). Looking at the comorbidity of alcohol abuse and infection with HIV, Sassoon et al. (2007) found worse visuospatial and speeded motor performance (as measured with the Digit Symbol test) in alcoholic HIV-positive adults compared to adults with either diagnosis alone. Similar findings were reported by Fama et al. (2007) with a composite measure of speeded fine finger movements, disease comorbidity showed compounded deficits. On the other hand, results are mixed whether comorbid substance abuse exacerbates cognitive deficits in HIV-positive adults. For example, Grassi et al. (1995) reported increased cognitive decline in HIV-positive substance abusers, but others have not (Concha et al. 1992; Stern 1994). With alcohol abuse, because each condition (HIV infection and alcoholism) is known to affect brain function, metabolism, and structure, a recent magnetic resonance spectroscopy study found significant deficits or decreases in two metabolites (*N*-acetylaspartate and creatine) in the superior parietal-occipital cortex in HIV-positive adults with alcoholism compared to either diagnosis alone (Pfefferbaum et al. 2005). The relevant question here is whether older HIV-positive adults are more likely to be abusers. In a large sample of 1,803 adults (1,047 who were HIV-positive), although rates of alcohol abuse and substance abuse were generally higher in the HIV-positive adults, abuse appears to be most prevalent in younger ages (younger than 60 years old) in both HIV-negative and HIV-positive groups (Justice et al. 2004). In the Valcour et al. (2006) study, there was no difference in rate of substance dependence between 95 younger HIV-positive adults and

103 older HIV-positive adults 50 years or older. On the other hand, in the Cherner et al. (2004) study, older HIV-positive adults (n=67) tended to report higher rates of substance abuse disorders than younger HIV-positive adults (n=52) across a variety of drugs, although it is not clear which, if any, group differences are statistically significant. It is not clear from these studies whether alcohol or substance abuse is more prevalent in older HIV-positive adults. It is interesting to note that in the Valcour et al. (2006) study, even after statistically controlling for substance dependence, the odds of having HAD in the older group was still 3.26 times that of the younger group.

The present review also indicates that exacerbated cognitive deficits will be present at least in a subset of the population of older HIV-positive adults. This finding has real world consequences for these individuals. For example, Hinkin et al. (2003) found in a sample of 148 HIV-positive adults between the ages of 25 and 69 years that adherence to protease inhibitors was better in older adults (87.5%) compared to younger adults (78.3%). In fact, HIV-positive adults age 50 years or older were three times more likely to achieve a 95% adherence rate compared to the younger group. However, of those older adults with impairments in executive ability or memory, 74% and 67% were classified as poor adherers respectively. In a follow-up study (Barclay et al. 2007), they found neurocognitive status to be associated with poor adherence, but only in the older adults, not in the younger poor adherers. Thus, there is a subgroup of older HIV-positive adults who may be at increased risk for cognitive impairment resulting in reduced medication adherence. With an adherence rate of 95% needed for optimal viral suppression, such cognitive declines can negatively impact health outcomes.

Converging evidence also suggests that problems with processes of attention may be an early marker of cognitive decline (neurological impairment) in older HIV-positive adults. This is not entirely unexpected. Attention deficits have been reported as the most frequent impairment in HIV (Heaton et al. 1995). In addition, there is a large literature showing a variety of alterations in attention in older adults (Hartley 1992). In fact, attention has been proposed as the first cognitive indicator of cortical dysfunction in Alzheimer's dementia (Parasuraman and Haxby 1993), an age-related dementia. Neurophysiological evidence also supports the proposal of attention processes being particularly susceptible to the combined effects of aging and HIV. For instance, in the Ernst and Chang (2004) study, normal aging effects on frontal white matter (via measures of choline compounds and myoinositol) were five times larger in HIV-positive adults. Frontal regions in general are associated with processes of executive control and attention (Beer et al. 2004), and declines in both have been shown in normal aging (Raz and Rodrigue 2006). Impairment of specific aspects of attention (and working memory) has also been linked to the presence of APOE4 in healthy older adults, impairments similar to that seen in Alzheimer's dementia (Parasuraman et al. 2002). As discussed earlier in this review, results from Valcour, Shikuma, Shiramizu et al. (2004) indicate that the presence of at least one E4 allele is associated with a greater chance of developing HAD in older but not younger HIV-positive adults. Similarly, Cherner et al. (2004) found that older HIV-positive adults who had a detectable viral load were more likely to be impaired than younger HIV-positive adults who had a detectable viral load on tests of attention and working memory. Perhaps attention (and closely related cognitive domains) is a particularly sensitive aspect of cognition to the presence of APOE4 and to a detectable viral load in older HIV-positive adults. This remains to be tested.

The proposal that attention may be the focus of early cognitive decline in older HIV-positive adults is also compatible with more general findings. For instance, in a comparison of education and age effects on neuropsychological test performance, Heaton, Grant, and Matthews (1986) found that age accounted for more variance in tests that required speed of processing and attention (including the Trails Making Test Part B), while education accounted for more variance in tests tapping into verbal skills and knowledge. Related to this issue of impaired attention deficits in older HIV-positive adults is the operation of complex attention-demanding systems such as driving a car. For instance, it has been shown in HIV-positive adults that impairment in attention, executive functioning, speed of information processing, and motor abilities is associated with decreased driving ability (Marcotte et al. 1999; Marcotte et al. 2006; Marcotte et al. 2004). Although no data on driving ability exists to date specifically in older HIV-positive adults, the preliminary results from the Hardy et al. (2004) study cited in this review suggest that these older adults may be at risk for impairment in demanding complex scenarios such as driving a car, flying aircraft, and so on.

In conclusion, in the United States, the number of adults 50 years old or over with HIV/AIDS has risen from 65,655 cases in 2001 to 104,260 cases in 2004, an increase of 59% (Centers for Disease Control and Prevention 2007). As the population ages and HAART extends the life span of those already infected, addressing the neuropsychological needs of older HIV-positive adults will grow. Although it does appear that cognitive impairment may be an issue that a subpopulation of older HIV-positive adults will confront, this appears to be a complex issue. In fact, individual differences must be considered when accounting for such cognitive impairments. The differences may be accounted for by such factors as APOE4, viral load, and CD4 lymphocyte cell counts. With regard to neuropsychological

assessment, although a dementia categorization might be more clinically relevant than analyzing separate test score outliers, analysis of individual tests scores may be a useful adjunct in research on HIV and aging. This may especially be the case in the discovery of an early behavioral marker of cognitive decline (such as in attention processing) before the onset of clinically detectable dementia.

References

Arendt, G., Hefter, H., Nelles, H. W., Hilperath, F., & Strohmeyer, G. (1993). Age-dependent decline in cognitive information processing of HIV-positive individuals detected by event-related potential recordings. *Journal of the Neurological Sciences*, *115*, 223–229. doi:10.1016/0022-510X(93)90229-R.

Barclay, T. R., Hinkin, C. H., Castellon, S. A., Mason, K. I., Reinhard, M. J., Marion, S. D., et al. (2007). Age-associated predictors of medication adherence in HIV-positive adults: health beliefs, self-efficacy, and neurocognitive status. *Health Psychology*, *26*, 40–49. doi:10.1037/0278-6133.26.1.40.

Bashore, T. R. (1993). Differential effects of aging on the neurocognitive functions subserving speeded mental processing. In J. Cerella, J. Rybash, W. Hoyer, & M. L. Commons (Eds.), *Adult information processing: Limits on loss* (pp. 37–76). San Diego: Academic Press.

Becker, J. T., Sanchez, J., Dew, M. A., Lopez, O. L., Dorst, S. K., & Banks, G. (1997). Neuropsychological abnormalities among HIV-infected individuals in a community-based sample. *Neuropsychology*, *11*, 592–601. doi:10.1037/0894-4105.11.4.592.

Becker, J. T., Lopez, O. L., Dew, M. A., & Aizenstein, H. J. (2004). Prevalence of cognitive disorders differs as a function of age in HIV virus infection. *AIDS (London, England)*, *18*, 11–18. doi:10.1097/00002030-200401001-00003.

Beer, J. S., Shimamura, A. P., & Knight, R. T. (2004). Frontal lobe contributions to executive control of cognitive and social behavior. In M. S. Gazzaniga (Ed.), *The cognitive neurosciences, 3rd edn* (pp. 1091–1104). Cambridge: MIT Press.

Brew, B. J. (2004). Evidence for a change in AIDS dementia complex in the era of highly active antiretroviral therapy and the possibility of new forms of AIDS dementia complex. *AIDS (London, England)*, *18*, 75–78. doi:10.1097/00002030-200401001-00011.

Centers for Disease Control and Prevention. (2007). Estimated numbers of persons living with HIV/AIDS, by year and selected characteristics, 2001–2004. Cited at www.cdc.gov/hiv/topics/surveillance/resources/reports/2004report/table8.htm.

Cherner, M., Ellis, R. J., Lazzaretto, D., Young, C., Mindt, M. R., Atkinson, J. H., et al. (2004). Effects of HIV-1 infection and aging on neurobehavioral functioning: preliminary findings. *AIDS (London, England)*, *18*, 27–34. doi:10.1097/00002030-200401001-00005.

Comstock, J. R., & Arnegard, R. J. (1992). *The multi-attribute task battery for human operator workload and strategic behavior research (Tech. Memorandum No. 104174)*. Hampton: NASA Langley Research Center.

Concha, M., Graham, N. M. H., Munoz, A., Vlahov, D., Royal, W., Updike, M., et al. (1992). Effect of chronic substance abuse on the neuropsychological performance of intravenous drug users with a high prevalence of HIV-1 seropositivity. *American Journal of Epidemiology*, *136*, 1338–1348.

Conigliaro, J., Justice, A. C., Gordon, A. J., & Bryant, K. (2006). Role of alcohol in determining human immunodeficiency virus (HIV)-relevant outcomes: a conceptual model to guide the implementation of evidence-based interventions into practice. *Medical Care*, *44*, 1–6. doi:10.1097/01.mlr.0000223659.36369.cf.

Connor, M. D., Lammie, G. A., Bell, J. E., Warlow, C. P., Simmonds, P., & Brettle, R. D. (2000). Cerebral infarction in adult AIDS patients: observation from the Edinburgh HIV autopsy cohort. *Stroke*, *31*, 2117–2126.

Cook, R. L., Sereika, S. M., Hunt, S. C., Woodward, W. C., Erlen, J. A., & Conigliaro, J. (2001). Problem drinking and medication adherence among persons with HIV infection. *Journal of General Internal Medicine*, *16*, 83–88. doi:10.1111/j.1525-1497.2001.00122.x.

Craik, F. I. M., & Salthouse, T. A. (Eds.), (1992). *The handbook of aging and cognition*. Hillsdale, NJ: Lawrence Erlbaum and Associates.

Craik, F. I. M., & Salthouse, T. A. (Eds.), (2000). *The handbook of aging and cognition (2nd ed.)*. Hillsdale, NJ: Lawrence Erlbaum and Associates.

Czigler, I., Csibra, G., & Ambro, A. (1997). Age and information processing: event-related potential studies. *European Psychologist*, *2*, 247–257. doi:10.1027/1016-9040.2.3.247.

El Yagoubi, R., Lemaire, P., & Besson, M. (2005). Effects of aging on arithmetic problem-solving: an even-related brain potential study. *Journal of Cognitive Neuroscience*, *17*, 37–50. doi:10.1162/0898929052880084.

Ernst, T., & Chang, L. (2004). Effect of aging on brain metabolism in antiretroviral-naïve HIV patients. *AIDS (London, England)*, *18*, 61–67. doi:10.1097/00002030-200401001-00009.

Fama, R., Pfefferbaum, A., & Sullivan, E. V. (2004). Perceptual learning in detoxified alcoholic men: contributions from explicit memory, executive function, and age. *Alcoholism, Clinical and Experimental Research*, *28*, 1657–1665. doi:10.1097/01.ALC.0000145690.48510.DA.

Fama, R., Eisen, J. C., Rosenbloom, M. J., Sassoon, S. A., Kemper, C. A., Deresinski, S., et al. (2007). Upper and lower limb motor impairments in alcoholism, HIV infection, and their comorbidity. *Alcoholism, Clinical and Experimental Research*, *31*, 1038–1044. doi:10.1111/j.1530-0277.2007.00385.x.

Galvan, F. H., Bing, E. G., Fleishman, J. A., London, A. S., Caetano, R., Burnam, M. A., et al. (2002). The prevalence of alcohol consumption and heavy drinking among people with HIV in the United States: results from the HIV Cost and Services Utilization Study. *Journal of Studies on Alcohol*, *63*, 179–186.

Gordon, S. M., Kennedy, B. P., & McPeake, J. D. (1988). Neuropsychologically impaired alcoholics: assessment, treatment considerations, and rehabilitation. *Journal of Substance Abuse Treatment*, *5*, 99–104. doi:10.1016/0740-5472(88)90019-0.

Gottlieb, M. S., Schanker, H. M., Fan, P. T., Saxon, A., Weisman, J. D., & Pozalski, I. (1981). Pneumocystis pneumonia—Los Angeles. *Morbidity and Mortality Weekly Report*, *30*(21), 1–3.

Grant, I., & Martin, A. (1994). *Neuropsychology of HIV infection*. New York: Oxford University Press.

Grassi, M. P., Clerci, F., Perin, C., Zocchetti, C., Borella, M., Cargnel, A., & Mangoni, A. (1995). HIV infection and drug use: influence on cognitive function. *AIDS (London, England)*, *9*, 165–170. doi:10.1097/00002030-199509020-00008.

Grotemeyer, K. H., Husstedt, I. W., Brundermann, H., Busch, H., Schlake, H. P., & Zidek, W. (1991). Event-related potentials in HIV-infected outpatients. *AIDS Research and Human Retroviruses*, *7*, 629–635.

Hardy, D. J., Hinkin, C. H., Satz, P., Stenquist, P. K., van Gorp, W. G., & Moore, L. H. (1999). Age differences and neurocognitive performance in HIV-infected adults. *New Zealand Journal of Psychology*, *28*, 94–101.

Hardy, D. J., Satz, P., Stefaniak, M., van Gorp, W. G., Hinkin, C. H., & Stenquist, P. K. (1999). *Cognition in older adults with AIDS*. Poster presented at the 4th Annual UCLA Research Conference on Aging.

Hardy, D. J., Borghi, S., Lodato, J., Zolnikof, B., Miller, E. N., Green, M., et al. (2004). *Older HIV-infected adults and multi-task performance*. Poster presented at the 24th Annual Conference of the National Academy of Neuropsychology, Seattle, Washington.

Hartley, A. A. (1992). Attention. In F. I. M. Craik, & T. A. Salthouse (Eds.), *The handbook of aging and cognition* (pp. 3–49). Hillsdale: Lawrence Erlbaum Associates.

Heaton, R. K., Grant, I., Butters, N., White, D. A., Kirson, D., Atkinson, J. H., et al. (1995). The HNRC 500—Neuropsychology of HIV infection at different disease stages. *Journal of the International Neuropsychological Society*, *1*, 231–251.

Heaton, R. K., Grant, I., & Matthews, C. G. (1986). Differences in neuropsychological test performance associated with age, education and sex. In I. Grant, & K. M. Adams (Eds.), *Neuropsychological Assessment of Neuropsychiatric Disorders* (pp. 100–120). New York: Oxford University Press.

Hicks, L. H., & Birren, J. E. (1970). Aging, brain damage, and psychomotor slowing. *Psychological Bulletin*, *74*, 377–396. doi:10.1037/h0033064.

Hinkin, C. H., Cummings, J. L., van Gorp, W. G., Satz, P., Mitrushina, M., & Freeman, D. (1990). Frontal/subcortical features of normal aging: an empirical analysis. *Canadian Journal on Aging*, *9*, 104–119.

Hinkin, C. H., Castellon, S. A., van Gorp, W. G., & Satz, P. (1998). Neuropsychological features of HIV disease. In W. G. van Gorp, & S. L. Buckingham (Eds.), *Practitioner's guide to the neuropsychiatry of HIV/AIDS* (pp. 1–41). New York: The Guilford Press.

Hinkin, C. H., Castellon, S. A., Atkinson, J. H., & Goodkin, K. (2001). Neuropsychiatric aspects of HIV infection among older adults. *Journal of Clinical Epidemiology*, *54*, 44–52. doi:10.1016/S0895-4356(01)00446-2.

Hinkin, C. H., Hardy, D. J., Mason, K. I., Castellon, S. A., Durvasula, R. S., Lam, M. N., & Stefaniak, M. (2003). Medication adherence in HIV-infected adults: effect of patient age, cognitive status, and substance abuse. *AIDS (London, England)*, *17*, 1–7. doi:10.1097/00002030-200301030-00003.

Justice, A. C., McGinnis, K. A., Atkinson, J. H., Heaton, R. K., Young, C., Sadek, J., et al. (2004). Psychiatric and neurocognitive disorders among HIV-positive and negative veterans in care: veterans Aging Cohort Five-Site Study. *AIDS (London, England)*, *18*, 49–59. doi:10.1097/00002030-200401001-00008.

Linnville, S. E., Elliott, F. S., & Larson, G. E. (1996). Event-related potentials as indices of subclinical neurological differences in HIV patients during rapid decision making. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *8*, 293–304.

Mahncke, H. W., Bronstone, A., & Merzenich, M. M. (2006). Brain plasticity and functional losses in the aged: scientific bases for novel intervention. *Progress in Brain Research*, *157*, 81–109. doi:10.1016/S0079-6123(06)57006-2.

Marcotte, T. D., Heaton, R. K., Wolfson, T., Taylor, M. J., Alhassoon, O., Arfaa, K., et al. (1999). The impact of HIV-related neuropsychological dysfunction on driving behavior. *Journal of the International Neuropsychological Society*, *5*, 579–592. doi:10.1017/S1355617799577011.

Marcotte, T. D., Wolfson, T., Rosenthal, T. J., Heaton, R. K., Gonzalez, R., Ellis, R. J., et al. (2004). A multimodal assessment of driving performance in HIV infection. *Neurology*, *63*, 1417–1422.

Marcotte, T. D., Lazzaretto, D., Scott, J. C., Roberts, E., Woods, S. P., Letendre, S., et al. (2006). Visual attention deficits are associated with driving accidents in cognitively-impaired HIV-infected individuals. *Journal of Clinical and Experimental Neuropsychology*, *28*, 13–28. doi:10.1080/13803390490918048.

McArthur, J. C., & Grant, I. (1998). HIV neurocognitive disorders. In H. E. Gendelman, S. A. Lipton, L. Epstein, & S. Swindells (Eds.), *The neurology of AIDS* (pp. 499–523). New York: Chapman & Hall.

Nelson, E. A., & Dannefer, D. (1992). Aged heterogeneity: fact or fiction? The fate of diversity in gerontological research. *The Gerontologist*, *32*, 17–23. doi:10.1159/000116781.

Parasuraman, R., & Haxby, J. V. (1993). Attention and brain function in Alzheimer's Disease. *Neuropsychology*, *7*, 242–272. doi:10.1037/0894-4105.7.3.242.

Parasuraman, R., Greenwood, P. M., & Sunderland, T. (2002). The apolipoprotein E gene, attention, and brain function. *Neuropsychology*, *16*, 254–274. doi:10.1037/0894-4105.16.2.254.

Pfefferbaum, A., Ford, J. M., Wenegrat, B. G., Roth, W. T., & Kopell, B. S. (1984). Clinical application of the p3 component of event-related potentials. I. Normal aging. *Electroencephalography and Clinical Neurophysiology*, *59*, 85–103. doi:10.1016/0168-5597(84)90026-1.

Pfefferbaum, A., Adalsteinsson, E., & Sullivan, E. V. (2005). Cortical NAA deficits in HIV infection without dementia: influence of alcoholism comorbidity. *Neuropsychopharmacology*, *30*, 1392–1399. doi:10.1038/sj.npp.1300623.

Picton, T. W., Stuss, D. T., Champagne, S. C., & Nelson, R. F. (1984). The effects of age on human event-related potentials. *Psychophysiology*, *21*, 312–325. doi:10.1111/j.1469-8986.1984.tb02941.x.

Polich, J., Ilan, A., Poceta, J. S., Mitler, M. M., & Darko, D. F. (2000). Neuroelectric assessment of HIV: EEG, ERP, and viral load. *International Journal of Psychophysiology*, *38*, 97–108. doi:10.1016/S0167-8760(00)00133-1.

Raz, N., & Rodrigue, K. M. (2006). Differential aging of the brain: patterns, cognitive correlates and modifiers. *Neuroscience and Biobehavioral Reviews*, *30*, 730–748. doi:10.1016/j.neubiorev.2006.07.001.

Rugg, M. D., & Coles, M. G. H. (Eds.), (1995). *Electrophysiology of mind*. Oxford: Oxford University Press.

Salthouse, T. A. (1994). How many causes are there of aging-related decrements in cognitive functioning? *Developmental Review*, *14*, 413–437. doi:10.1006/drev.1994.1016.

Sassoon, S. A., Fama, R., Rosenbloom, M. J., O'Reilly, A., Pfefferbaum, A., & Sullivan, E. V. (2007). Component cognitive and motor processes of the Digit Symbol Test: differential deficits in alcoholism, HIV infection, and their comorbidity. *Alcoholism, Clinical and Experimental Research*, *31*, 1315–1324. doi:10.1111/j.1530-0277.2007.00426.x.

Schaie, K. W. (1996). Intellectual development in adulthood. In J. E. Birren, & K. W. Schaie (Eds.), *Handbook of the psychology of aging, 4th edn* (pp. 266–286). San Diego: Academic Press.

Stern, Y. (1994). Neuropsychological assessment of seropositive intravenous drug users. In I. Grant, & A. Martin (Eds.), *Neuropsychology of HIV infection* (pp. 220–233). New York: Oxford University Press.

Stoff, D. M. (2004). Mental health research in HIV/AIDS and aging: problems and prospects. *AIDS (London, England)*, *18*, 3–10. doi:10.1097/00002030-200401001-00002.

Stoff, D. M., Khalsa, J. H., Monjan, A., & Portegies, P. (2004). Introduction: HIV/AIDS and aging. *AIDS (London, England)*, *18*, 1–2. doi:10.1097/00002030-200401001-00001.

Takakuwa, K. M., Callaway, E., Naylor, H., Herzig, K. E., & Yano, L. M. (1993). The effects of the Human Immunodeficiency Virus on visual information processing. *Biological Psychiatry*, *34*, 194–197. doi:10.1016/0006-3223(93)90392-Q.

Tartar, J. L., Sheehan, C. M., Nash, A. J., Starratt, C., Puga, A., & Widmayer, S. (2004). ERPs differ from neurometric tests in assessing HIV-associated cognitive deficit. *Neuroreport*, *15*, 1675–1678. doi:10.1097/01.wnr.0000134992.74181.4b.

Valcour, V., Shikuma, C., Shiramizu, M., Watters, M., Poff, P., Selnes, O. A., et al. (2004). Age, apolipoprotein E4, and the risk of HIV dementia: the Hawaii Aging with HIV Cohort. *Journal of Neuroimmunology*, *157*, 197–202. doi:10.1016/j.jneuroim.2004.08.029.

Valcour, V. G., Shikuma, C. M., Watters, M. R., & Sactor, N. C. (2004). Cognitive impairment in older HIV-1-seropositive individuals: prevalence and potential mechanisms. *AIDS (London, England)*, *18*, 79–86. doi:10.1097/00002030-200401001-00012.

Valcour, V., Shikuma, C., Shiramizu, B., Watters, M., Poff, P., Selnes, O., et al. (2006). Higher frequency of dementia in older HIV-1 individuals. The Hawaii Aging with HIV-1 Cohort. *Neurology*, *63*, 822–827.

van Gorp, W. G., & Mahler, M. (1990). Subcortical features of normal aging. In J. L. Cummings (Ed.), *Subcortical dementia* (pp. 231–250). New York: Oxford University Press.

van Gorp, W. G., Mitrushina, M., Cummings, J. L., Satz, P., & Modesitt, J. (1989). Normal aging and the subcortical encephalopathy of AIDS. A neuropsychological comparison. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, *2*, 5–20.

van Gorp, W. G., Miller, E. N., Marcotte, T. D., Dixon, W., Paz, D., Selnes, O., et al. (1994). The relationship between age and cognitive impairment in HIV-1 infection: findings from the Multicenter AIDS Cohort Study and a clinical cohort. *Neurology*, *44*, 929–935.

Vance, D. E. (2004). Cortical and subcortical dynamics of aging with HIV infection. *Perceptual and Motor Skills*, *98*, 647–655. doi:10.2466/PMS.98.2.647-655.

Vance, D. E., & Robinson, F. P. (2004). Reconciling successful aging with HIV: a biopsychosocial overview. *Journal of HIV/AIDS & Social Services*, *3*, 59–78. doi:10.1300/J187v03n01_06.

Vance, D. E., & Burrage Jr., J. W. (2006). Promoting successful cognitive aging in adults with HIV: strategies for intervention. *Journal of Gerontological Nursing*, *32*(11), 34–41.

Vance, D. E., Woodley, R. A., & Burrage Jr., J. A. (2007). Predictors of cognitive ability in adults aging with HIV: a pilot study. *Clinical Gerontologist*, *30*(3), 83–101. doi:10.1300/J018v30n03_07.

West, R., & Schwarb, H. (2006). The influence of aging and frontal function on the neural correlates of regulative and evaluative aspects of cognitive control. *Neuropsychology*, *20*, 468–481. doi:10.1037/0894-4105.20.4.468.

Wilkie, F. L., Goodkin, K., Khamis, I., van Zuilen, M. H., Lee, D., Lecusy, R., et al. (2003). Cognitive functioning in younger and older HIV-1-infected adults. *Journal of Acquired Immune Deficiency Syndromes*, *33*, 93–105.

Woodruff-Pak, D. S. (1997). *The neuropsychology of aging*. Malden: Blackwell Publishers Inc.