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Incidence and Nature of Cognitive Decline Over One Year Among HIV-infected Former Plasma Donors in China

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Abstract

Objective—To quantify and characterize the nature of cognitive change over one year in a cohort of HIV+ former plasma donors in rural China.

Design—Observational cohort study

Methods—192 HIV+ and 101 demographically comparable HIV– individuals, all former plasma donors, who lived in a rural part of China, received comprehensive medical and neuropsychological (NP) examinations. At study entry 56% of HIV+ group was on combination antiretroviral treatment (cART) and 60.9% at followup. Multiple regression change score approach was used with the HIV – sample to develop norms for change that would be then applied to the HIV+ participants. Followup test scores adjusted for the control group practice effect.

Results—53 HIV+ individuals (27%) developed significant cognitive decline as compared to five (5%) of HIV– individuals. Cognitive decline was predicted at baseline by AIDS status, lower nadir CD4, and worse processing speed; at follow-up, it was associated with lower current CD4 and failure of viral suppression on cART. NP decline also was associated with decreased independence in activities of daily living. Using NP-impairment scores that were corrected for “practice” on repeated testing, we found that among the decliners, 41.5% (N=22) had incident impairment, while 38% (N=20) declined within the impaired range and another 20.7% (N=11) declined within the normal range.

Conclusions—This study demonstrates that despite ongoing cART, cognitive decline in HIV+ people is common over a one year follow-up. Regression-based norms for change on Western NP tests can be used to detect disease-related cognitive decline in a developing country.

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Keywords

HIV/AIDS; Neurocognitive Disorders; Incidence Studies; China; Longitudinal Studies; Neuropsychological Tests; Antiretroviral Therapy; Highly Active

Introduction

Several recent studies have provided prevalence estimates of HIV-associated neurocognitive disorders (HAND) [1] in “non-Western” regions of the world, such as sub-Saharan Africa [2, 3] India [4], China [5,6] and South East Asia [7]. Taken together, the findings of these studies have demonstrated that HAND can be validly assessed in resource limited countries, when using appropriate control samples. HAND prevalence appears to be similar in these areas of the world to the estimates reported with Western HIV-positive (HIV+) cohorts (i.e., 20–50%, depending upon disease stages and comorbid conditions [8]).

Combination antiretroviral therapy (cART) has greatly decreased HIV-associated mortality and medical morbidity, including HIV-associated dementia (HAD), but the prevalence of milder forms of HAND remains high [8]. Several longitudinal cohort studies in Western countries have assessed cognitive decline and its potential contributing factors in the cART era [9–13]. Published studies, after varying followup periods, have found that between 22% and 63% of participants on cART demonstrated continuing impairment and at least 21% had incident impairment [12,13]. Variability in these estimates of cognitive impairment and change probably is related to methodological factors, such as inclusion of appropriate normative standards for detecting these outcomes [14].

Just as it is important to define cross-sectional neuropsychological (NP)-impairment in individual cases, rather than relying on group mean comparisons, longitudinal methods for classifying meaningful NP change in individuals also are needed. Advantages of reliably detecting cognitive change at the individual level include understanding factors responsible for variable manifestations and course of HAND, and alerting clinicians to consider changes in ARV regimens early (e.g., to include agents with better CNS penetration [15], or adjunctive treatments that may specifically benefit the CNS [16]).

To our knowledge, the current study is the first to assess long-term neurocognitive outcomes in a large cohort of HIV+ persons in China and in the cART era. Our aim was to detect and quantify NP decline over a one-year period in 192 individual HIV+ former plasma donors (FPDs) in the Chinese province of Anhui. For this we developed norms for change using longitudinal data of a fairly large sample (N=101) of demographically comparable HIV-negative (HIV-) individuals. The norms for change were derived using a regression change score approach [17,18]. Here we propose an extension of this method by introducing a battery approach to derive a *normed summary change score* for each individual. In addition, we propose an adaptation of the Global Deficit Score method [19,20] to estimate followup impairment rate corrected for practice effect.

Methods

Participants

Details regarding participant recruitment procedures and baseline results were published in Heaton et al. [6]. Briefly, at baseline 203 HIV+ and 198 HIV- participants, virtually all of whom were farmers in the rural area of Anhui province, were enrolled into the study at a local hospital in Fuyang City. By design, at 12 months post-baseline, half of the baseline HIV- participants (N=101) were re-assessed. In addition, all available HIV+ participants were re-

assessed (N=192) yielding a 5.4% (11/203) attrition rate. The causes for drop-out were: 1 case of cerebral infarct; 2 cases of blindness and an additional case of substantial vision decline precluding valid NP testing; 4 moved away for work; and 3 deaths. The 101 HIV– participants had been randomly selected in order to compose a sample representative of the total baseline group with respect to demographic and baseline NP characteristics. This sample of HIV– participants was followed up at one year in order to develop normative standards for NP change (see also e-data analysis). At baseline 106 (55.2%) of the 192 HIV+ participants met CDC-1993 criteria for AIDS. Virtually the same subgroup (N=107; 55.7%) was being prescribed cART at baseline consistent with prevailing antiretroviral initiation guidelines in China. HIV duration estimated from self-report averaged 154 months (SD= 42). When they were re-tested after 12 months, 20 additional HIV+ participants had transitioned to AIDS, and at that time 60.9% of the total group was receiving cART.

Procedure

As in the baseline assessment, participants underwent comprehensive neurocognitive and neuromedical evaluations, and a structured psychiatric examination, as well as a self-report assessment of daily functioning. Examinations were performed by the same Chinese psychiatric staff who had conducted the baseline assessments the previous year. They had been trained and certified in the standardized testing procedures by the U.S. research team (RKH, DF and HJ). Prior to starting the second annual testing phase, the Chinese examiners participated in another training session in order to review and practice test administration and test scoring procedures.

Details of the NP battery selection and adaptation for use in China are provided in Cysique et al. [5] and in Heaton et al. [6] (see also Table e-1 & e-2). Clinical significance of any NP-impairment or change was examined with standard instruments measuring participants' experience of cognitive difficulties in everyday life (Patient's Assessment of Own Functioning Inventory – PAOFI [21]), and decreases in degree of independence in activities of daily living (modified version of the Lawton & Brody IADL scale [22]). Participants also completed the Beck Depression Inventory-II (BDI-II [23,24]).

Data Analysis

To identify individuals who presented with overall NP change, we used a statistical methodology based on the multivariate regression change score approach (see [17,18] for review of this change score approach). The advantage of the regression based change score approach is that it accounts for practice effect, regression towards the mean and other factors that may influence normal test-retest variability in neurologically stable people (e.g., test-retest interval, demographics, and overall baseline NP competence [18]). Our detailed method is available in the supplemental file e-Data analysis. Briefly, to define NP decline in the HIV+ sample, the 101 HIV– individuals were used as a reference sample to develop normative regression formulas. The final regression formulas were then applied to the HIV+ sample providing a Z-score for each of 17 NP variables. These z-scores reflect how well or poorly the person performed at followup, relative to normal expectation for someone with same baseline NP and other relevant characteristics. The z-scores were then summed to provide a *summary regression change score* (sRCS). We determined a 90% confidence interval on the sRCS to define “no change” on the test battery. That is, the cut-off for the top 5% of the sRCS distribution of the HIV– controls defined the “improved” range and the cut-off for the bottom 5% defined the “decliners” range. This was applied to the HIV+ sample (Figure 1).

Secondary analyses were conducted to clarify the nature and both baseline predictors and followup correlates of cognitive decline in this population. The HIV+ decliners and non-decliners (as defined by the sRCS) were compared on baseline and followup demographic,

HIV disease-related laboratory measures, AIDS status, Global Deficit Score (GDS), and ability domain summary scores on the NP test battery, treatment-related variables, cognitive complaints, IADL, and BDI-II using t-test or Chi-square as appropriate. We also conducted standard multivariate analyses to define which combination of baseline factors provided the most robust prediction of NP decline (defined by the sRCS).

The GDS and ability domain T-scores at followup were corrected for the HIV- sample median practice effect (see also e-Data analysis [6; 19, 20]).

Results

The baseline demographic characteristics of the HIV- and HIV+ persons who participated in the 12 months followup assessment are presented in Table 1. Test-retest correlations on the NP battery were robust for both groups [HIV- group's mean scaled score $r_{tt} = .85$; HIV+ group's mean scaled score $r_{tt} = .84$].

Incidence of NP decline in the HIV+ group (27.6%) was significantly greater than in our reference HIV- sample (5%) as defined by the sRCS approach [$X^2_{(1)} = 21.4$; $p < .0001$]. We found that 53 HIV+ individuals were classified as having NP decline at the 12 months followup (i.e., they performed below the 5% cut-off reference range that defined the “decliners” in the HIV- sample; confidence interval of 95% 1-tailed) (see Figure 1).

When comparing the 53 HIV+ participants who were classified as decliners at the 12 months followup with the 139 HIV+ nondecliners, we found that decliners tended to be older ($p < .08$), were more likely to have AIDS at baseline ($p < .03$), and had lower nadir CD4 ($p < .05$). At followup, they had lower current CD4 ($p < .03$), and also were more likely to have detectable virus in plasma when on cART ($p < .01$) (Table 2). To explore further the CD4 finding at followup and take into account any cART effect, a 2-way ANOVA was performed with the CD4 at followup as the outcome variable, and the decliner status as well as the treatment status at baseline (whether receiving cART or not *at baseline*) as predictors, and their interaction. We found that the followup CD4 still tended to differ between the decliners and non-decliners ($p = .06$). No other findings approached statistical significance. Importantly, the decliner and nondecliner groups did not differ in education and gender characteristics, or for prevalence of HCV infection or cART duration. They also did not differ on overall baseline NP performance (GDS) or prevalence of baseline NP-impairment.

About one quarter of both the decliners and nondecliners evidenced clinically significant level of depressive symptoms (BDI-II ≥ 17) at baseline (26.4% vs. 25.2%). At followup, neither group showed an increase in rates of depression, but the nondecliners improved somewhat more (see Table 2). Decliners and non-decliners did not differ in their numbers of reported cognitive problems either at baseline ($p = .22$) or followup ($p = .60$), nor in the difference between baseline and followup ($p = .13$). Results remain comparable when the BDI-II was entered as a covariate. However, decliners were more likely to have significant decrease in IADL independence at followup [9.4% versus 1.4%; $p < .007$] (significant decrease in IADL was defined as decrease in dependence in at least two everyday functioning areas [22]).

Although NP-impairment rates for the decliners and non decliners were almost identical at baseline (37.7% vs. 36.7% respectively), not surprisingly a much higher prevalence of impairment was seen in the decliners at followup [79.25% vs. 28.78%; $p < .0001$]. Overall impairment rate in the HIV+ group at followup was 42.71% (82/192) which was just slightly higher than at baseline (36.9%; 71/192).

When using the followup scores that were uncorrected for practice effect, 51% of decliners and 15.1% of non decliners would be classified NP-impaired at followup (and only 25% in the

total HIV+ group – see also Table e-2 e-Data analysis). Importantly, without correction for practice effect, impairment prevalence estimates in the HIV– controls also dropped from an expected 14% to only 2% ($p=.0004$). There is no known biological reason for such change; this result should therefore be considered as evidence for error due to failure to correct for practice.

Although overall NP performance at baseline did not differ between decliners and non-decliners, we did find that Speed of Information Processing (SIP) at baseline was significantly lower in the HIV+ who would go on to decline as compared to the nondecliners (medium effect size, $d = 0.51$ - see Table 3). At followup and using the practice effect corrected NP scores to derive demographically corrected ability domain T-scores, we found that the decliners demonstrated significantly lower performance in all domains when compared to the non-decliners, with the greatest difference found in learning, memory and SIP (all large effect sizes; $d > 0.8$).

We found that among the 53 HIV+ decliners, 22 (41.5%) showed incident impairment on the corrected GDS at followup. Eleven (20.7%) declined within the normal range and another 20 (38%) declined within the impaired range. These subgroups did not statistically differ on the sRCS.

Finally, we tested predictors of cognitive change using a stagewise regression approach. First, in a multivariate model with the sRCS as the outcome and including the predictors that were found [$p < .10$] to be different between HIV+ decliners and non-decliners *at baseline* – see Table 2), we found that SIP ($p=.004$) and AIDS at baseline (trending at $p=.06$) remained unique contributors to the model ($R^2 = .10$; $p=.007$; baseline age did not uniquely predict change). Secondly, In a final two-covariates logistic regression model that predicted decliners' status, baseline SIP mean T-score had an odds ratio of 1.07 [CI: 1.03–1.13] for a one-unit decrease, and baseline AIDS had an odds ratio of 1.94 [CI: 0.98–3.84] relative to baseline Non-AIDS.

Discussion

This study demonstrated that performance on the NP tests originally developed in Western regions of the world was quite reliable over time in both the infected and uninfected rural Chinese participants. Together with the earlier finding of greater baseline impairment associated with HIV and HCV infections, and associations of NP-impairment with both HIV disease severity and indications of decreases in everyday functioning [6], this suggests that NP tests standardized and widely used in Western regions of the world (here historically and geographically defined as Europe, Australia, and North America) generalize to people having very different cultural, linguistic and educational backgrounds. It may be, therefore, that the abilities assessed by most or all of these tests capture some universal features of cognition.

Moreover, using the regression change score approach that has been validated mainly in non-HIV populations in the U.S., we found that we could detect cognitive decline in 27.6% of the HIV+ participants after a one year interval. This greatly exceeded the expected 5% normative cut-off of the HIV– sample. Even though our infected sample remained relatively healthy from a general medical point of view (average immune status improved and few participants had new AIDS-defining illnesses) and reported excellent adherence to their cART (Table 2), many evidenced worsening of their neurocognitive status and slightly fewer than expected showed any improvement. Thus, while cART has dramatically improved the mortality and medical morbidity associated with HIV disease, such treatment appears less effective in alleviating or reversing CNS compromise that has been observed since the beginning of the HIV epidemic [25].

The minimal 12 month dropout rate (5%) for our HIV+ former plasma donors is remarkable and reflects high levels of cooperation and dedication of the Chinese participants and examiners. Of the 11 baseline HIV+ subjects who could not be retested, 7 were presumed to be due to HIV disease phenomena (3 deaths, 1 stroke, 3 with recent severe visual impairment), so their loss to followup may have slightly underestimated rates of HIV related NP decline.

Similar to prior longitudinal NP findings in Western studies [26–29], test-retest interval in our rural Chinese population was not a significant predictor of variability in cognitive performance. Still, the variation in retest interval was restricted by design (actual range 237–494 days), and it is possible that more discrepant test-retest intervals may have yielded different results. Also similar to results in Western studies, we found that the most robust predictors of followup NP scores were baseline scores on the same tests, as well as overall NP competence at baseline [18;27,28;30,31], and to a lesser extent age [27] (see also e-Data analysis).

Supporting the current method for classifying change is the fact that NP decline was associated with markers of advanced HIV disease, such as AIDS at baseline and lower nadir CD4. The same disease-related predictors were associated with NP-impairment at baseline [6]. Worse immune recovery, as reflected by lower current CD4 counts at follow-up, also was associated with cognitive decline. Even though both groups' CD4 counts improved at followup, immune recovery was slightly worse for the decliners. Although cART use and duration did not differ between the groups, the cART of the decliners was less likely to be effective (they were more likely to have detectable viral loads at followup, suggesting more treatment failure in the decliner group).

Altogether, our findings would imply that *current* virological response to cART and *past* immune injury are important factors for HAND prognosis. Lower nadir CD4 cell counts may reflect prior HIV-related brain injury, representing a neuropathogenic process that may persist despite partial immune recovery, while current viral load detection would reflect ineffective cART. In any event, our results regarding long-lasting effects of earlier immunosuppression are consistent with several reports in Western regions [10;13;32–34] as are findings suggesting that successful cART is an important factor for maintaining stable cognitive functions [9]. Together, these findings strengthen the hypothesis that effective cART initiated earlier in HIV disease may be more efficient at preventing HAND [35].

As has been noted in relation to studies of NeuroAIDS in the West, the precise timing and nature of the neuropathological mechanisms occurring in Chinese HIV+ persons with stable or incident HAND are not well understood [36]. Co-infection with HCV, although associated with somewhat increased risk of NP-impairment in this population at baseline, was unrelated to further cognitive decline over the next year. One explanation for this observation is that the brain injury that was previously linked to HCV had already occurred and was static and non-progressive. Another is that some individuals who tested positive for HCV antibodies at baseline no longer had active HCV viral replication, although this hypothesis was not tested in this study. Future longitudinal research with co-infected (and HCV mono-infected) samples should determine whether detectable HCV in plasma confers an increased risk for NP decline over time.

Another confirmatory finding with the previous literature in NeuroAIDS is that lower Speed of Information Processing performance was predictive of future NP decline [37]. Impairment of this ability appears to be a common and possibly early feature of both HAND and HAND progression. If so, the presence of even fairly isolated deficiencies in information processing speed may suggest the possibility of an evolving process. Studies in other countries should be undertaken to see whether this is a generalizable feature of HAND, independently of the cultural context.

We showed that our estimate of cognitive decline was associated with decreased independence in activities of daily living, but not change in cognitive complaints nor depressive symptoms. Independence in everyday life serves as an important benchmark to distinguish asymptomatic from symptomatic forms of HAND [1]. We had previously demonstrated that NP criteria for HAND could be effectively adapted to the Chinese rural context cross-sectionally [6], and that NP-impairment was associated with reported decrease in performance of IADL. This longitudinal finding is the first to be reported in a Chinese HIV+ cohort, and supports our definition of NP change and its clinical meaningfulness.

In conclusion, this study demonstrates that despite ongoing cART, cognitive decline in HIV+ people is common over a one year follow-up. Regression-based norms for change on Western NP tests can be used to detect disease-related cognitive decline in a developing country.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

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Figure 1. Percentage of NP change as defined by the summary regression change score in the HIV+ and HIV- samples

% participants who were classified as being stable or decliners on the summary regression change score (sRCS; 95% confidence interval, 1-tailed).

Table 1

Baseline characteristics of 101 HIV– and 192 HIV+ participants at one year followup

	HIV– (n=101)	HIV+ (n=192)	<i>p</i>	<i>d</i>
BASELINE				
Age (years) Mean (SD)	40.8 (6.7)	40.2 (6.3)	.42	.09
Education (years) Mean (SD)	5.8 (2.1)	5.5 (2.3)	.15	.13
Gender % Male	56%	61%	.40	.10
AIDS %	-	55%	-	-
Plasma HIV RNA ¹ Median (IQR)	-	4.2 (3.5–4.7)	-	-
Plasma HIV RNA % Undetectable	-	34%	-	-
On cART %	-	56.3% (N=107)	-	-
Current CD4 Median (IQR)	-	346 (204–454)	-	-
Nadir CD4 Median (IQR)	-	200 (159–360)	-	-
HCV+ %	67.3%	92.7%	<.0001	.43
FOLLOWUP				
New AIDS diagnosis %	-	10% (N=20)	-	-
Plasma HIV RNA ² Median (IQR)	-	4.2 (3.6–4.8)	-	-
Plasma HIV RNA % Undetectable	-	39%	-	-
On cART ³ %	-	60.9% (N=117)	-	-
Current CD4 Median (IQR)	-	375 (11–1173)	-	-

ART: antiretroviral treatment

d= Cohen's *d*¹
(N= 127 detectable)²
(N= 117 detectable)

³ At follow-up, among the participants on ART, all were on cART defined as a regimen composed of at least 3 antiretroviral drugs except for one patient who was on monotherapy. This is higher than baseline where, in this sample, 89% were on cART; 9% on dual-therapy and 2% on monotherapy. Most commonly prescribed ART drugs were: D4T (N=103); Nevirapine (N=98); DDI (N=77); and 3TC (N=51). Other drugs prescribed less frequently were: Efavirenz (N=10); Atazanavir (N=7); and Zidovudine (N=8). The restricted range did not allow testing CNS penetration effectiveness [15]. However, it should be noted that overall the CPE is fairly low in the cohort, suggesting that some individuals may be suboptimally treated for their CNS HIV-related injury.

Table 2

Baseline and followup characteristics in HIV+ persons who declined versus those who did not decline on the NP battery

	Declined N = 53	Did not decline N= 139	p	d
Age Mean (SD)	41.6 (6.6)	39.6 (6.2)	<.08	.32
Education Mean (SD)	5.2 (2.4)	5.6 (2.2)	.34	.17
Sex %	60.4%	61.9%	.85	.03
NP-impaired baseline %	37.7%	36.7%	.89	.02
NP-impaired followup (corrected ¹) %	79.2%	28.8%	<.0001	1.2
Global Deficit Score baseline Mean (SD)	0.52 (0.4)	0.49 (0.5)	.65	.06
Global Deficit Score followup (corrected ¹) Mean (SD)	0.91 (0.5)	0.40 (0.4)	<.0001	1.2
HCV+ %	94.3%	92.1%	.59	.08
Estimated HIV duration (months) Mean (SD)	161 (36)	152 (44)	.13	.21
AIDS % baseline	68.0%	50.4%	<.03	.36
AIDS % followup	71.1%	63.8%	.30	.17
New AIDS-defining illnesses %	9.4%	10.1%	.89	.03
BDI-II baseline (% clinically depressed) ²	26.4%	25.2%	.86	.02
BDI-II followup (% clinically depressed) ²	20.7%	8.6%	.02	.32
On cART baseline (Total N=107; 35 decliners, 72 non-decliners) %	66.0%	52.5%	.09	.27
On cART at followup (Total N=117; 38 decliners, 79 non-decliners) %	71.7%	56.8%	.06	.32
cART duration at follow-up (months) Mean (SD)	139 (58)	124 (70)	.22	.22
CD4 current baseline Mean (SD)	324 (186)	365 (203)	.19	.20
CD4 current followup Mean (SD)	352 (184)	422 (225)	<.03	.32
CD4 nadir Mean (SD)	233 (159)	268 (156)	.17	.22
CD4 nadir <200 %	62.3%	46.0%	<.05	.33
% Undetectable VL baseline (<50 cpy/mL, total sample %)	33.9%	33.8%	.98	.01
% Undetectable VL followup (<50 cpy/mL, total sample %)	32.1%	41.2%	.22	.20
% Undetectable VL followup (<50 cpy/mL, on cART at baseline %)	40% (14/35)	55.5% (40/72)	.13	.24
% Undetectable VL followup (<50 cpy/mL, on cART at followup %)	39.5% (15/38)	64.5% (51/79)	<.01	.42

¹The Global Deficit Score was based on Mean T-scores corrected for HIV– median practice effect.

²BDI-II: Beck Depression Inventory-II; (a score ≥ 17 reflects threshold for clinical level of depressive complaints).

Test-retest interval did not differ between the decliners and nondecliners (333 ± 37 vs. 331 ± 45 ; $p=.79$).

Level of adherence was high in this sample and there were no significant differences between decliners and nondecliners at baseline: 100% of decliners on ART reported that they took their medication "Almost all of the time", and 98.5% of non-decliners on ART reported that they took their medication "Almost all of the time". At followup, 94.7% of decliners on ART reported that they took their medication "Almost all of the time", and 98.8% of non-decliners on ART reported that they took their medication "Almost all of the time".

There were no significant differences in baseline demographics (age, $p=.44$; education, $p=.86$; gender, $p=.10$) and baseline overall neuropsychological performance ($p=.35$) between the 5 HIV- decliners and 96 HIV-nondecliners.

VL: Viral load

d= Cohen's d

Table 3

Mean and domains T-scores in HIV+ persons who decline versus those who did not decline

	Declined N = 53	Did not decline N= 139	<i>p</i>	<i>d</i>
Mean T-score baseline Mean (SD)	44.5 (5.2)	46.1 (6.1)	.08	.27
Executive baseline Mean (SD)	45.1 (8.8)	45.9 (9.3)	.57	.09
Verbal baseline Mean (SD)	46.3 (7.2)	46.6 (8.1)	.81	.04
Attention / WM baseline Mean (SD)	45.1 (7.3)	47.2 (8.4)	.09	.26
Learning baseline Mean (SD)	45.2 (7.8)	46.0 (8.9)	.52	.06
Memory baseline Mean (SD)	44.2 (7.2)	45.8 (8.3)	.18	.20
Motor baseline Mean (SD)	46.5 (8.6)	45.2 (10.3)	.37	.13
SIP baseline Mean (SD)	42.5 (5.7)	46.0 (7.2)	.0005	.51
Mean T-score followup ^{<i>I</i>} Mean (SD)	40.2 (3.9)	46.9 (5.4)	<.0001	1.31
Executive followup ^{<i>I</i>} Mean (SD)	40.6 (8.2)	46.1 (7.9)	<.0001	.68
Verbal followup ^{<i>I</i>} Mean (SD)	42.3 (7.4)	47.4 (8.1)	<.0001	.64
Attention / WM followup ^{<i>I</i>} Mean (SD)	42.4 (6.0)	48.4 (8.4)	<.0001	.76
Learning followup ^{<i>I</i>} Mean (SD)	39.4 (6.5)	46.9 (8.4)	<.0001	.93
Memory followup ^{<i>I</i>} Mean (SD)	37.2 (7.1)	45.8 (8.3)	<.0001	1.06
Motor followup ^{<i>I</i>} Mean (SD)	42.4 (9.1)	47.9 (9.4)	.002	.58
SIP followup ^{<i>I</i>} Mean (SD)	38.6 (5.0)	46.2 (6.7)	<.0001	1.19

^{*I*} T-scores corrected for HIV– median practice effect

SIP: Speed of Information Processing

WM: Working Memory