

Corrigendum

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This corrigendum concerns the following article published in the Journal of Neurovirology: Heaton RK, Cysique LA, Jin H, *et al*: Neurobehavioral effects of human immunodeficiency virus infection among former plasma donors in rural China. Journal of Neurovirology, 7:1-14, 2008. In this article we reported that 26% of the HIV uninfected (HIV-) sample and 46% of the HIV infected (HIV+) sample were also infected with the Hepatitis C virus (HCV).

Recently we discovered that there was a change in the laboratory personnel at the China CDC during the first year of data collection. The new person made a systematic transcription error when processing the hepatitis and liver panel data. This error resulted in an underestimation of HCV prevalence in our samples. The new (corrected) rates of HCV infection are as follows: 62.5% of the HIV- sample and 93% of the HIV+ sample were infected with HCV ($p = .001$).

The revised Table 1 provides extended demographic information about the four reconstituted groups. There was a trend for a greater proportion of males in the uninfected control group, and the HIV/HCV coinfecting group had many more prior plasma donations (and associated increased infection risk) than all other groups. Otherwise, the four groups were comparable with respect to age, ethnicity, and educational, family, linguistic, employment and rural living backgrounds.

Table 2 compares the HIV disease history and treatment characteristics of our two HIV infected groups. These groups were quite comparable in terms of distribution of CDC stages, as well as current and nadir CD4 cell counts and percent receiving ARV treatment. However, participants in the correctly constituted HIV monoinfected group had a longer duration of HIV infection, and those who were receiving ART were less likely to be on HAART

regimens and had regimens with lower CNS Penetration Effectiveness (CPE) ranks. These differences were not seen in the original HIV infected groups that were classified on the basis of incorrect HCV information, and potentially could place the HIV monoinfected group at greater risk for CNS injury than their coinfecting counterparts (Cysique *et al*, 2009; Tozzi *et al*, 2009; Letendre *et al*, 2008).

A central issue was whether the previously reported HIV effect on neurocognitive functioning was changed by the revised HCV prevalence rates. We found that it was not: the results concerning the effects of HIV infection on neuropsychological (NP) functioning remain highly significant. Although we were not able to detect an HCV effect in our HIV+ sample (37% impairment in the coinfecting group vs. 36% impairment in the HIV monoinfected group; $p = .92$), a modest effect of HCV on NP functioning was evident in the HIV- control sample: Using the Global NP summary score, as described in our report, NP impairment was found in 23.3% of the HCV monoinfected group, vs. only 12.5% of controls uninfected with either virus ($p = .06$).

The new Table 3 and Figure 1 provide details of the NP comparisons of the three infected groups with the uninfected controls. As reported in the original publication, both HIV infected groups evidenced substantial impairment across all ability domains. The somewhat larger effect for the HIV monoinfected than the coinfecting group was not anticipated, but could relate to the above mentioned differences in ARV regimens for these two groups. Although the HCV monoinfected group evidenced some increased impairment versus controls on the NP summary score (23.3% vs. 12.5%), this rather subtle difference was not as apparent on the individual NP tests and ability domains (Table 3 and Figure 1). As reported in the original article,

Table 1 Extended demographic characteristics of Controls, HCV monoinfected HIV monoinfected and co-infected- groups

	Controls (n = 72)	HCV monoinfected (n = 120)	HIV monoinfected (n = 14)	HIV/HCV coinfectd (n = 187)	Comparisons*
Age (years)	40.81 (7.509)	40.15 (5.509)	39.14 (8.264)	40.34 (6.20)	.80
Education (years)	5.82 (2.14)	5.72 (2.08)	6.43 (2.38)	5.39 (2.28)	.19
Gender % <i>Male</i>	70.8%	53.3%	50%	61.5%	.09
Speaks Fuyang dialect	100.0%	100.0%	100.0%	100.0%	1.00
Speaks Mandarin	15.3%	10.8%	28.6%	12.8%	.29
Han Ethnicity	98.6%	100.0%	100.0%	99.5%	.47
Grew up in rural area	100.0%	100.0%	100.0%	98.3%	.99
Resides in rural area	100.0%	100.0%	100.0%	99.5%	.99
Engaged in Farming	90.3%	91.2%	85.7%	86.6%	.85
Number of family members in home	5.05 (1.12)	5.25 (1.28)	4.78 (1.31)	5.18 (1.41)	.53
Currently married	98.6%	94.2%	85.7%	88.8%	.17
Widowed	1.4%	5.8%	14.3%	10.2%	.17
Number of plasma donations ¹	6.66 (12.9)	17.38 (28.21)	9.857 (12.95)	55.80 (98.54)	<.0001

*One-way Anova or overall Chi-Square comparison as appropriate.

¹HIV/HCV Co-infected > all other groups ($p < .05$).

Eight participants (6 HIV- and 2 HIV+) are not included here because their HCV status is unknown.

Table 2 Clinical and laboratory characteristics in the HIV monoinfected and coinfectd groups

	HIV monoinfected (n = 14)	HIV/HCV coinfectd (n = 187)	<i>p</i>
Current CD4 count	392 (IQR: 309–478)	316 (IQR: 186–365)	.28
Nadir CD4 count	262 (169–375)	200 (IQR: 152–350)	.82
Plasma HIV viral load in 132 detectable ¹	3.75 (0.59)	4.11 (0.84)	.10
HIV RNA % detectable	71.43%	64.24%	.63
Duration of known HIV seropositivity in months (SD)	156.7 (22.6)	141.8 (43.5)	.04
% AIDS	64.3%	55.6%	.53
CDC stages %			
A1	7.2%	7%	-
A2	21.5%	26.4%	-
A3	35.7%	20.4%	-
B1	7.1%	0.0%	-
B2	0.0%	10.7%	-
B3	7.1%	21%	-
C2	7.1%	3.2%	-
C3	14.3%	11.3%	-
On ARV drugs (%)	64.3%	56.1%	.55
Type of ART regimen among treated ²			
HAART (≥ 3 drugs)	66.7%	89.5%	.04
Dual-therapy	33.3%	7.6%	
Monotherapy	0.0%	2.9%	
ARV treatment duration in months (SD)	92 (48)	96 (59)	.87
CNS Penetration-Effectiveness (CPE) Ranks ³	1.28 (0.36)	1.56 (0.35)	.02
Self-reported adherence as “always”	100%	98%	.91%

Eight participants (6 HIV- and 2 HIV+) are not included here because their HCV status is unknown.

ARV: antiretroviral.

¹NucliSens EasyQ HIV-1 from bioMérieux Easy Q assay uses real-time NASBA amplification and molecular beacon detection technology and has a range of 50 to 3 million IU(copies)/mL.

²Comparisons were conducted for HAART versus non HAART.

³See Letendre *et al*, 2008 for more details in the computation of the CPE Ranks.

Table 3 Raw scores and effect sizes on individual NP test measures

		Controls (n = 72) Mean (SD)	HCV monoinfected (n = 120) Mean (SD)	HIV monoinfected (n = 14) Mean (SD)	HIV/HCV coinfected (n = 187) Mean (SD)
Executive function	Color Trails II (time seconds)	110.08 (32.42)	121.17 (38.64) ^a	140.57 (50.42) ^b	130.48 (44.15) ^b
	WCST (Preservative errors)	15.97 (8.19)	16.03 (9.14)	16.36 (8.51)	15.65 (8.40)
	Category Test (errors)	68.64 (22.01)	63.74 (25.44) ^a	69.64 (32.19)	73.13 (27.50)
Verbal fluency	Animal fluency (total correct)	13.56 (3.30)	13.08 (3.38)	12.14 (3.94) ^a	12.16 (3.09) ^a
	Action fluency (total correct)	7.94 (3.04)	7.33 (2.87)	6.57 (4.25) ^a	6.87 (2.65) ^a
Attention/WM	PASAT-50 (total correct)	27.89 (9.82)	27.63 (9.43)	21.07 (13.31) ^b	24.84 (9.08) ^a
	WMS-III Spatial Span	14.72 (3.47)	13.70 (3.26) ^a	13.36 (3.65) ^a	13.09 (3.30) ^b
Learning	HVLT-R Learning (total 3 trials)	17.88 (4.22)	17.99 (5.18)	15.71 (5.61) ^a	16.62 (5.16) ^a
	BVMT-R Learning (total correct)	15.94 (6.59)	16.20 (7.34)	12.71 (7.94) ^a	13.43 (6.95) ^a
Memory	HVLT-R Delayed Recall (total correct)	6.06 (2.10)	6.32 (2.44)	5.64 (2.56) ^b	5.58 (2.37) ^a
	BVMT-R Delayed Recall (total correct)	7.50 (2.73)	7.32 (3.16)	5.71 (3.49) ^b	6.04 (3.01) ^b
Motor	Grooved Pegboard DH (time seconds)	79.17 (17.18)	78.71 (17.14)	85.64 (17.86) ^a	84.58 (25.22) ^a
	Grooved Pegboard NDH (time seconds)	83.89 (21.34)	82.23 (21.20)	93.93 (36.86) ^a	88.53 (24.22) ^a
SIP	WAIS-III Digit Symbol (total correct)	42.11 (14.79)	41.22 (12.49)	35.57 (10.19) ^a	35.06 (12.39) ^b
	WAIS-III Symbol Search (total correct)	18.94 (7.59)	17.75 (6.89)	12.79 (5.59) ^b	14.34 (6.74) ^b
	Trail Making Test A (time seconds)	58.69 (18.16)	61.84 (18.13)	66.00 (19.16) ^a	66.99 (19.15) ^a
	Color Trails I (time seconds)	58.58 (18.36)	61.22 (19.29)	73.07 (30.21) ^b	66.40 (22.18) ^a
	Stroop color (total completed in 90s)	44.68 (13.20)	46.23 (13.02)	45.07 (15.41)	39.78 (12.41) ^a

Eight participants (6 HIV- and 2 HIV+) are not included here because their HCV status is unknown.

SIP: Speed of Information Processing, WM: Working Memory, WCST: Wisconsin Card Sorting Test, HVLT-R: Hopkins Verbal Learning Test –Revised, BVMT-R: Benton Visual Retention Test-Revised.

^aSmall effect size (d=.20–.49) with controls as reference.

^bMedium effect size (d=.50–.79) with controls as reference.

Effect size computations were corrected for small sample size (N<20) using Hedges procedure when appropriate.

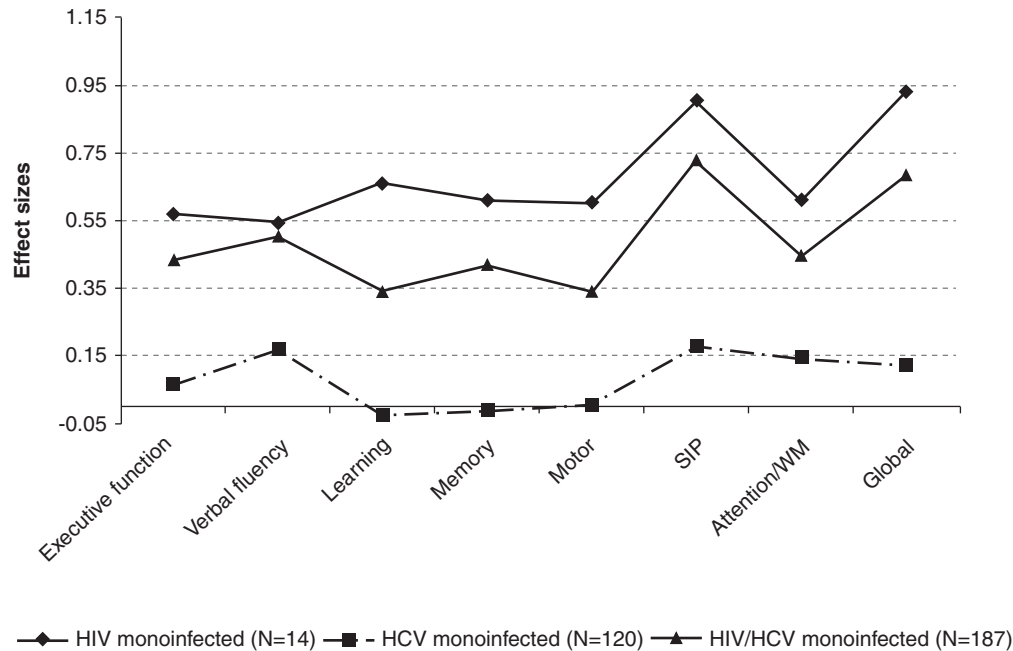


Figure 1 Effect sizes on ability domains (Mean domain T-scores) and the total test battery (Global Mean T-scores) for infected groups as compared to 72 controls

Table 4 Cognitive complaints, IADL dependence and employment in controls, HCV monoinfected, HIV monoinfected, and coinfecting groups

	Controls (<i>n</i> = 72) Mean (SD)	HCV monoinfected (<i>n</i> = 120) Mean (SD)	HIV monoinfected (<i>n</i> = 14) Mean (SD)	HIV/HCV coinfecting (<i>n</i> = 187) Mean (SD)	<i>P</i>
Cognitive complaints (PAOFI) ¹	3.35 (4.12)	3.59 (4.82)	4.93 (5.65)	5.28 (5.96)	<.02
Decreased IADL independence ²	0.15 (0.81)	0.13 (0.72)	0.64 (1.28)	0.46 (1.32)	.02
Currently unemployed (%) ³	4.2%	4.2%	28.6%	20.8%	<.0001
Months worked in the last year ⁴	7.33 (3.03)	7.56 (3.02)	4.57 (3.46)	5.15 (3.46)	<.0001

Mean comparisons with Dunnett's Method, control group as a reference.

¹Co-infected different from controls (*p* <.03).

²HIV mono-infected different from controls (*p* = .09).

³HIV mono-infected different from controls (*p* = .002), Co-infected different from controls (*p* = .001).

⁴Co-infected different from controls (*p* < .0001), HIV mono-infected different from controls (*p* = .01).

HIV+ former plasma donors with more advanced HIV disease (AIDS, *n* = 114) evidenced a significantly higher rate of NP impairment than those with less advanced disease (non-AIDS; *n* = 89) (43% vs. 29.2%; *p* < .05).

Table 4 shows that, after the groups were reconstituted with the correct HCV status, only the HIV monoinfected and coinfecting groups reported

increased unemployment. Also the coinfecting group reported increased cognitive difficulties in everyday functioning, and a trend towards decreased independence in instrumental activities of daily living (IADLs). As stated in the original article, in the three infected groups combined, NP impairment was significantly associated with cognitive complaints and reduced independence in IADLs.

References

- Cysique LA, Vaida F, Letendre S, Gibson S, Cherner M, Woods SP, McCutchan JA, Heaton RK, Ellis RJ (2009). Dynamics of cognitive change in impaired HIV+ individuals initiating antiretroviral therapy. *Neurology* **73**: 342–348
- Letendre S, Marquie-Beck J, Capparelli E, Best B, Clifford D, Collier AC, Gelman BB, McArthur JC, McCutchan JA, Morgello S, Simpson D, Grant I, Ellis RJ; and the CHARTER Group (2008). Validation of the CNS Penetration-Effectiveness rank for quantifying antiretroviral penetration into the central nervous system. *Arch Neurol.* **65**: 65–70.
- Tozzi V, Balestra P, Salvatori MF, Vlassi C, Liuzzi G, Giancola ML, Giulianelli M, Narciso P, Antinori AJ (2009). Changes in cognition during antiretroviral therapy: comparison of 2 different ranking systems to measure antiretroviral drug efficacy on HIV-associated neurocognitive disorders. *Acquir Immune Defic Syndr.* **52**: 56–63. Erratum in: *J Acquir Immune Defic Syndr.* **52**: 529.