

Supplementary Table S1. Associations between pNfL and neuroimaging, cognitive and disease and treatment related variables

	plasma Neurofilament Light (pNfL)	
Variables association analysis	Coefficient (95% CI)	Adjusted <i>p</i> -value
Neuroimaging		
White matter volume #	0.01 (-0.006 – 0.018)	0.351
Grey matter volume	0.001 (-0.008 – 0.011)	0.773
White matter hyperintensities #	-0.17 (-1.63 – 1.33)	0.828
Mean diffusivity #	-0.002 (-0.012 – 0.007)	0.750
Axial diffusivity #	-0.003 (-0.014 – 0.005)	0.455
Fractional anisotropy #	-0.003 (-0.004 – 0.010)	0.395
Radial diffusivity #	-2.40 (-7.01 – 2.13)	0.323
Cognitive function		
Executive function #	0.33 (-0.43 – 1.11)	0.412
Processing speed #	-1.06 (-6.29 – 4.38)	0.698
Learning ability #	0.296 (-0.14 – 0.75)	0.200
Visual motor function	0.09 (-0.01 – 0.20)	0.091
Working memory #	-0.32 (-1.36 – 0.73)	0.548
Intelligence quotient #	1.7 (-0.02 – 0.06)	0.143
HIV- and cART related variables		
CDC-C	-0.06 (-0.24 – 0.12)	0.536
Age at diagnosis	0.02 (-0.07 – 0.11)	0.676
Zenith HIV VL #	0.29 (-0.353 – 0.938)	0.599
Nadir CD4+ T-cell	0.06 (-0.33 – 0.46)	0.288
Duration of cART (y)	0.01 (-0.07 – 0.10)	0.823
Age at start cART (y)	-0.04 (-0.08 – 0.07)	0.960
Undetectable HIV VL at second assessment	1.33 (-7.18 – 9.83)	0.780
Undetectable HIV VL between first and second assessment	1.9 (-5.45 – 9.31)	0.631

Linear mixed model formulas were used for longitudinal association analysis adjusted for age, sex and BMI; # These variables were transformed using natural logarithm prior to analysis. AIDS = acquired immunodeficiency syndrome; cART = combination antiretroviral therapy; CI = 95% confidence interval; CDC = Centers for Disease Control and Prevention, classification system used to classify HIV- stage (N = no symptoms, A = minimal symptoms, B = moderate symptoms, C = severely symptomatic/immunodeficiency syndrome); VL = viral load; y = year; Zenith VL values extracted for duration of follow-up and transformed using 10-base logarithm prior to analysis; CD4+ T-cell were compared to appropriate age and HIV- controls using Z-scores; Executive function and learning ability are compared to HIV- controls by Z-scores; HIV = human immunodeficiency virus; IQ and processing speed are compared with regular population; *p*-values were adjusted for age, sex, BMI;

Supplementary Table S2. Different cART regimens at first and second assessment in PHIV adolescents

cART Regimens	PHIV (n = 19)
Protease inhibitors (PIs)	
First assessment	7 (41%)
Second assessment	4 (24%)
Integrase strand transfer inhibitors (INSTIs)	
First assessment	1 (6%)
Second assessment	10 (58%)
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	
First assessment	9 (53%)
Second assessment	3 (18%)
Efavirenz	
First assessment	8 (47%)
Second assessment	3 (18%)
Ritonavir	
First assessment	6 (35%)
Second assessment	2 (11%)
Abacavir	
First assessment	10 (58%)
Second assessment	8 (47%)

Abbreviations: Values are reported in number and percentage (No %). PHIV (n = 19), with one missing value in first and second assessment; cART = Combination antiretroviral therapy; INSTIs = integrase strand transfer inhibitors; PIs = protease inhibitors; NNRTIs = non-nucleoside reverse transcriptase inhibitors;

Supplementary Table S3. Different cART regimens and association with pNfL and cognitive function variables over time

Association analysis of different cART regimens						
	PIs exposure	INSTIs exposure	NNRTIs exposure	Efavirenz exposure	Ritonavir exposure	Abacavir exposure
	Group x time	Group x time	Group x time	Group x time	Group x time	Group x time
Executive function [#]						
Coefficient (95% CI)	-0.3 (-1.1 – 0.5)	0.5 (-0.2 – 1.9)	0.6 (-0.2 – 1.3)	0.6 (-0.1 – 1.3)	-0.5 (-1.3 – 0.4)	0.3 (-0.7 – 1.3)
<i>p</i> -value	0.418	0.174	0.113	0.116	0.244	0.525
Processing speed [#]						
Coefficient (95% CI)	0.09 (-0.01 – 0.2)	-0.07 (-0.1 – 0.005)	0.01 (-0.06 – 0.09)	0.03 (-0.05 – 0.1)	0.03 (-0.06 – 0.12)	-0.04 (-0.1 – 0.03)
<i>p</i> -value	0.075	0.086	0.743	0.424	0.533	0.246
Learning ability [#]						
Coefficient (95% CI)	-0.1 (-0.9 – 0.7)	-0.3 (-0.7 – 0.5)	-0.4 (-1.0 – 0.3)	-0.2 (-0.9 – 0.5)	0.7 (-0.2 – 1.4)	-0.1 (-0.7 – 0.5)
<i>p</i> -value	0.789	0.489	0.222	0.547	0.093	0.706
Visual motor function [#]						
Coefficient (95% CI)	-0.13 (-0.08 – 0.3)	-0.15 (-0.3 – 0.04)	0.04 (-0.2 – 0.2)	0.09 (-0.1 – 0.3)	0.08 (-0.2 – 0.3)	-0.08 (-0.3 – 0.09)
<i>p</i> -value	0.256	0.135	0.647	0.392	0.513	0.391
Working memory [#]						
Coefficient (95% CI)	-0.001 (-0.3 – 0.3)	-0.09 (-0.4 – 0.19)	0.09 (-0.2 – 0.4)	0.1 (-0.2 – 0.4)	-0.03 (-0.03 – 0.4)	0.05 (-0.2 – 0.3)
<i>p</i> -value	0.994	0.556	0.523	0.525	0.849	0.695
Intelligence Quotient						
Coefficient (95% CI)	-0.5 (-9.0 – 7.8)	-0.8 (-7.8 – 6.7)	1.1 (-6.0 – 8.3)	3.0 (-4.3 – 10.2)	-5.2 (-13.5 – 3.1)	2.8 (-2.6 – 8.5)
<i>p</i> -value	0.911	0.834	0.762	0.428	0.240	0.332
pNfL (log pg/ml) [#]						
Coefficient (95% CI)	0.17 (-0.3 – 0.7)	0.09 (-0.5 – 0.6)	-0.3 (-0.7 – 0.3)	-0.2 (-0.7 – 0.3)	0.4 (-0.2 – 0.9)	0.03 (-0.4 – 0.04)
<i>p</i> -value	0.520	0.755	0.347	0.427	0.254	0.910

Abbreviations: pNfL = plasma Neurofilament light; 95% CI = 95% Confidence Interval; Group x time = group by time interaction; INSTIs = integrase strand transfer inhibitors; PIs = protease inhibitors; NNRTIs = non-nucleoside reverse transcriptase inhibitors; Executive function and learning ability are compared to HIV- controls by Z-scores; Visual motor function, working memory, IQ and processing speed are compared with regular population; CD4+ T-cell were compared to appropriate age and HIV- controls using Z-scores. Linear mixed models' formulas were used for longitudinal association analysis. # These variables were transformed using natural logarithm prior to analysis.