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HIV DNA and Neurocognitive Impairment in Older and Younger Subjects on Suppressive ART

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Background

- Older HIV-infected adults have a higher risk of developing neurocognitive impairment.
- The underlying mechanisms are poorly understood.

Objective

To address viral and immunological factors associated with neurocognitive impairment during suppressive antiretroviral therapy (ART) in older and younger HIV-infected adults.

Methods

- Paired blood and cerebrospinal fluid (CSF) from HIV+ adults on suppressive ART (<50 copies/ml blood plasma):
  - N=26 (59.1%) older adults (>50 years)
  - N=18 (40.9%) younger adults (<40 years)
- Levels of HIV DNA (pol) in peripheral CD4 T cells:
  - by droplet digital PCR (ddPCR)
- Levels of inflammatory markers in CSF and blood plasma:
  - by ELISA: sCD163 and neopterin
  - by Mesoscale: MCP-1, IL-8, IL-6 and TNF-α
- Neurocognitive functioning:
  - clinical battery of 7 ability areas (Frascati criteria)
  - Global deficit score (GDS): >0.5 = neurocognitive impairment
- Differences between age groups (Mann-Whitney U test) for:
  - HIV DNA, inflammatory markers, GDS, CD4 counts, estimated duration of infection [EDI])
- Associations (regression analysis adjusted for EDI)
  - GDS versus HIV DNA, inflammatory markers and clinical variables separately by age groups

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Results

- After adjusting for EDI, older individuals have higher levels of monocyte activation and trafficking in blood (sCD163) and CSF (sCD163 and MCP-1) compared to their younger counterparts. **See table.**

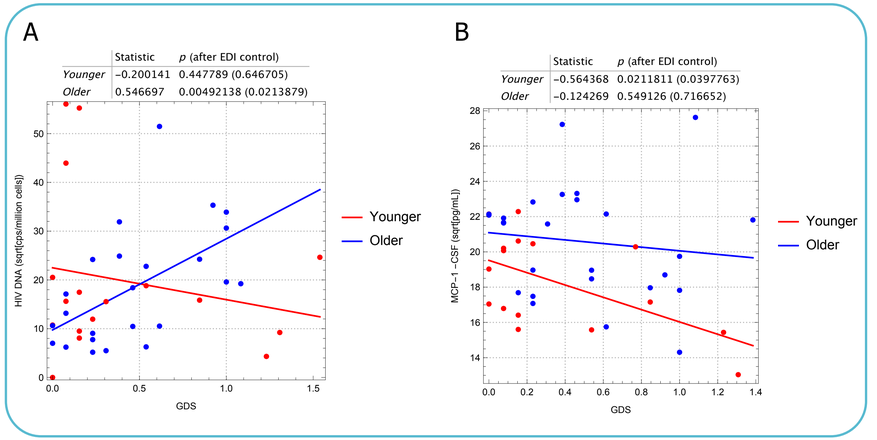
TABLE. Clinical and demographic characteristics, HIV DNA and cytokine levels between age groups.

Parameters n=44	Younger group (N= 18)	Older group (N= 26)	Mann-Whitney p	Multivariate (EDI) p
Characteristics				
Education (years) [a]	13 [12,13]	13.5 [12,16]	0.12	
EDI (years) [a]	8.4 [2.6, 12.6]	17.4 [15.2,21]	**<0.01**	
Current CD4[a]	606 [494, 685]	722 [463.3, 901.3]	0.48	
Nadir CD4[a]	216.5 [121.8, 321.8]	231 [92, 317.3]	0.73	
CNS Penetration Effectiveness[a]	7 [7, 7.8]	7 [6, 8]	0.5	
GDS[a]	0.2 [0.1, 0.7]	0.4 [0.2, 0.8]	0.24	
HIV DNA (cps/million cells; log_{10})	2.4 [1.9, 2.6]	2.5 [1.9, 2.7]	0.96	0.21
Cytokines				
CSF				
sCD163 (ng/mL)	36.3 [24.6, 39.4]	61.3 [50.5, 69.1]	**<0.01**	**0.01**
IL-6 (pg/mL)	1 [0.7, 1.2]	1 [0.7, 1.2]	0.25	0.12
IL-8 (pg/mL)	40.1 [34, 47.4]	47.4 [42.7, 54.9]	**0.03**	0.21
MCP-1 (pg/mL)	328.2 [262.9, 413.3]	467 [327.3, 490.4]	**0.03**	**0.06**
Neopterin (ng/mL)	1.4 [1.3, 2.5]	1.9 [1.3, 2.4]	0.54	0.43
Plasma				
sCD163 (ng/mL)	982.6 [786.8, 1441.8]	1501.9 [962.5, 1853.8]	0.07	**0.03**
IL-6 (pg/mL)	0.7 [0.6, 1.3]	0.9 [0.7, 1.2]	**0.03**	0.16
IL-8 (pg/mL)	5.1 [3.4, 7.6]	5.9 [4.8, 7.2]	0.17	0.19
TNF-α (pg/mL)	1.6 [1.1, 2.1]	1.5 [1.2, 1.8]	0.73	0.99
MCP-1 (pg/mL)	109.7 [85.2, 137]	131.9 [113.8, 157.3]	**0.01**	0.10
Neopterin (ng/mL)	2.4 [2, 3.2]	2.5 [1.9, 3.1]	0.86	0.46

[a]Data shown as median [interquartile range]

Figure: Predictors of neurocognitive impairment across age groups.

- Higher levels of HIV DNA in blood CD4+ T cells were associated with impairment (p=0.003) in older individuals (but not in younger). **Figure 1A.**
- Lower levels of MCP-1 in CSF were associated with impairment (p=0.04) in younger individuals (but not in older) **Figure 1B.**



- No association between GDS and any of the other tested variables in any age group (p>0.1).
- Higher levels of HIV DNA blood CD4+ T cells (p=0.004) in older and lower levels of MCP-1 (CSF) (p=0.02) in younger were both associated with deficits in executive functioning.

Conclusions

- **Higher HIV DNA levels in blood CD4+ T cells might indicate higher total HIV DNA in brain.**
- **Correlates of neurocognitive impairment differ between younger and older adults, which suggest future treatment strategies for HIV-associated neurocognitive disorders may need to be based on age.**