Poster #484

Cystatin C is Associated with Neurocognitive Impairment in Older HIV+ Adults

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HNRP HIV NEUROBEHAVIORAL RESEARCH PROGRAM
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Background

- The incidence and prevalence of HIV infection among older adults is on the rise.
- Older age appears to increase the risk of neurocognitive impairment (NCI) among HIV+ adults.
- Understanding the correlates, and potential predictors, of NCI in older HIV+ adults is important; particularly biomarkers in readily accessible body fluids.
- Among older HIV- adults, elevated cystatin C predicts neurocognitive (NC) decline and mortality[1,2].
- Cystatin C is elevated in HIV+ persons[3], but the association of cystatin C and NCI has yet to be studied.

Objective

- To examine differences in cystatin C between HIV-infected (HIV+) and -uninfected (HIV-) older adults, and within the HIV+ adults to examine the association of cystatin C with neurocognitive impairment (NCI).

Method

Participants: 77 HIV+ and 47 HIV- adults ≥50 years old. HIV+ participants were on antiretroviral therapy (ART) and had an undetectable plasma viral load.
Cystatin C: Measured from plasma using quantitative sandwich enzyme immunoassay. Cystatin C was log-transformed for analyses.
NCI: Determined via standardized seven domain battery based on global deficit scores derived from best available normative corrections (Blackstone et al., 2012).
Covariates: All Table 1 variables were tested for associations with global NCI or cystatin C to determine relevant covariates.
Statistical Analyses: Association of the continuous, log-transformed cystatin C values was analyzed. Recursive partitioning was used to determine whether there was an optimal threshold at which cystatin C levels were most sensitive to NCI in the HIV+ sample.

Results

Table 1. Sample Characteristics (N=124)

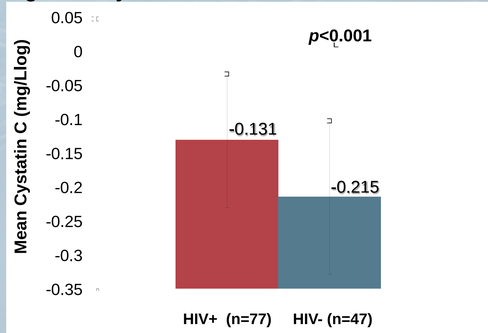
	HIV+ (n=77)		HIV- (n=47)		
	M(SD) or No. (%)	Range	M(SD) or No. (%)	Range	p-value
Age (years)	58.3 (6.1)	50-79	59.7 (7.3)	50-79	0.2
No. Male (%)	66 (86%)		27 (57%)		<0.01
Education (years)	14.6 (2.6)	8-20	14.1 (2.7)	6-19	0.3
Race [No. White] (%)	63 (82%)		30 (64%)		0.02
Current CD4 (cells/mL)	646 (341)	6-1606	---	---	---
Nadir CD4 (cells/mL)	185 (192)	2-850	---	---	---
AIDS Status (Yes) (%)	52 (68%)	---	---	---	---
EDI (yrs)	18.34 (8.0)	1-31	---	---	---
Lifetime MDD Dx (Yes) (%)	48 (62%)	---	14 (30%)	---	<0.01
Current MDD Dx (Yes) (%)	12 (16%)	---	1 (2%)	---	0.02
Lifetime Substance Disorder Dx (Yes) (%)	52 (68%)	---	25 (54%)	---	0.12
Current Substance Disorder Dx (Yes) (%)	2 (3%)	---	0	---	0.3

- A two-sample T-test revealed mean log-transformed plasma cystatin C concentration was significantly different between the HIV+ and HIV- subjects (p<0.001). (Figure 1)
- The HIV+ group mean cystatin C of -0.131 mg/L_{log} (0.740 mg/L) was higher than the HIV- group mean of -0.215 mg/L_{log} (0.610 mg/L). (Table 2)
- This association remained after adjusting for race (associated with cystatin C).

Table 2. Cystatin C Characteristics

	HIV+ (n=77)	HIV- (n=47)
Mean in (mg/L)	0.740	0.610
Mean (mg/L_{log})	-0.131	-0.215
Lower 95% - Upper 95% (mg/L)	0.701 - 0.780	0.565 – 0.660

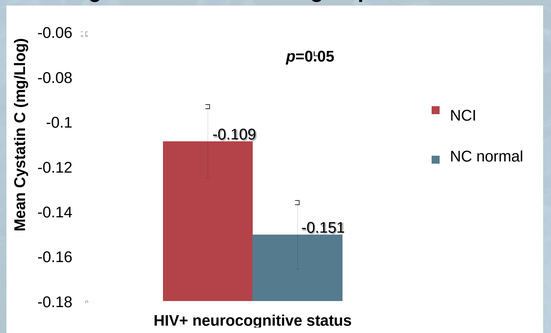
Figure 1. Cystatin C association with HIV status



Note: Cystatin C (mg/L) was log transformed for analyses. Bars represent standard deviations.

Results (cont.)

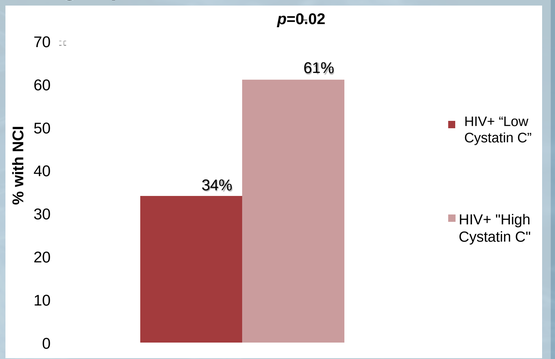
Figure 2. Association of Cystatin C with neurocognitive status in HIV+ group



Note: Cystatin C (mg/L) was logarithmically transformed for analyses.

- Within the HIV+ group, there was a trend level association between higher cystatin C and NCI (p=0.05). (Figure 2)
- The NCI group had a higher mean cystatin C at -0.109 mg/L_{log} (0.778 mg/L) compared to the neurocognitively normal group at -0.151 mg/L_{log} (0.707 mg/L).
- Higher cystatin C levels were not associated with NCI in the HIV- group (p=0.70).
- In order to further explore this interaction, we looked for a categorical cut point for cystatin C.

Figure 3. Rate of NCI in high vs. low Cystatin C HIV+ groups



- A categorical cut point determined using recursive partitioning grouped the HIV+ subjects into "high" and "low" cystatin C groups.
- Recursive partitioning identified that HIV+ subjects who had log-transformed cystatin C levels ≥-0.12 mg/L_{log} (0.75 mg/L) had a 79% increased relative risk of NCI (p=0.02). (Figure 3)

Conclusions

- HIV+ adults had higher cystatin C concentrations than HIV- adults, consistent with prior reports[3].
- Higher plasma cystatin C was associated with NCI in older HIV+ adults but not in HIV- adults.
- Cystatin C may be a useful clinical biomarker to identify HIV-infected persons at increased risk for NCI.
- A significant limitation of the present study is the cross-sectional design.
- Future projects should investigate the role of cystatin C in neurocognitive decline over time among older persons living with HIV.

References

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