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Association Between Plasma Homocysteine Levels and Neuronal Injury in Untreated HIV

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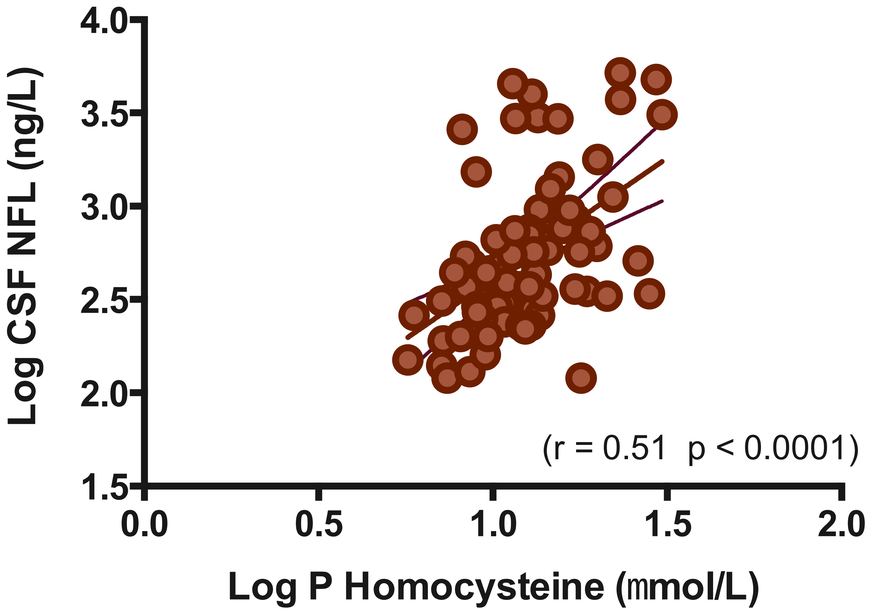
Background

Many HIV-1 infected patients without antiretroviral treatment suffer from neurological symptoms in a varying range of severity. Most patients with, and several without, neurological symptoms have elevated levels of neurofilament light protein (NFL) in cerebrospinal fluid (CSF), a marker of ongoing axonal injury. Hyperhomocysteinemia, related to vitamin B12 and folic acid deficiency, is associated with neurological symptoms. HIV-negative subjects with hyperhomocysteinemia and mild cognitive impairment show a significant reduction of brain atrophy in parts of the brain related to Alzheimer's disease when treated with vitamin B12.

The aim of this study was to investigate the correlation between homocysteine levels in plasma and signs of axonal injury in HIV-1 infected patients.

Methods

Homocysteine and B12-vitamin levels were analyzed in plasma with stable isotope dilution liquid chromatography tandem mass spectrometry (LC-MS/MS), and electrochemilluminescence immunoassay, respectively, from 80 neurological asymptomatic HIV-1 infected patients without antiretroviral treatment. NFL was measured, by an enzymatic 2-site quantitative immunoassay (UmanDiagnostics, Umea, Sweden), in CSF, and HIV RNA, neopterin and albumin in blood and CSF. 22 patients provided a second CSF and blood sample, in median 12.5 months, after antiretroviral treatment initiation.



Results

We found a significant correlation between the plasma level of homocysteine and CSF level of NFL in untreated patients, (r = 0.51, p <0.0001). 20 patients had hyperhomocysteinemia (>15 µmol/L) and 20 had elevated levels of CSF NFL (age dependent). As expected, there was also a significant inverse correlation between homocysteine and B12 levels (r = -0.36. p = 0.001) but no significant correlation between B12 and CSF NFL. CSF neopterin correlated with CSF NFL (r = 0.38, p = 0.001) but not with serum homocysteine. In a multiple linear regression analysis homocysteine stood out as an independent predictor of CSF NFL in HIV-1 infected individuals. No significant difference was found in homocysteine levels before and after initiation of antiretroviral treatment.

Predicting Log P Homocysteine

	Univariable		Multivariable	
Predictor	Std β (r)	p	Std β_{adj}	p
Age	0.403	<0.001	0.365	<0.001
Log CD4	-0.411	<0.001	-0.193	0.06
Log P HIV RNA	0.395	<0.001	0.275	<0.01
Log S Neopterin	0.340	0.002		
Log P B12	-0.363	0.001	-0.236	0.01

Predicting Log CSF NFL

	Univariable		Multivariable	
Predictor	Std β (r)	p	Std β_{adj}	p
Age	0.475	<0.001	0.347	<0.001
Log CD4	-0.469	<0.001	-0.278	<0.01
Log CSF HIV RNA	0.058	0.61		
Log CSF Neopterin	0.379	0.001	0.258	<0.01
Log CSF/P albumin ratio	0.267	0.01		
Log P B12	-0.165	0.14		
Log P Homocysteine	0.507	<0.001	0.223	<0.05

Conclusion

A significant correlation was found between plasma homocysteine and CSF NFL levels in neurologically asymptomatic HIV-1 infected individuals without antiretroviral treatment.

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