Pro-Inflammatory Glycomic Dysregulations Define HIV-Associated Neurocognitive Impairments

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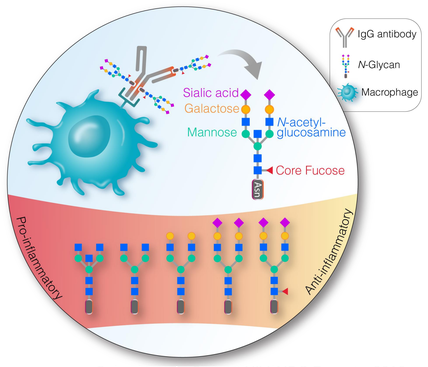
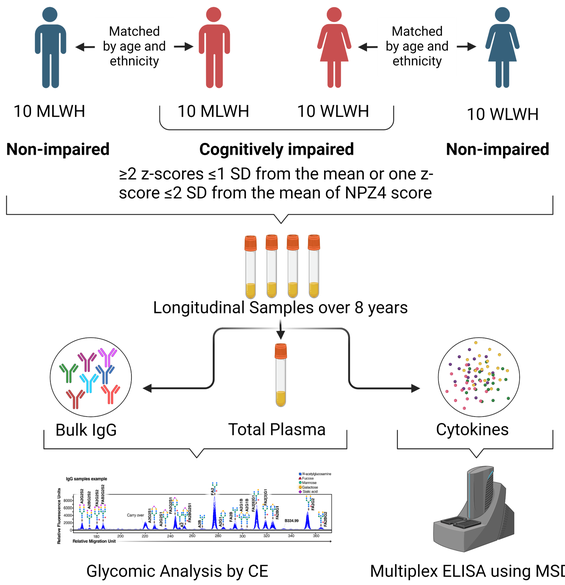
BACKGROUND

- In the general population, host glycomic alterations drive inflammation and precede the onset of inflammation-associated diseases.
- However, it remains unclear whether glycomic alterations are associated with the development of inflammation-associated diseases, including cognitive impairment (CI), in people with HIV (PLWH) on suppressive antiretroviral therapy (ART).



Colomb et al., Current HIV/AIDS Reports, 2019

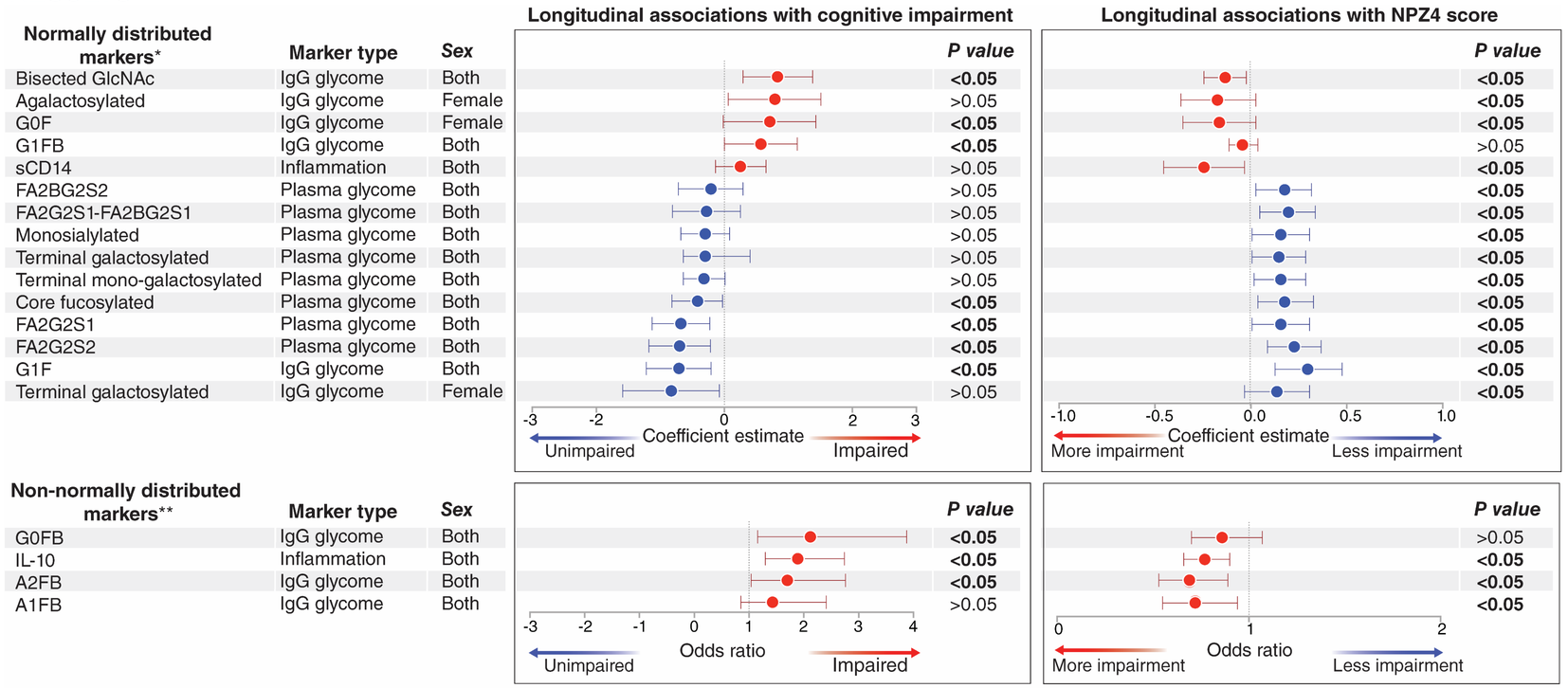
METHODS



NPZ4 scores were calculated by the mean of Trail Making A and B tests, the Wechsler Adult Intelligence Scale-Revised Digit Symbol test, and Hopkins Verbal Learning Test-Revised)

	Male (n=20)		Female (n=20)	
	Impaired (n=10)	Unimpaired (n=10)	Impaired (n=10)	Unimpaired (n=10)
Number of visits	8	8	7	7
Age (years-median)	52	51	52	51
Race White, non-Hispanic	60%	60%	30%	40%
Black, non-Hispanic	10%	10%	20%	30%
Hispanic (Regardless of race)	30%	30%	50%	30%
BMI (kg/m^2 - median)	25	27	30	28
CD4 Count (cells/mm^3- median)	747	744	796	689
Pre-ART viral Load (log copies/ml - median)	4.55	4.70	4.65	4.60
ART duration (years-median)	5.6	8.4	6.9	10.5
Nadir CD4 (cells/mm^3 - median)	267	217	252	182

RESULTS



*Linear models: data were normalized to μ=0, σ=1 before modeling; **ordinal models: data were converted to deciles before modeling.

Figure 1. Glycan traits are associated with cognitive impairment and/or NPZ4 scores in PLWH on ART. Cognitive impairment and lower NPZ4 scores were associated with higher levels of several pro-inflammatory bisected and agalactosylated IgG glycans in both sexes or in women only. Consistent with their pro-inflammatory roles, these glycans, specifically G0FB, correlated with higher levels of the inflammatory marker TNFα (not shown). Conversely, cognitive impairment and lower NPZ4 scores were associated with lower levels of glycans that contain the anti-inflammatory sialic acid and fucose. Among inflammation markers, IL-10 and sCD14 exhibited positive correlations with neurocognitive impairment and negative correlations with NPZ4 scores.

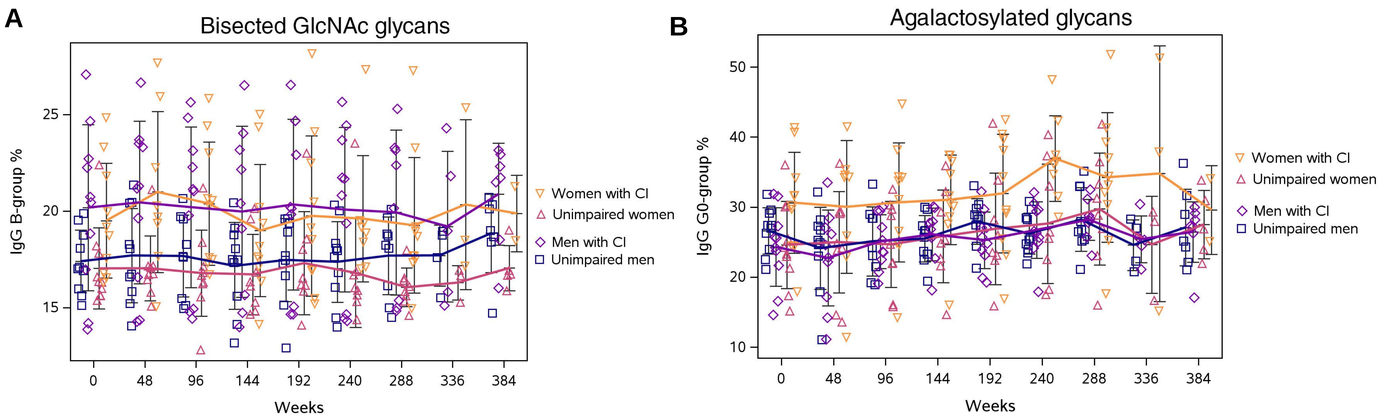


Figure 2: Examples of: (A) a marker that differs between CI and non-CI in both sexes and **(B)** a marker that differs between CI and non-CI in women only.

Aging- and inflammation-associated host glycomic dysregulations are linked to the presence of neurological impairments in people with HIV on ART in a sex-dependent manner.

Future studies are warranted to validate these exploratory findings and to examine the potential prognostic and functional significance of host glycans and inflammatory markers in the pathogenesis of neurological impairments in people with HIV.

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