Increased Immune Activation Following Acute Sleep Deprivation in People with HIV on ART

#00351

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Introduction

- Up to 70% of people with HIV (PWH) complain of sleep disturbances
- Extracellular adenosine (ADO) is a potent immune regulatory nucleoside that mediates immune activation
- ADO metabolism is dysregulated in PWH
- Sleep behaviors alter ADO metabolism
  - Our prior research demonstrated that CD73 expression was upregulated in PWH with obstructive sleep apnea
- It is unknown if total sleep deprivation (TSD) alters peripheral adenosine regulation and levels of inflammation and immune activation in virally suppressed PWH on ART

Figure 1 Extracellular Purinergic Metabolism

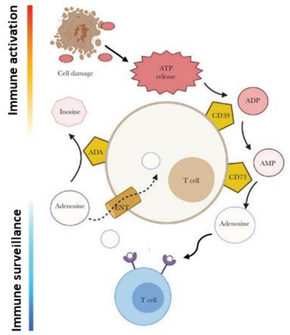


Figure adapted from: Hixson, Borker, et al. (2021)

Ectonucleosidase Expression by Obstructive Sleep Apnea Exposure

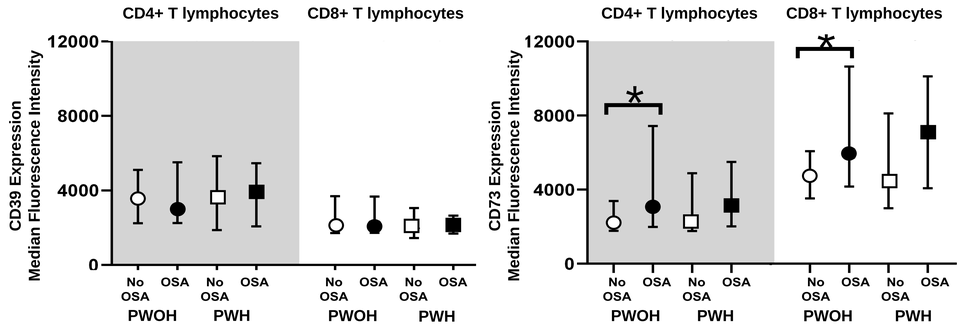
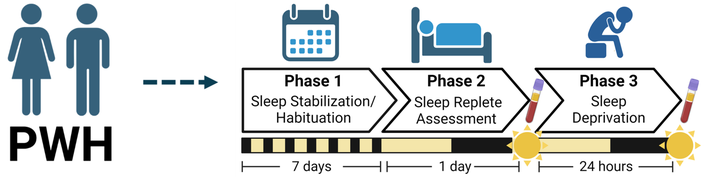


Table 1 Participant Demographics

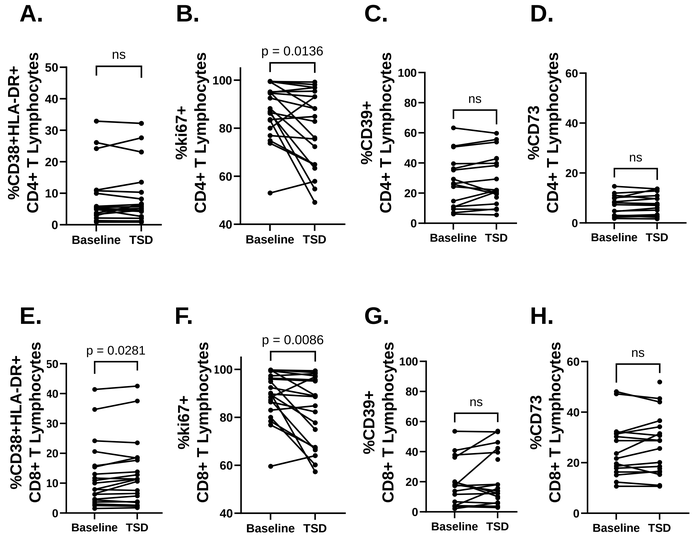
	PWH (n=20)
	Median (IQR)
Age (yrs)	59.8 (58.5. 63.5)
Male (n,%)	15 (75%)
Black Race (n, %)	7 (35%)
Body mass index (kg/m²)	26.7 (22.7, 31.0)
CD4+ count (cells/mm³)	760 (678, 883)
Apnea Hypopnea Index (4%)	4.7 (1.7, 9.8)

Methods

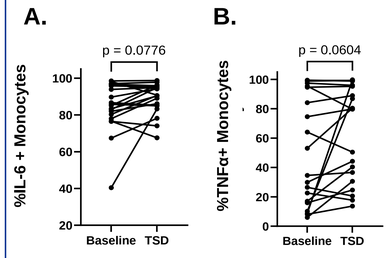


- People with HIV (PWH n = 20) underwent sleep deprivation with fasting blood draws
- Peripheral mononuclear cells (PBMCs) were extracted and analyzed by flow cytometry.
  - CD4⁺ and CD8⁺ T cells were evaluated for:
    - CD39 and CD73 expression
    - HLA-DR/CD38 co-expression
  - Monocytes were identified by CD14 and CD16 expression and intracellularly stained for
    - IL-6 and TNFα
- Plasma was analyzed for:
  - Levels of Soluble Markers (using Luminex)
    - IL-6, sCD14, sCD163, TNFα
  - Plasma adenosine metabolites were identified by mass spectroscopy/HPLC:
    - Adenosine, inosine, hypoxanthine, xanthine, 3'5'-cAMP, 3'5'-cGMP

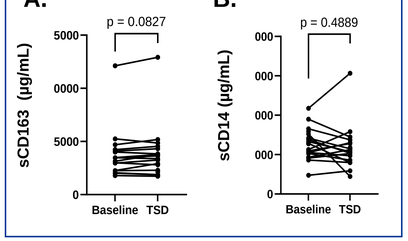
T Lymphocytes



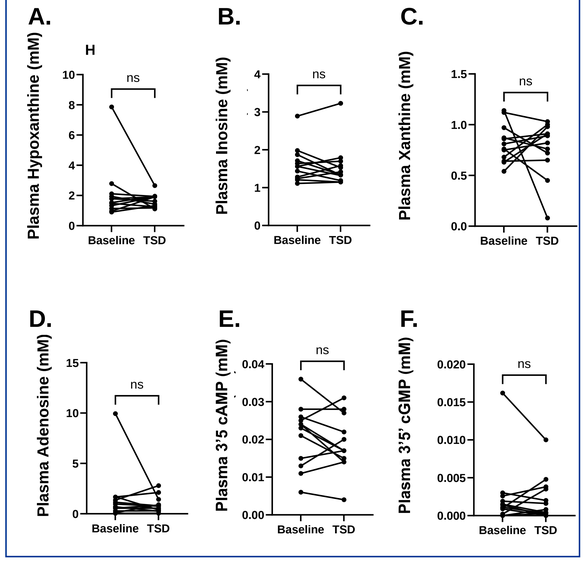
Monocytes



Soluble Markers



Plasma Adenosine Metabolites



Discussion

- Among virally suppressed PWH on ART, total sleep deprivation resulted in a significant increase in CD8+ T cell activation and trend for increased monocyte and macrophage activation.
- Total sleep deprivation did not result in a compensatory increase in ectoenzyme expression or in the plasma levels of adenosine.
- Interventions targeting sleep disturbances among PWH could be beneficial in addressing chronic inflammation in HIV.

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