Alcohol Use Is Associated with Degradation of Brain White Matter in HIV Infection

Mollie A. Monnig[1], Peter M. Monti[1], Karen Tashima[2], Joseph M. Gullett[3], Eric Porges[3], Neda Jahanshad[4], Paul Thompson[4], Talia Nir[4], and Ronald A. Cohen[3]
[1]Brown University, Providence, RI, USA, [2]The Miriam Hospital, Providence, RI, USA, [3]University of Florida, Gainesville, FL, USA, [4]University of Southern California, Los Angeles, CA, USA

0399

BACKGROUND

- HIV infection is associated with damage to the brain's white matter, as is heavy alcohol use.
- Few neuroimaging studies of people living with HIV (PLWH) have included heavy drinkers. As a result, little is known about brain white matter health in the context of co-occurring HIV and heavy drinking.
- This issue is important to public health because 15% of PLWH report heavy drinking in the past month.

METHODS

- **Participants:** PLWH and controls were recruited from an immunology clinic for the Brown University Alcohol Research Center on HIV (ARCH). Participants were categorized as non-drinkers, moderate drinkers, or heavy drinkers based on NIH guidelines.
- **Magnetic resonance imaging (MRI):** Diffusion tensor imaging was used to quantify fractional anisotropy, radial diffusivity, and axial diffusivity in white matter. Whole-brain voxelwise analyses (tract-based spatial statistics) tested effects of HIV, age, drinking group, sex, smoking, marijuana use, and the HIV x drinking group interaction. Region-of-interest analyses probed group differences.

TABLE 1	Entire Sample (N=108)	PLWH (n=62)	Control group (n=46)	p-value for group difference
Age	45.2 ± 11.1	48.9 ± 8.6	40.3 ± 12.2	p < .001*
Sex (% female)	42%	29%	59%	p = .002*
Race/ethnicity	68% White, 24% African-American, 7% Hispanic/Latino	66% White, 23% African-American, 10% Hispanic/Latino	70% White, 26% African-American, 4% Hispanic/Latino	p = .586
Current smoker	42%	42%	43%	p = .873
Years since diagnosis	----	18.8 ± 18.2	----	----
On ART	----	93.5%	----	----
Virally suppressed	----	69.4%	----	----
CD4 count	----	581 ± 275	----	----
CD4 nadir	----	214 ± 171	----	----
HCV co-infection	----	19%	----	----
Drinking status	28% non-drinker, 55% moderate drinker, 17% heavy drinker	32% non-drinker, 53% moderate drinker, 15% heavy drinker	22% non-drinker, 58% moderate drinker, 20% heavy drinker	p = .450
Diagnosis of alcohol use disorder (AUD)	27% never AUD, 57% remote AUD, 16% current AUD	35% never AUD, 50% remote AUD, 15% current AUD	21% never AUD, 63% remote AUD, 16% current AUD	p = .265
Percent days using marijuana	12.7 ± 27.5	17.1 ± 30.4	6.9 ± 22.1	p = .055

Alcohol use was associated with degradation of the brain's white matter in people living with HIV.

RESULTS

- **Table 1:** PLWH and controls were matched on alcohol use, heavy drinking, alcohol use disorder diagnosis, smoking, & other drug use.
- **Figure 1**: Greater alcohol use was associated with lower fractional anisotropy (**1A**) and with higher radial diffusivity (**1B**) and axial diffusivity (**1C**).
- **Figure 2**: Non-drinkers had the highest fractional anisotropy values in several white matter structures, including corpus callosum (**2A**), cingulate gyrus (**2B**), and posterior thalamic radiation (**2C**). Moderate drinkers were intermediate to non-drinkers and heavy drinkers. The interaction of HIV with drinking group was **not** significant.
- Older age predicted lower fractional anisotropy (p<.05).
- HIV diagnosis and clinical characteristics were **not** associated with white matter metrics.

Fig 1A. Heavier drinking was associated with lower fractional anisotropy in broad white matter regions (in all figures, significant voxels are yellow-red).

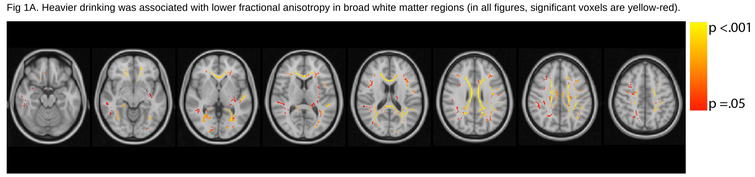


Fig 1B. Heavier drinking was associated with higher radial diffusivity in regions that largely overlapped with areas of lower fractional anisotropy (see above).

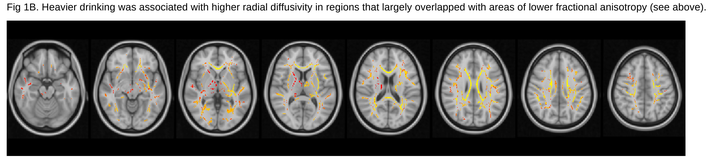


Fig 1C. Heavier drinking was associated with higher axial diffusivity in corona radiata and internal capsule.

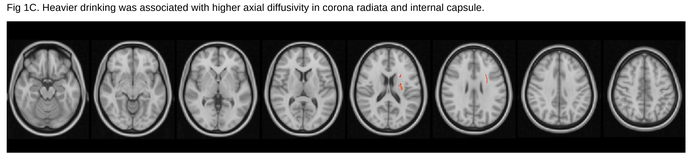


Figure 2A

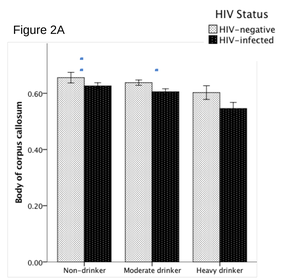


Figure 2B

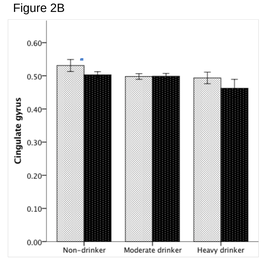
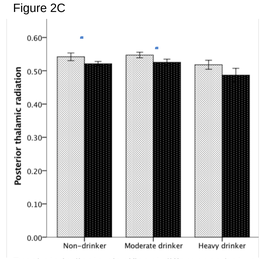


Figure 2C



Brackets indicate significant differences between drinking groups. Bars are +/- 1 standard error.

CONCLUSIONS

- Alcohol use significantly predicted degradation of white matter microstructure in this sample of PLWH in care and seronegative controls.
- Results are consistent with a dose-dependent association of alcohol use with lower coherence of white matter microstructure.

Diffusion-weighted MRI showed strong and widespread associations of heavier alcohol use with lower fractional anisotropy and higher radial diffusivity in white matter. Fractional anisotropy is a summary metric that reflects fiber density, myelination quality, and axonal integrity. Lower fractional anisotropy reflects degradation of white matter in many clinical conditions. Radial diffusivity reflects water diffusion perpendicular to the primary axis, and higher values can be indicative of damage to the myelin sheath. The high degree of spatial overlap between fractional anisotropy and radial diffusivity findings points to myelin damage as a possible mechanism of alcohol-related white matter degradation.

Although prior studies have reported compromised white matter microstructure in individuals with HIV and alcohol dependence, our study is the first to compare groups matched on alcohol use, other drug use, and smoking. As a result, we can conclude that our findings were not likely to have been confounded by other substance use.

ADDITIONAL KEY INFORMATION

Author Contact Information: Please contact Mollie Monnig, PhD, at mollie_monnig@brown.edu with comments or questions.

Funding Acknowledgements: This research was supported by National Institute on Alcohol Abuse and Alcoholism grants K23AA024704 (PI: Monnig), P01AA019072 (PI: Monti), U01AA020797 (Co-I: Gullett), K01AA025306 (PI: Porges); and by National Institute of Biomedical Imaging and Bioengineering grant U54EB020403 (PI: Thompson).