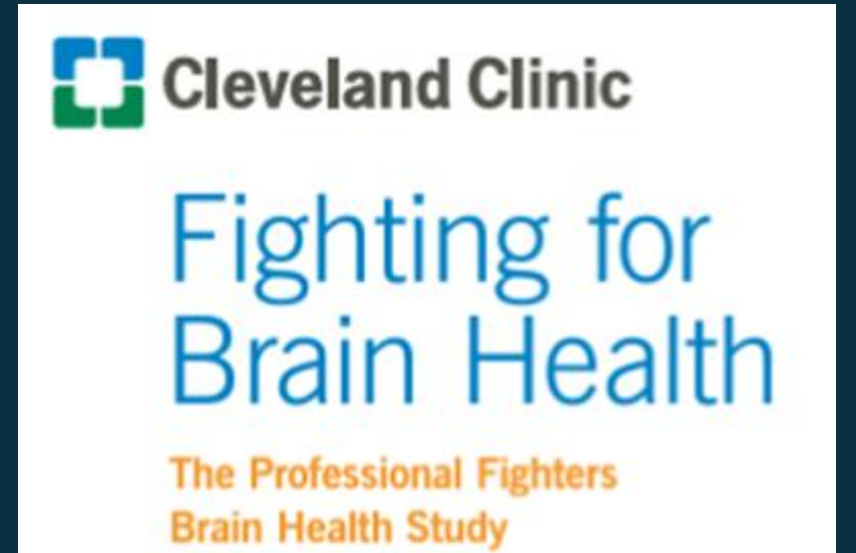




Xiaowei Zhuang, Ph.D., Andrea John, B.S., Dietmar Cordes, Ph.D., Charles Bernick, M.D.

¹Lou Ruvo Center for Brain Health, Cleveland Clinic Nevada, Las Vegas, NV



BACKGROUND

- Professional fighters exposed to repetitive head injury (RHI) experience elevated risk for chronic traumatic encephalopathy (CTE)[1].
- The role of sex in RHI/CTE has not been studied historically due to data limitation.
- This study aim to explore whether there is a sex difference in long-term RHI-related trajectory changes of blood-based biomarkers in **retired/inactive** fighters, using data from the Professional Athletes Brain Health Study (PABHS) [2].

METHODS

- Participants:** Fighters and mixed martial artists (MMAs) drawn from the Professional Athletes Brain Health Study (PABHS). Included longitudinal visits that are 1) with a blood draw; 2) at least two years after last documented professional fights. **Sample Characteristics.**
- Blood Biomarkers:** GFAP (Glial fibrillary acidic protein) and NfL (Neurofilament light chain), ultrasensitive molecule array assays (Quanterix). Log-transformed to reduce right skewness.
- Statistical Analyses--Linear mixed effect models:**
 - Fixed effect:** Sex; Time (Visit); Number of professional fights (NOF); and hierarchical model comparisons
 - Three-way interaction (Sex:Visit:NOF)if sex-specific longitudinal biomarkers changes depend on NOF (removed if non-significant)
 - Two-way interactions tested and removed if non-significant:
 - Sex:Visit if longitudinal biomarker changes depend on sex;
 - Sex:NOF if NOF-associated biomarker changes depends on sex;
 - Visit:NOF if longitudinal biomarker changes depends on NOF
 - Random effect:** random intercepts and time slopes for subjects.
 - Covariates:** Age; Education (years); Race; Types of fighting.

SAMPLE CHARACTERISTICS

Mean(std)	Female	Male	pValue ¹
N-sub (N-visit)	28 (54)	268 (672)	
N-visit: Mean [range]	1.93 [1, 7]	2.51 [1, 11]	
Age at Baseline:	39.17 (8.06)	40.57 (10.07)	
Race	18 White; 1 African American; 9 others	128 White; 79 African American; 61 others	0.003
Education	15.09 (1.73)	13.07 (2.35)	<0.001
Type of Fighting	10 Boxing; 18 MMA	160 Boxing; 108 MMA	0.01
Number of Fights at Baseline	17.39 (15.05)	23.05 (18.66)	

¹. Sex-differences: Chi-square tests for categorical variables and two-sample t-tests for continuous variables

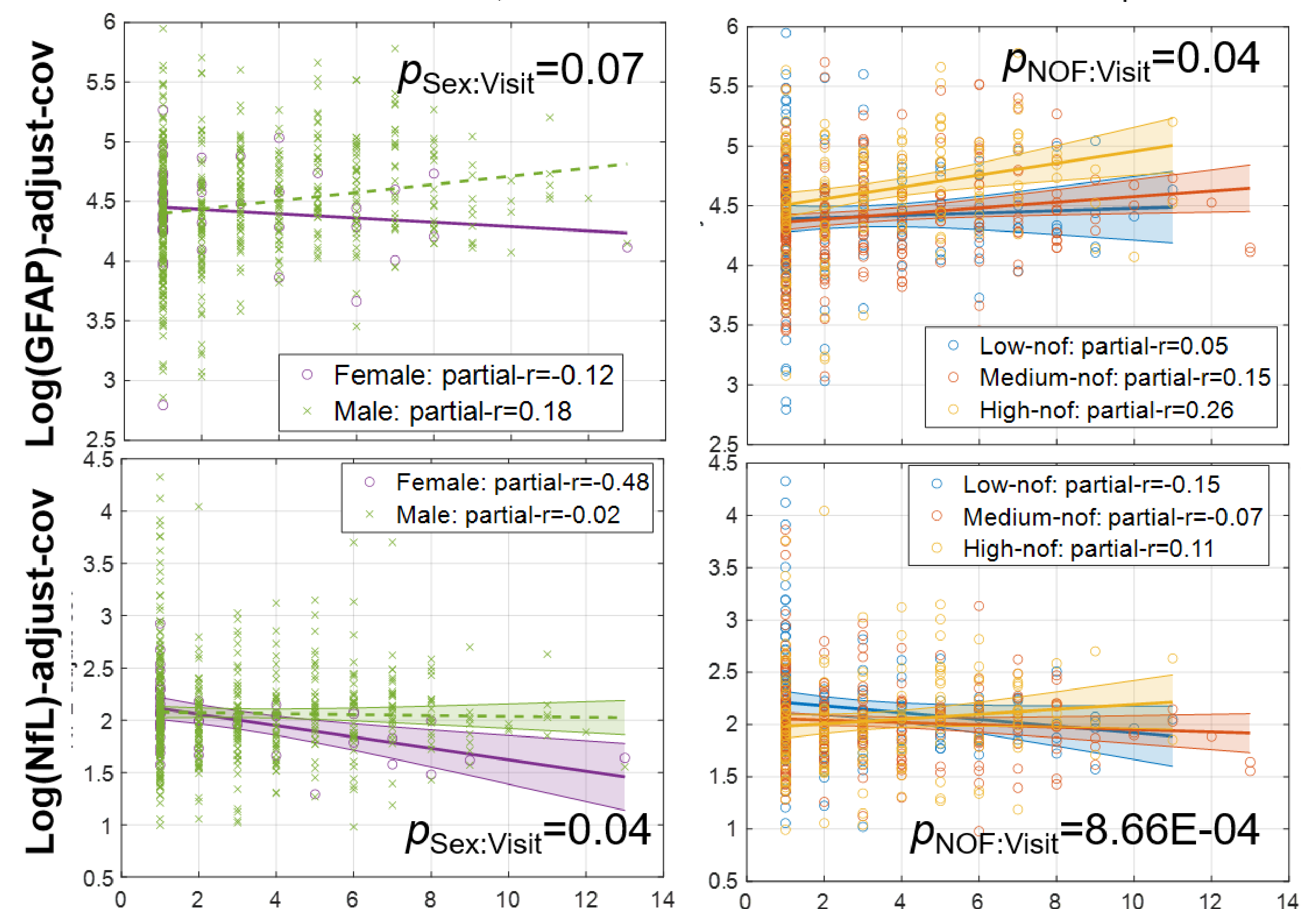
RESULTS

- Table below:** Three-way interaction was not significant for either GFAP or NfL
- Figure below:** Female inactive fighters tend to show longitudinal reduction in both GFAP and NfL; males demonstrate continued GFAP increase and stable NfL levels.
- Figure below:** Longitudinal increases of GFAP and NfL are most pronounced among fighters in the highest quartile of NOF, whereas fighters in the lowest quartile exhibit stable GFAP levels and greatest recovery in NfL over time.

Term	Log (GFAP)			Log (NfL)		
	LRstats ¹	deltaDF ¹	pValue	LRstats	deltaDF	pValue
Sex:Visit:NOF	0.05	1	0.82	1.12	1	0.29
Sex:NOF	0.99	1	0.32	0.15	1	0.69
Sex:Visit	4.06	1	0.04	4.94	1	0.03
Visit:NOF	4.51	1	0.03	11.31	1	7.70E-04

LME hierarchical model comparisons; Terms with p<0.05 were included in the final LME.

¹LRstats: Likelihood Ratio Statistics; deltaDF: difference in number of estimated parameters



CONCLUSIONS

- Despite the limited number of female participants, we preliminarily show that long-term biomarker trajectory following cessation of RHI exposure is influenced by both sex and cumulative fighting exposure in inactive fighters.**

ACKNOWLEDGEMENTS

[1] Mckee et al., 2016; [2] Banks et al., 2016. Research reported in this study was supported by Lincy Foundation, Belator, Ultimate Fighting Championship Company (UFC), the August Rapone Family Foundation, Top Rank, Haymon Boxing, and the National Institutes of Health (NIA-grant 1RF1AG071566, NIGMS-grant P20GM109025 and NIA-grant P20AG068053).