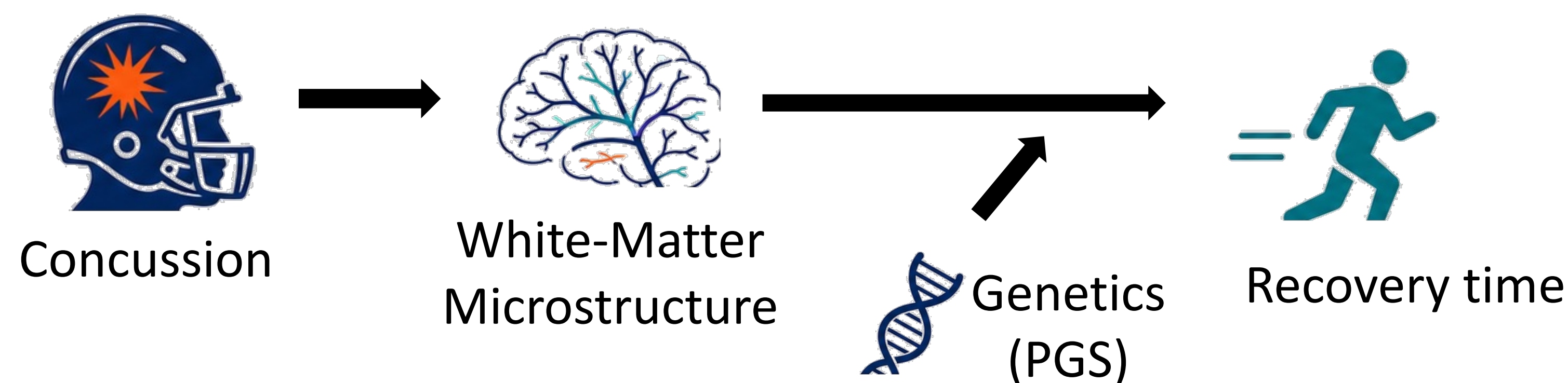


1 Background and Initial Aims

- Sport-related concussion (SRC) is common among service academy members and collegiate athletes, but recovery time varies substantially across individuals.
- Polygenic score (PGS) summarizes genetic variation that may contribute to differences in concussion recovery.
- Diffusion tensor imaging (DTI) captures white-matter microstructural alterations after SRC.
- Aim:** Evaluate whether integrating DTI-derived diffusion metrics with PGS improves prediction of time to return-to-asymptomatic after SRC.



2 Methods

	CARE Cohort	108 concussed collegiate athletes; mean (SD) age at injury: 20.12 (1.12); 16.7% female.
	Outcome	Time to Return-to-Asymptomatic after concussion.
	PGS	PGS was developed using data from 768 CARE participants (Zhang et al., <i>Sports Medicine</i> , 2026).
	DTI metrics	Mean diffusivity (MD) was measured in 27 major white-matter tracts 24-48h post injury.
	Factor Analysis	Tract-level MD were summarized into latent diffusion factors.
	Data Split	Training N = 86; Validation N = 22.
	Feature Selection	Network-based robust variable selection (Ren et al., 2019) combined with stability selection.
	Model Evaluation	Selected predictors were evaluated using a log-logistic accelerated failure time (AFT) model.
	Validation	C-statistic was calculated on the validation set.

3 Results

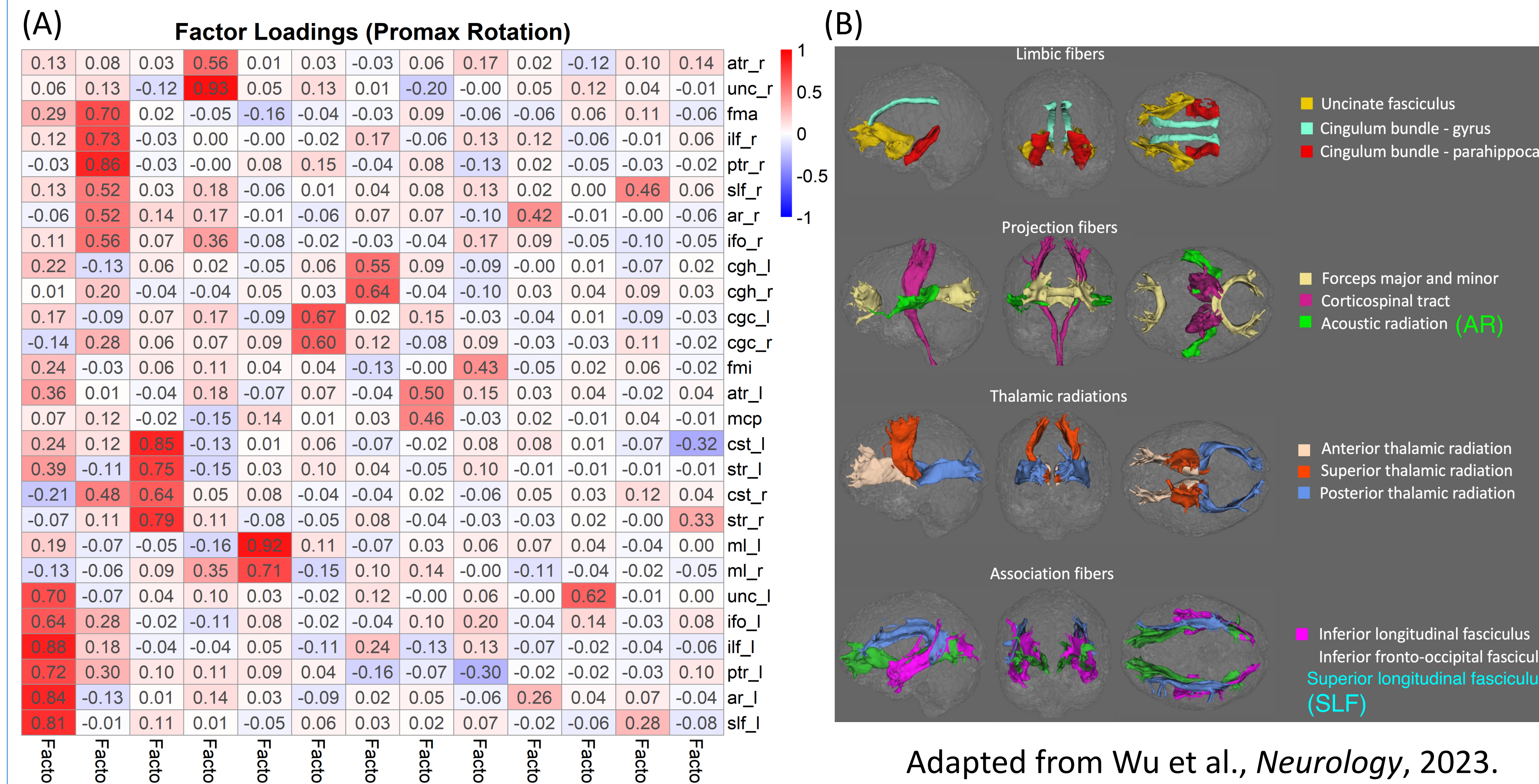


Figure 1. (A) Factor-loading structure. MD measures from 27 white-matter tracts were summarized into 13 latent diffusion factors. In the tract labels, *l* and *r* denote the left and right hemispheres, respectively. **(B)** Anatomical locations of the white-matter tracts.

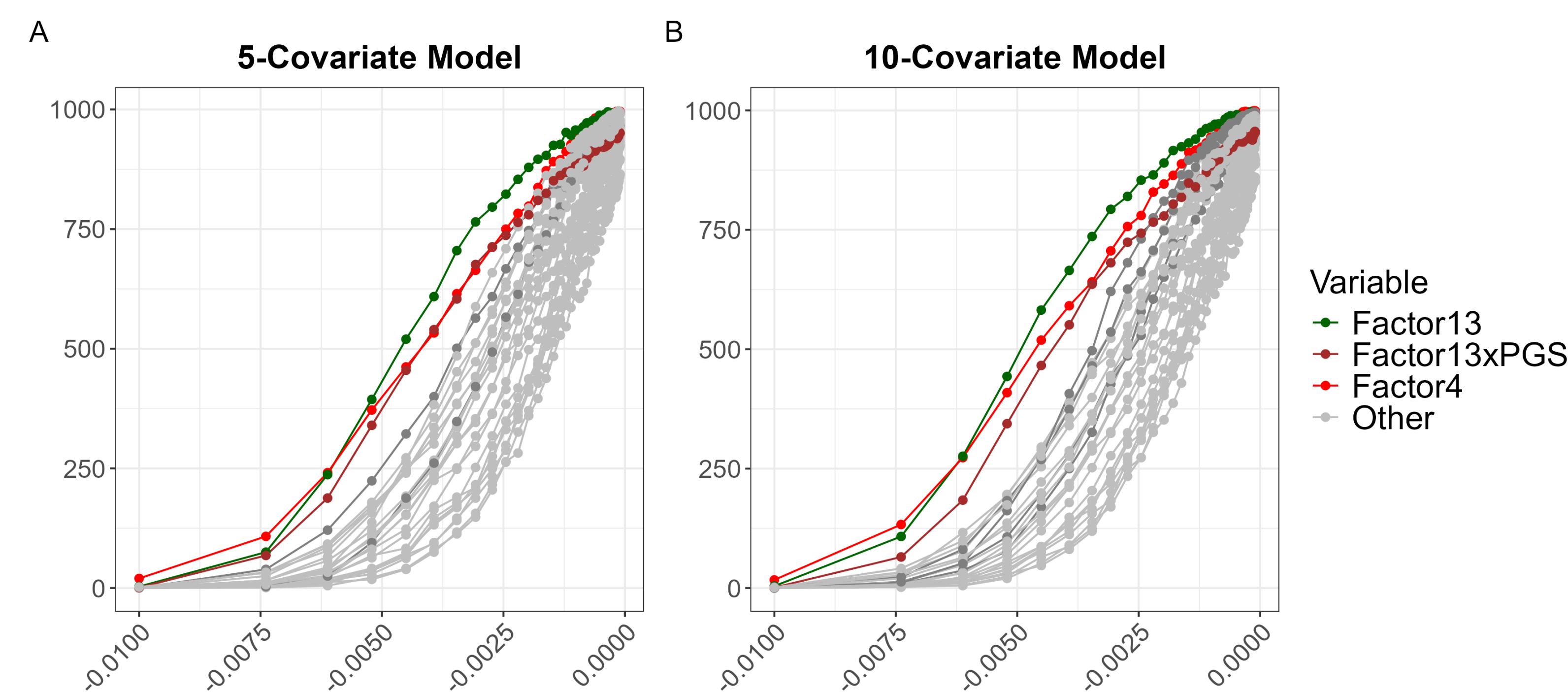


Figure 2. Feature selection. Selection frequencies for diffusion factors and factor $\times$ PGS interactions across values of the regularization parameter λ . (A) Adjusted for PGS, SCAT severity at 24-48h post-injury, sex, injury situation and previous concussion. (B) Additionally adjusted for the first 5 genetic ancestry PCs.

Most Consistently Selected Predictors	
Factor 13	bilateral superior longitudinal fasciculus (SLF) -loading
Factor 4	bilateral acoustic radiation (AR) -loading
Factor 13 $\times$ PGS	interaction between the SLF-loading factor and PGS

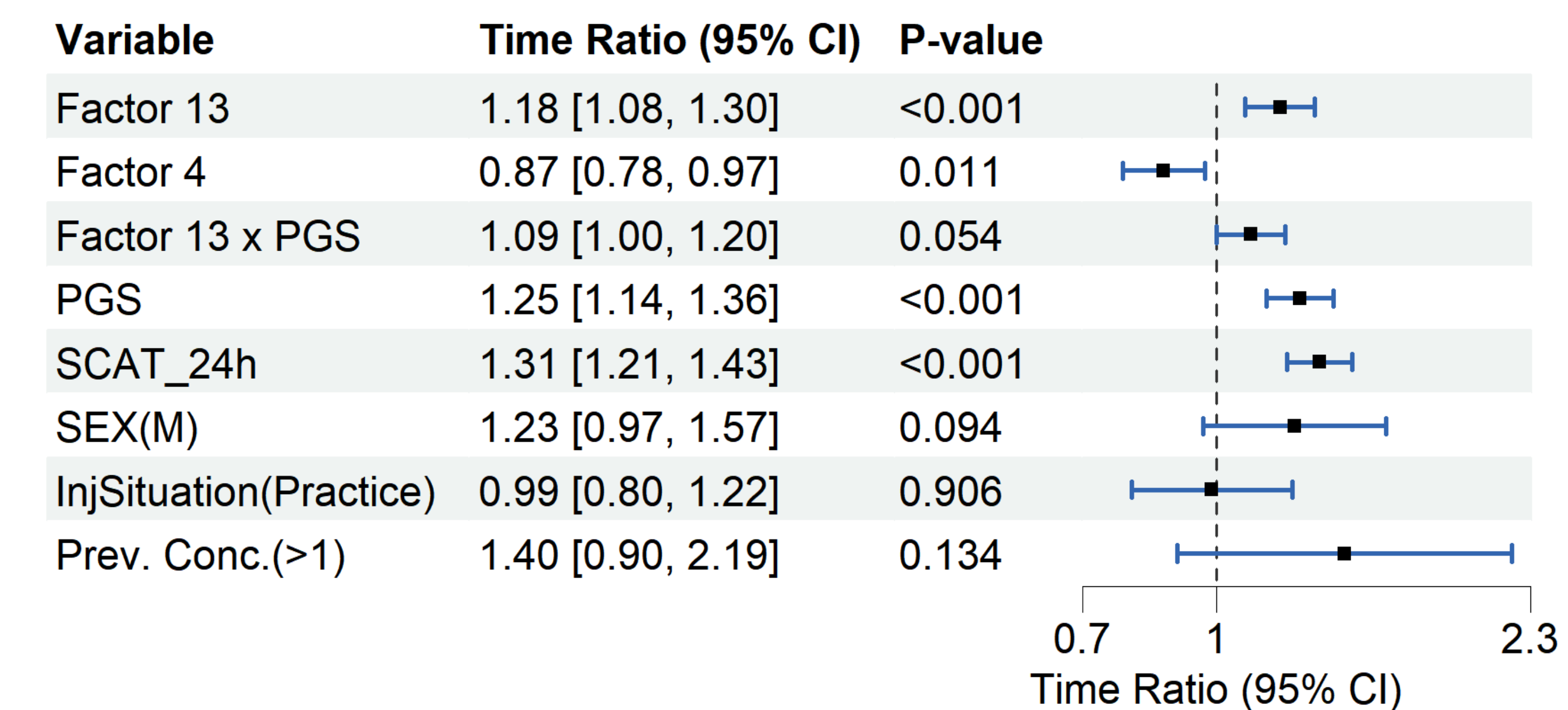


Figure 3. Final AFT model fitted in the training set.

Effects on Time to Return-to-Asymptomatic

- SLF-loading factor:** 18% longer recovery time per 1-SD increase.
- AR-loading factor:** 13% shorter recovery time per 1-SD increase.
- SLF $\times$ PGS:** the SLF effect increased by approximately 9% per 1-SD increase in PGS.

Validation Set C-statistics (95% CI)

Base model (covariates + PGS):	0.651 (0.489, 0.813)
Integrated model:	0.703 (0.547, 0.859)

4 Discussion & Future Directions

- Our preliminary findings show that adding diffusion factors and the SLF $\times$ PGS interaction improved prediction of time to return-to-asymptomatic after SRC.
- The association between white-matter microstructure and recovery time varied by genetic background (PGS).
- Integrating genetic and neuroimaging information may help identify individuals who could benefit from closer monitoring during concussion recovery.

Future Directions

- Extend the analysis to other DTI metrics, such as radial diffusivity.
- Evaluate model stability using 5-fold cross-validation.
- Validate the model in independent cohorts, including service academy members, to assess the generalizability of the findings.