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Investigating the reliability of ComBat for harmonizing diffusion MR images acquired at a single site with multiple echo times

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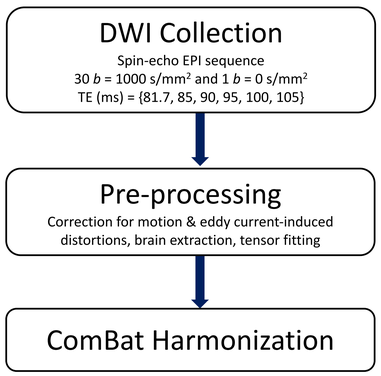
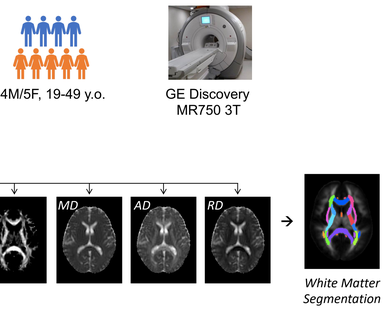
INTRODUCTION

- Precision of diffusion MRI measures is prone to different scanners, acquisition parameters, and other confounding factors such as vendor, bandwidth, head coils, and signal-to-noise ratio. Notably, a strong TE dependence of echo time (TE) was observed for DTI metrics. To date, many harmonization techniques for diffusion MRI have been proposed to perform data pooling from multiple sites and scanners.
- Combined association test (ComBat) has gained popularity for harmonizing MRI data by removing variability introduced by sites and scanners in parametric maps while preserving biological variability.
- **This work aims to investigate whether ComBat can harmonize diffusion MRI data acquired at a single site with multiple TE values.**

METHODS





- Performed for the mean FA, MD, AD, and RD within the 48 WM ROIs
- Biological covariates included age, gender, and weight
- Compared TE dependence at Pre- vs. Post-ComBat
- From ANOVA, calculated proportion of variance explained using

$$\frac{SSE_{\text{variable}}}{\sum SSE_{\text{variable}} + SSE_{\text{residuals}}} \times 100\%$$

Fig 1: Workflow of collecting and harmonizing single-site multi-TE DWI data.

Table 1: TE dependence before and after ComBat harmonization

		Pre-ComBat		Post-ComBat	
	White Matter Tracts	β_{TE}	p_{TE}	β_{TE}	p_{TE}
FA					
	Splenium of corpus callosum	**3.39 × 10⁻⁴**	**0.017**	1.64 × 10⁻⁴	0.211
	Right posterior limb of internal capsule	**4.17 × 10⁻⁴**	**0.012**	2.10 × 10⁻⁴	0.169
	Right medial lemniscus	**5.29 × 10⁻⁴**	**0.012**	2.08 × 10⁻⁴	0.243
	Right corticospinal tract	**5.22 × 10⁻⁴**	**0.034**	2.14 × 10⁻⁴	0.343
	Left superior corona radiata	**4.73 × 10⁻⁴**	**0.025**	2.22 × 10⁻⁴	0.260
	Left medial lemniscus	**4.76 × 10⁻⁴**	**0.021**	1.90 × 10⁻⁴	0.303
MD					
	Right cerebral peduncle	**6.42 × 10⁻⁷**	**0.022**	3.11 × 10⁻⁷	0.221
AD					
	Right cerebral peduncle	**1.49 × 10⁻⁶**	**<0.001**	**7.81 × 10⁻⁷**	0.017
	Left posterior limb of internal capsule	**9.41 × 10⁻⁷**	**0.003**	4.33 × 10⁻⁷	0.121
	Left external capsule	**8.63 × 10⁻⁷**	**0.031**	3.08 × 10⁻⁷	0.405
	Left corticospinal tract	**1.63 × 10⁻⁶**	**0.027**	6.32 × 10⁻⁷	0.349
	Left cerebral peduncle	**1.48 × 10⁻⁶**	**0.001**	7.04 × 10⁻⁷	0.081
RD					
	Right superior corona radiata	**-3.91 × 10⁻⁷**	**0.022**	**-3.10 × 10⁻⁷**	0.048
	Right posterior limb of internal capsule	**-3.21 × 10⁻⁷**	**0.023**	-2.48E-07	0.056
	Left external capsule	**5.02 × 10⁻⁷**	**0.032**	2.51 × 10⁻⁷	0.248

Significant

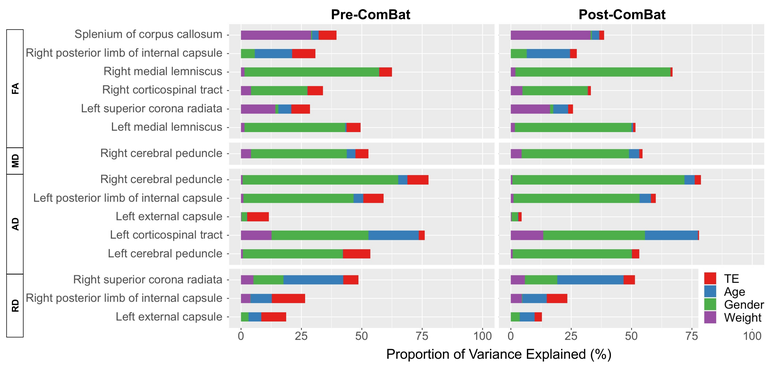


Fig 2: Bar plots illustrating proportion of variance explained by each variable before and after ComBat harmonization.

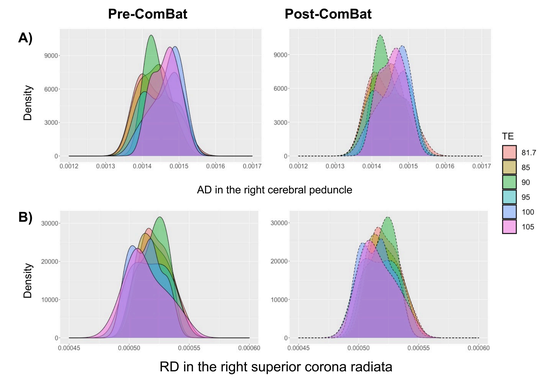


Fig 3: Density plots of A) AD in the right cerebral peduncle and B) RD in the right superior corona radiata, where TE dependence remained after ComBat harmonization.

RESULTS & DISCUSSION

- After ComBat, most of the TE dependence was corrected (*Table 1*), the biological variabilities were preserved, and the proportion of variance explained by TE was reduced (*Fig 2*). However, the TE dependence persisted for AD within the right cerebral peduncle (*Fig 3A*), and for RD within the right superior corona radiata (*Fig 3B*).
- The removal of TE dependence by ComBat was not always consistent across the ROIs. Because ComBat takes parametric maps as inputs, harmonization may be prone to cases where assumptions on parametric prior distributions are violated.

CONCLUSION

Implement ComBat with caution, even if DWI data are collected from a single site.

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